

# Pediatric Infections

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**Part II Symptoms and Signs**

<b>11</b>	<b>Fever: Pathogenesis and Treatment</b> .....	133
	Edhem Ünver, Nuray Bayar Muluk, and Oleg Khorov	
<b>12</b>	<b>Headache in Children</b> .....	145
	Hülya Maraş Genç, Bülent Kara, and Çiçek Wöber-Bingöl	
<b>13</b>	<b>Otalgia: Pathogenesis, Diagnosis, and Treatment</b> .....	161
	Mümtaz Taner Torun, Nuray Bayar Muluk, and Ahmed El-Saggan	
<b>14</b>	<b>Otorrhea: Pathogenesis, Diagnosis, and Treatment</b> .....	169
	Fatma Ceyda Akin Öçal, Yavuz Fuat Yılmaz, and Kevin A. Peng	
<b>15</b>	<b>Hearing Loss</b> .....	179
	Özlem Yüksel Coşar, Nuray Bayar Muluk, and Slobodan Spremo	
<b>16</b>	<b>Vertigo and Dizziness in Children</b> .....	191
	Utku Mete, Nuray Bayar Muluk, and Claudio Vicini	
<b>17</b>	<b>Nasal Obstruction in Childhood</b> .....	201
	Sinem Gökçe Kütük, Sema Başak, and Gordon Soo	
<b>18</b>	<b>Rhinorrhea: Pathogenesis, Diagnosis, and Treatment</b> .....	211
	Murat Koçyiğit, Cemal Cingi, and Ali Arslantaş	
<b>19</b>	<b>Dysphonia</b> .....	221
	Yücel Kurt, Cemal Cingi, and Bert Schmelzer	
<b>20</b>	<b>Sore Throat</b> .....	231
	Bülent Saat, Cemal Cingi, and Glenis Scadding	
<b>21</b>	<b>Tonsillar Hypertrophy in Childhood</b> .....	239
	Sertaç Düzer, Nihat Susaman, and Andrew A. Winkler	
<b>22</b>	<b>Cervical Lymphadenopathy in Children</b> .....	251
	Nazan Sarper and Giulio Cesare Passali	
<b>23</b>	<b>Halitosis in Children Secondary to ENT Infections</b> .....	263
	Tuğçe Küçükoğlu Çiçek, Nuray Bayar Muluk, and William Reisacher	
<b>24</b>	<b>Facial Paralysis in Children</b> .....	273
	Sena Genç Elden, Deniz Demir, and Chae-Seo Rhee	
<b>25</b>	<b>Snoring in Children</b> .....	287
	Taşkın Tokat, Deniz Demir, and Refika Ersu	
<b>26</b>	<b>Dysphagia in Children</b> .....	299
	Bilal Sizer, Nuray Bayar Muluk, and Nitin R. Ankle	
<b>27</b>	<b>Cough in Children</b> .....	311
	Emine Atağ, Zeynep Seda Uyan, and Refika Ersu	



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## 26.1 Introduction

311/1093



Dysphagia refers to discomfort experienced during the process of deglutition involves transfer of a solid or liquid bolus from the oral cavity into the pharynx, thence to the oesophagus and finally to the stomach. Problems affecting any of these stages may lead to dysphagia. There are multiple causes for difficulty in feeding or deglutition, anatomical and physiological, in children, and they affect individuals whose development is in other respects abnormal as well as those whose development is otherwise healthy. If there is an anomalous anatomical configuration of the mouth, throat or oesophagus, this may interfere with feeding normally [1, 2].

## 26.2 Dysphagia in Children

Deglutition involves a complex sequence of muscular contractions co-ordinated by several different nerves, both cranial and cervical, and located in the labial, lingual, palatal, oropharyngeal, pharyngeal, laryngeal, oesophageal and retrosternal regions.

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Dysphagia may result from any disorder which has the potential to disturb the co-ordination between these different actors in the process of deglutition [3–5].

The upper aerodigestive tract of a child, unlike that of an adult, undergoes a series of alterations as the child grows and matures, which means that the pathogenesis of disorders causing dysphagia and feeding difficulty is distinctly different between children and adults. In early childhood, the mouth, throat and larynx are continuously undergoing alterations in their anatomical configuration. The physiological control of deglutition also matures step by step to allow for a change from the reflex actions of suckling to the movements involved in chewing and to address the need to permit both breathing and swallowing of food. Where the child lacks the ability to adapt to the alterations in anatomy or where neurological control mechanisms are impaired, deglutition may be hindered, with the result that chronic lung disorders or malnutrition develop.

The number of cases of dysphagia seen in children is rising, which may be attributed to higher numbers of infants born prematurely or with low birth weight who survive and then go on to develop complicated disorders which may impinge on the anatomical integrity of the structures involved in deglutition or their physiological actions [6–8].

312/1093



## 26.3 The Physiology of Healthy Deglutition

The neurological control mechanisms involved in deglutition are somewhat complex. There is integration of sensory information carried by afferent fibres at the level of the brainstem. The efferent outflow involves the generation of a pattern of impulses that allow deglutition to occur efficiently and safely. Neural control co-ordinates the actions of the pharyngeal, laryngeal and oesophageal musculature.

There are four elements of this neurological control mechanism which have been extensively characterised:

1. The cranial nerves carry the afferent sensory input required.
2. Motor efferent fibres within the cranial nerves and the ansa-cervicalis.
3. The cerebrum, midbrain and cerebellum have projections which form synaptic connections at the level of the midbrain.
4. The brainstem contains twin deglutition centres.

When the child swallows, a bolus (whether solid or liquid) moves in succession from the oral cavity to the pharynx, then descends through the oesophagus before entry into the stomach. This movement depends upon synchronisation by the nervous system of the action of muscles lying under voluntary as well as involuntary control. Descriptions of deglutition usually consider the process to consist of three separate stages, involving the mouth, pharynx and oesophagus in turn. The stages each accomplish a specific goal. Dysphagia arises when there is an abnormality affecting at least one of these stages [6, 8].

### 26.3.1 Mouth (Oral) Stage

The mouth stage involves the action of muscles that are controlled voluntarily. It starts with food entering the oral cavity. The tongue and the muscles of mastication act in a co-ordinated fashion to form the chewed food into a bolus. Mechanoreceptors provide the necessary feedback to achieve this objective. The bolus is gathered in the middle of the lingual upper surface, which rises, propelling the bolus towards the pharynx in a manner resembling gut peristalsis. As the bolus is propelled towards the throat, an involuntary reflex is activated to swallow the bolus. This is the swallowing reflex [6, 8].

The mouth stage of swallowing calls for a high degree of co-ordination between the sensory input and motor output. The muscles of facial expression are supplied by the seventh cranial nerve, whereas the muscles that move the mandible are supplied by the trigeminal nerve. For the tongue to move in a co-ordinated way, there must be co-ordinated action by the four intrinsic muscles of the tongue and four extrinsic muscles. The former are supplied by the twelfth cranial nerve, the latter being supplied by branches of the ansa-cervicalis. The palatal, pharyngeal and laryngeal muscles are supplied by the ninth and tenth cranial nerves. There is sensory input from the second division of the fifth and the seventh, ninth and tenth cranial nerves. In infants, deglutition is almost entirely controlled at the brainstem level. However, with the introduction of the cerebral cortex, voluntary control over swallowing develops gradually to include

313/1093

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### 26.3.2 Pharyngeal Stage

For the most part, the pharyngeal stage in deglutition does not call for voluntary control. This stage is triggered to occur by the presence of food or saliva within the pharynx, and involves a number of responses occurring one after the other. The pharyngeal mechanoreceptors supply sensory input to the deglutition centre within the medulla oblongata. This sensory input is carried by the fifth, ninth and tenth cranial nerves [10]. The deglutition centre within the medulla relays the signal to begin the motor sequence of swallowing to the nucleus ambiguus and the medial nucleus of Cranial Nerve X. The velum takes up position against the posterior wall of the pharynx, separating the oropharynx from the nasopharynx and ensuring that the bolus descends rather than entering the nasal cavity. The oropharyngeal constrictor muscle contracts against the lingual base and thus the bolus is conveyed downwards. There is some adjustment to the exact muscular movements that depends on mechanoreceptors, which is needed to accommodate the variation in bolus volume and consistency expected during eating [6, 9, 11].

Since the pharynx forms part of the aerodigestive tract, it fulfils a dual purpose as an airway and a passage for food. This situation necessitates reciprocal inhibition of the respiratory and gastrointestinal systems. At the beginning of the pharyngeal stage, breathing halts and the larynx undergoes traction upwards and forwards, preventing it from obstructing the bolus on its descent. Both pairs of vocal cords

and the epiglottis bends backwards, closing off the entrance to the laryngeal lumen, as the larynx moves superiorly. This action of raising the larynx widens the entrance to the oesophagus, and the constrictor muscles within the pharynx constrict to produce a peristaltic wave that carries the bolus towards the oesophageal entrance [6, 12]. Beyond this stage onwards, deglutition enters involuntary phase.

If food does perchance enter the larynx, its presence will be detected by mechano- and chemoreceptors, which trigger the vocal folds to snap shut and produces a halt in breathing. This failure to carry on breathing persists whilst the food remains lodged in the larynx. In neonates, there is inadequate respiratory reserve, so this protective reflex may make the child hypoxic. At the same time, coughing may also be triggered by food entering the larynx. Coughing may be initiated by sensory input originating in the larynx itself or from tracheal receptors. Nonetheless, this extra layer of protection is not found in three quarters of babies born prematurely, nor in half of those born at term. Furthermore, infants who sustain impairment to the nervous system may also lack the coughing reflex [6, 12].

### 26.3.3 Oesophageal Stage

314/1093

The oesophagus acts as a tube connecting the pharynx with the stomach, closed at both ends by default. Muscular sphincters keep the ends closed except when deglutition occurs. The upper muscular ring of the oesophagus opens to permit deglutition and this opening is further assisted by the upwards movement of the larynx. A peristaltic wave actively moves the bolus in the direction of the gastric entrance. The lower muscular ring needs to remain contracted at times other than swallowing, otherwise the stomach contents risk being refluxed back up the oesophagus. Peristalsis is orchestrated by the myenteric plexus of the oesophagus acting with impulses provided by the tenth cranial nerve [6, 12].

The term oral dysphagia is applied to a variety of different problems affecting the oral stage. Such problems include over- and under-sensitivity to the taste or texture of food, losing food out of the mouth or being impaired in the ability to form food into a bolus and move it within the oral cavity. Pharyngeal dysphagia results from weak muscular action by the musculature of this region, misjudged initiation of deglutition, inadequate repositioning of the larynx and failure to protect the airway and a reduced ability to sense the passage of bolus. The consequences of pharyngeal dysphagia may include the passage of bolus upwards into the nasal cavity, food remaining in the pharynx when swallowing has finished, penetrative injury to the pharynx, aspirated bolus and choking. Oesophageal dysphagia encompasses a number of issues including cricopharyngeal achalasia, in which the upper oesophageal muscular ring does not open to let the bolus pass and the oesophagus suffers from abnormal motility.

Dysphagia may be noticed in the following circumstances: the child cannot retain food in the oral cavity, food and saliva are inadequately under the child's control, the voice sounds wet, the child coughs when eating or there are attempts to clear the throat at any point prior to, during or post deglutition [1–3].

For most cases, a thorough and precise history should allow the correct diagnosis to become obvious. Some important specific items to enquire about when taking the

history include whether the child has been seen swallowing non-food matter, or if some items of small size appear missing (such as watch batteries), if the child may have swallowed a corrosive substance, loss of voice, pyrexia (particularly if there are lesions within the mouth), excessive salivation, pharyngitis, jaw muscle spasm or nuchal rigidity. Some causes of paediatric dysphagia are detailed in Table 26.1 [8].

**Table 26.1** Causes of dysphagia in children [8]

Life-threatening	Foreign body within oesophagus Stevens-Johnson syndrome Corrosive substance ingestion Retropharyngeal abscess Epiglottitis Central nervous system infection (e.g. meningitis, encephalitis, cerebral abscess) Impairment of deglutition (e.g. cerebral palsy, myasthenia gravis, botulism, Miller Fisher syndrome) Tetanus Diphtheria Poliomyelitis Central nervous system tumours Perforation of the oesophagus
Common	Stomatitis Infectious pharyngitis Quinsy Dystonic reaction Injury to the oropharynx
Oesophageal causes	Oesophagitis Megaoesophagus Diverticula, Membranes, Rings, Dysphagia lusoria, Stenosis, Tracheo-oesophageal fistula
Other	Achalasia Rheumatic disease (e.g. juvenile systemic sclerosis, dermatomyositis) Myasthenia gravis Crohn's disease Thyroid enlargement (e.g. acute suppurative thyroiditis) Tumour of the oesophagus Vascular ring Globus sensation Macroglossia Cleft anomalies Lingual goitre Cervical cysts Ranula Soft palate palsy in diphtheria Acromegaly CNS diseases like bulbar paralysis Cerebral ischaemia Amyotrophic lateral sclerosis

315/1093

Frequently occurring infections of the upper respiratory tract may be responsible for cases of paediatric dysphagia. Although it has been known since the 1970s that tonsillitis may worsen dysphagia through alteration to the action of muscles involved in swallowing, there is minimal research available that has focused on the pharyngeal musculature in cases of tonsillitis [6, 8, 13].

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## 26.4 Stomatitis

Stomatitis refers to an inflammatory process involving the mucosae found within the oral cavity and oropharynx. It is amongst the most frequently occurring reasons for paediatric dysphagia and is characteristically found in association with a viral infective episode. Hand, foot and mouth disease is a disorder caused by Coxsackie A virus, one of the enteroviridae. It presents as pyrexia, vesicular lesions on the lining of the cheeks and the tongue, and tiny, painful skin lesions distributed over the hands, feet and buttocks. The same pathogen is also responsible for herpangina, a rash with vesicles found on the palatal tonsils and the velum, seen mainly in paediatric patients between the ages of 3 and 10 years. Herpangina produces a painful throat, pyrexia and pain on swallowing. It generally occurs during the summer months. Herpes simplex virus type 1 is the cause of herpetic gingivostomatitis. The usual age range is 1 to 5 years. This disorder presents with a prodromal pyrexia and malaise, after which lesions develop in the mouth and elsewhere. The lesions are initially vesicular, but then join together, producing areas of sore ulceration. The presentation often includes pyrexia, halitosis, painful swallowing, loss of appetite and swollen lymph nodes under the chin or in the neck.

Viral stomatitis secondary to enteroviruses may be treated by supporting the patient to drink enough liquid and providing analgesics to be given by mouth. For a subset of such cases, topical treatments may be efficacious. Where pain is of marked severity, consider using opiate pain killers. Sometimes a child may decline oral fluids and it may be necessary to supply fluids intravenously [14, 15].

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## 26.5 Infectious Pharyngitis

In a case of paediatric dysphagia where there are signs and symptoms of pharyngitis due to an infection, treatment depends on the most likely pathogen involved. Infectious agents that frequently occur include the enteroviruses, adenovirus, Epstein-Barr virus, Group A Streptococci or *Neisseria gonorrhoeae*. Some paediatric patients experience such severe odynophagia that oral fluid intake becomes inadequate to maintain hydration. How to go about diagnosing pharyngitis secondary to infection and the management of the dehydrated child is reported elsewhere in the literature. See, for example, Ref. [16].

## 26.6 Quinsy

Paediatric cases of quinsy are typically associated with marked pharyngitis, generally one-sided, and pyrexia. Patients are said to speak as if they were eating a hot potato. There may be excessive salivation, which may drip from the mouth. The symptom of muscular spasm, resulting from irritation to the internal pterygoid muscle, is seen in approaching 2 out of 3 cases of quinsy and is thus a useful sign diagnostically. The peak age at which this lesion occurs is during adolescence, but it does occur even in younger paediatric patients. Distinguishing between peritonsillar abscess and a retropharyngeal abscess or epiglottitis is sometimes challenging, since these conditions may also be associated with sialorrhoea and muscular spasm of the jaw [17, 18].

Physical examination of children with quinsy may reveal a highly oedematous tonsil that exhibits fluctuance and a uvula deviating away from the lesion. The posterior velum may be visibly swollen or bulging in the vicinity of the tonsil. It may feel full on palpation, and may be fluctuant.

The treatment for quinsy depends principally on surgically draining the abscess, supplying antibiotic pharmacotherapy and instigating supportive measures [17, 18].

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## 26.7 Epiglottitis

Cases where the clinician suspects epiglottitis need to be managed in a hospital setting. It is seldom seen amongst children who have received immunisation. Early diagnosis and rapid intervention are the only ways to prevent the high morbidity and mortality associated with the condition. Epiglottitis in paediatric patients classically presents as dysphagia that comes on suddenly and worsens in a matter of hours, coupled with hypersalivation in a distressed child. An abruptly beginning marked pyrexia (above 38.8 deg, but below 40 °C), painful swallowing and pharyngitis of marked severity are also common in cases of epiglottitis secondary to infection. Epiglottitis can also be triggered if a child drinks some corrosive liquid or very hot drinks [18, 19].

The usual appearance of a paediatric case of epiglottitis is toxic, possibly sitting down with the trunk bent forwards, neck sticking out and chin protruded, a manoeuvre that helps to make the airway as free from obstruction as possible. Such patients may refuse to lie flat. Whilst in some cases there is a history of a mild upper respiratory tract infection, generally the patient has only appeared sick for at most 24 h, sometimes even less than 12 h [8, 10, 19].

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## 26.8 Retropharyngeal Abscess

The peak age of occurrence for a retropharyngeal abscess is between 2 and 4 years old. This lesion is frequently the result of multiple pathogens. The main bacteria responsible are *Streptococcus pyogenes* (group A streptococcus), *Staphylococcus*

317/1093



*aureus* (including methicillin-resistant *S. aureus*), and anaerobic bacteria found in the respiratory tract, such as *Fusobacteria*, *Prevotella* or *Veillonella* spp. [8, 10].

In the first stages of a retropharyngeal abscess, there may be no features that differ from a simple sore throat. However, as the lesion matures, the upper aerodigestive tract becomes inflamed and obstructed, which produces more symptoms. Paediatric cases of this lesion start to appear unwell and a moderate pyrexia may be noted. They may have difficulty swallowing, pain when swallowing, hypersalivation, extending the neck may be painful, torticollis may be seen and they may speak as if eating a hot potato. Furthermore, such children may present with respiratory distress, stridor, cervical oedema or a mass lesion, and the lymph nodes may be swollen [8, 10].

## 26.9 Diphtheria

Diphtheria is no longer common in developed countries but remains common in less developed nations globally. This disease is caused by a Gram-positive bacillary pathogen. Respiratory diphtheria begins slowly, presenting as pharyngitis, painful swallowing, malaise and a pyrexia, which is not high. In a considerable number of cases, the bacterial toxin secreted by the pathogen leads to the development of a pseudomembranous covering, which may be found anywhere along the respiratory airways, from proximal to distal. It results in pain upon swallowing. Signs of associated neurological impairment, such as uncoordinated swallowing, difficulty in swallowing, blockage of the upper airways, with or without aspiration in the lungs rarely complicates this disorder when mild. However, in severe cases there is a risk of up to 75% that such complications will occur [8, 20, 21].

## 26.10 Stevens-Johnson Syndrome

The precise pathogenic mechanism behind Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) has not been established, but both disorders involve significant desquamation of skin or mucosa. Dysphagia and sialorrhoea are frequently seen when there is severe loss of mucosa within the oropharynx. If less than one tenth of the skin area is affected, such desquamation is termed Stevens-Johnson syndrome, whilst if at least three tenths of the skin is affected, toxic epidermal necrolysis is diagnosable. If between 10% and 30% of the skin is affected, there is said to be overlap between these two syndromes.

In virtually every case, TEN is linkable to a drug exposure, whereas SJS is both drug-associated as well as a possible consequence of infection. In both conditions there is a prodromal syndrome lasting between 1 and 3 days up to when the lesions appear on the mucosae or epidermis. During the prodrome, patients are pyrexial and have symptoms resembling an influenza episode. The lesions feature vesicles and bullae, which worsen over the course of a few days. It is possible for the disorder to involve multiple organ systems and the trachea and bronchi may also be affected [8, 22, 23].

## 26.11 Tetanus

The anaerobic bacterium, *Clostridium tetani*, synthesises a toxin that results in severe muscular spasm through its action on nervous tissue. Tetanus is currently seldom seen in developed countries, but is still present in developing nations. A frequent presentation in a child with systemic tetanus is dysphagia and spasm of the jaw muscles. It may also present with nuchal rigidity, opisthotonus and the so-called *risus sardonicus*.

Children suffering from generalised tetanus typically experience a prolonged contraction of the voluntary muscles, with severe muscle spasms occurring from time to time. Tetanus has no effect on how awake or aware patients are, and the prolonged contraction and muscular spasms generate a severe level of pain. These muscular spasms may be set off by a high noise level or intense sensory stimulation of other kinds, such as tactile or photic [8, 24, 25].

## 26.12 Cornelia de Lange Syndrome (CdLS)

319/1093



CdLS is an infrequently occurring congenital disorder that affects the auditory system and the aerodigestive tract. Its manifestations may be seen in a variety of organ systems, which then necessitate the involvement of a number of paediatric disciplines. ENT opinion is often required.

The initial description of this disorder was published in 1933 by the Dutch paediatrician and neuropathologist, Cornelia Catharina de Lange. She supplied a description of two children with a very specific dysmorphic facial appearance, delayed development and abnormal arms and legs. She used the term typhus degenerative Amstel Damensis, but it is today referred to as Cornelia de Lange Syndrome, in her honour. The incidence is 1 in 10,000 live births. It is equally common in both males and females [26, 27]. CdLS has a varied phenotype.

The multi-systemic nature of CdLS calls for multi-disciplinary management. Paediatric ENT specialists may treat auditory impairment, ensure a patent airway and address craniofacial anomalies. The long-term and multi-disciplinary nature of management imposes a considerable task on those caring for such children. There are, however, a number of centres where expertise has developed and an American foundation for CdLS also exists. This infrastructure helps to facilitate research and to offer social services to the affected families. The centres of expertise are valuable as models on which to base planning a service for patients affected by CdLS [28, 29].

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320/1093



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321/1093

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- Model viva and clinical examination questions, model short and long case records are liberally added in clinical methods.
- Anatomical basis of ENT diseases are answered by senior most Anatomy professor.

JAGADISH SUNKUM

# MANUAL OF ENT, HEAD & NECK SURGERY

Based on NMC /MCI new CBME curriculum for  
Indian Medical Graduate (IMG) GMER 2019

A text book for undergraduates and  
A Primer for Postgraduate students.

**FIRST EDITION**

**"IT IS NOT ABOUT WHAT YOU READ. IT IS ABOUT WHAT MAKES YOU READ"**

**JAGADISH SUNKUM**

**MBBS (Mys) MS( ENT) PGDHM (New Delhi)**

**Formerly**

Prof & HOD, ENT , AMC and SSRMC, Mauritius  
Medical Superintendent, K.M.C,M.M.C [ AP/TS] India  
Prof & HOD,ENT, KMC,MMC,NMC (AP/TS) India  
Asso Prof & HOD,ENT,Al- Tahaddi University,Sirte,Libya  
Asst /Assoc Prof AIISH, Mysore, JSS medical college, Mysore  
ENT Specialist , MOH, Saudi Arabia  
Flt Lt Medical Officer (IAF)

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## FOREWORD

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It's a privilege to write this foreword for this book titled "Manual of ENT-Head and Neck surgery" by Jagdish Sunkum. It certainly fulfils the purpose for which it was written, that it is to give clear cut basic information about various ENT issues for the benefit of the undergraduate student and in some cases also the post graduate student. The text has been very clearly and succinctly written and this is complemented by very clear and descriptive pictures which add great value to the book.

I feel this book would be of great help to the students of ENT both under graduate and the post graduate.

**Dr. M. V. Kirtane**

M.S. (ENT),D.O.R.L.  
PROF. EMERITUS, SETHI G.S.MEDICAL COLLEGE &  
K.E.M. HOSPITAL, MUMBAI  
CONSULTING ENT SURGEON AT  
THE P.D.HINDUJA NATIONAL HOSPITAL  
& MEDICAL RESEARCH CENTRE, MUMBAI,

BREACH CANDY HOSPITAL &  
PRINCE ALY KHAN HOSPITAL  
HON.ENT CONSULTANT TO HIS EXCELLENCY  
THE GOVERNOR OF MAHARASHTRA

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## FOREWORD

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I am very happy to know that Prof Jagdish Kumar has edited a book for undergraduates in Otorhinolaryngology, Head & Neck surgery. Even a casual glance through the book will reveal the extensive effort which has gone in creating this book. Even though the author has projected this book as a book for undergraduates I'm of the opinion that it can also serve the postgraduate residents in Otolaryngology as a ready reckoner and a quick reference guide. The chapters are well laid out and at the same time comprehensive and the information is presented with clarity. Illustrations add to the allure of the book.

I thoroughly enjoyed reading the chapters of the book and in my opinion this book fulfils a long felt need for a book of this kind. I'm sure the book will go a long way in introducing the specialty to undergraduates and satiating their quest for knowledge.

I have no hesitation in commending this book in the highest terms. The book deserves a place in every medical library.

Prof. Mohan Kameswaran MS, FRCS, FAMS, DSc  
Padma Sri awardee, Dr. B. C. Roy awardee, Indo-Australian awardee.  
Managing Director, Madras ENT Research Foundation ,Chennai,  
Hon' Prof of ENT,SRM medical college & RC, Kattankullathur, Hon'y Sr Lecturer, Edgehill university,  
Lancashire, UK. Regional Secretary, International Federation of Otorhinolaryngological Societies ( IFOS)

Dear Reader,

The first edition of **Manual of ENT ,Head and Neck Surgery** written and compiled by Professor Jagdish Sunkum, is an excellent overview for medical students, general practitioners and even post-graduate residents. This is a comprehensive review of the majority of specific ENT problems which patients encounter in their daily lives. I am overwhelmed by the extensive collection of illustrations and materials which have been a valuable contribution in bringing this textbook. Those doctors who are at the primary level of medical care, the ENT problems form a large segment of the general practitioner's patient evaluation and treatment.

This textbook offers a modern guide to ENT practice, teaching medical students and junior ENT doctors. Most chapters featuring the anatomy are well illustrated and have a general review of the diseases which may affect the area. In each overview, the student will be able to identify the most common conditions since they are well highlighted. The compilation of chapters in this book will definitely provide you with knowledge and structure you require in daily practice.

The Manual of ENT, Head and Neck surgery is an excellent reference for ENT related diagnoses and procedures, whereby the author demonstrates his extensive knowledge with succinct explanation and detailed illustration.

After reading this textbook, a GP will have refreshed his knowledge of common diseases in ENT including the emergencies, a student can fly high with roaring success in the MBBS examinations besides it can be of great help to a postgraduate in MS [ENT] and D.L.O going for exam.

**Dr. Beerdarshan Singh Caussy**

MBBS,MS[Gen Surg], MMSc [Scotland] & Fellow in Neurosurgery[UK]  
Regional Health Director  
Victoria Hospital  
Consultant in Charge Neurosurgery  
Ministry of Health and Quality of Life  
Mauritius.

## COMMENTS AND REVIEWS BY PROFESSORS IN VARIOUS MEDICAL COLLEGES

Chapter 50, 51-Carcinoma Larynx and Neck dissection, Speech and voice disorders. Well written, easy to understand, with good diagrams, excellent book for undergraduates. I went through the topic. It is well written with lots of information. Topics are written in points, easy to understand and remember. **Excellent book for both undergraduate and postgraduate** students, handy book for consultants to revise.

Thank you sir., Dr Chandrakiran.C

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Dr Mahendra Naik, Prof & HOD ENT, Maharaja Agrasena medical college, Agroha, Haryana, India  
Chapters 60,61,62-Thyroid, HIV/AIDS in ENT, Recent advances. This book meets with the requirements of the new curriculum, particularly the integration of basic sciences with clinical sciences. Applied and surgical anatomy have been given due mention. Overall a **student friendly book**, which will be **useful for undergraduates and postgraduates**

---

Dr Belaldavar, Senior consultant ,Prof & HOD, ENT ,JN medical college and Research centre, Belagavi, Karnataka, India

Chapter 42,43,44-Tumours of hypopharynx, Anatomy and physiology of Larynx, Congenital lesions of Larynx.

"The content of this text book is well charted keeping in mind, the tender understanding of the academic maturity of the undergraduate students. And also useful for the ready reference script for postgraduate students and faculty. I feel there is lot of shedding of sweat ,sparing of personal time and concern to bring such a **motivational book**. The standard by which this book has been penned suggests ,the highest acumen and experience of the author. I wish best of luck for his endeavours."

---

Dr Nitin Ankle, Prof and Senior Consultant, KLE HOSP & MRC JNMC, Belgavi Karnataka, India  
Chapter 58,59,60-Anatomy of Head, Infections of Head and Neck spaces, Neck, Thyroid. The book's cover looks impressive and the preface aptly reveals the objectives of the book. I agree **such a book is much needed** in present competitive times for our students

---

Dr Anjana Avinash Mohite, Associate Prof, DY Patil medical college, Kolhapur, Maharashtra, India  
Chapter 8, CSOM (IT) (AA) Cholesteatoma, Complications of CSOM. This ENT **book is superb** in its presentation. It contains all the fundamentals required for undergraduates and will definitely make ENT diseases an **interesting reading**.

---

Dr Arvind Sangavi.B. Associate Prof, Dept of ENT, Raichur Institute of Medical Sciences, Raichur., Karnataka.

Chapter 25,26 – Nasal polypi, Epistaxis. First of all, I would like to congratulate you for bringing out this excellent ENT textbook. we can see the efforts put in this book. Well written textbook written in a simplified way. **Excellent resource for** the undergraduate & PGs medical students. Topics have been covered in detail with large number of clinical photographs, radiographic images & diagrams making it easy to understand. **A must ENT textbook"**

---

Dr Nagaraj Gowda, Prof ENT,MVJ Medical College & Research HospitalHoskote, Bangalore, Karnataka.  
Chapters 66,67-Surgeries of Larynx and Bronchus, Surgeries of oesophagus; Hearty congratulations and best Wishes for your upcoming Text Book for MBBS and Post Graduate Students. Cover page looks very elegant. It has been well written, **easy to understand** and very concise for the undergraduate students.

---

Dr Remukananda, Prof of ENT, J J M medical college, Davanagere, Karnataka, India  
Chapter 23, 24-Allergic Rhinitis, Non-Allergic rhinitis; The book is very good for undergraduates. It is easy to read & remember. It is very concise. Even it is **good for Junior PG**. Sometimes during PG exam before entering exam hall students can have a glance.

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Dr B Jayaprakash Reddy,MS, DNB ,(ENT) Prof of ENT,Viswa Bharathi Medical college,Kurnool ,AP , India  
Chapter 52,Foreign bodies Airways. I have reviewed the text book authored by Dr Jagadish kumar. It is **simple superb** covering all the aspects. I can recommend this book to all the students appearing for exams.

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# SECTION 7- HEAD & NECK

## CHAPTER 58:

### ANATOMY OF HEAD

#### HEAD & NECK SPACE ANATOMY HEAD & NECK SPACE INFECTIONS: SKULL BASE SYNDROMES

##### Core competence

EN1.1.9 Describe the anatomy of head

##### Core competency:

EN 4.41: Describe the clinical features, investigations and principles of management of **Acute and Chronic Abscesses in relation to Pharynx.**

EN 4.37: Describe the clinical features, investigations and principles of management of Ludwig's angina

### ANATOMY OF HEAD

Following skull and facial bones are closely related to organs related to ENT diseases.

**Frontal bones** -has vertical squamous part which encloses frontal sinus, horizontal orbital plate which forms the roof of the orbit and third part called nasal part. Floor of the frontal sinus is thin and ideal for eliciting sinus tenderness.

**Ethmoid bone** – has three parts- ethmoid labyrinth, cribriform plate and perpendicular plate of ethmoid. Ethmoid labyrinth contains ethmoid sinuses, laterally separated from orbit by a thin plate of bone called lamina papyracea, olfactory nerve enters the cranium through the cribriform plate.

**Maxilla bone**-forms upper jaw, contains maxillary sinus, has four processes- frontal, zygomatic, palatine and alveolar. Palatine process forms hard palate and alveolar process contains dental sockets. Canine fossa in the anterior surface, is thin and hence it is the ideal point for examining the sinus tenderness.

**Sphenoid bone**- has central body which contains sphenoid sinus, two lateral great wings and two small wings and inferiorly two pterygoid processes. Superiorly, it has sella turcica, and pituitary fossa in which pituitary gland resides.. Hence pituitary lesions are easily approachable by nasal endoscope. It has four foramina – optic, rotundum, ovale and spinosum.

**Temporal bone** - has four parts- squamous, petrous, mastoid and tympanic. Squamous part forms roof of EAC. Petrous part forms roof of middle ear, anteriorly it has canal for tensor tympani and eustachian tube, and foramina for greater and lesser superficial petrosal nerves, posteriorly it has internal auditory canal, sulci for sigmoid

sinus, superior and inferior petrosal sinuses, inferiorly it has jugular fossa for jugular bulb. Tympanic and mastoid are not fully developed at birth and hence facial nerve lies exposed more superficially and can get injured during mastoidectomy with standard postaural incision in children. McEwen's triangle on the squamous part above the EAM is the surface anatomy of the mastoid antrum. Mastoid and petrous parts contain air cells, responsible for mastoiditis and Gradenigo syndrome.

**Mandible**-is largest and strongest bone of the face.

Condyle is weaker part and get fractured easily.

**Nasal bones**– upper half is thick and lower half is thin. Most common bone in the face to get fractured.

**Zygomatic bone** – called cheek bone, gives prominence to the cheek,

**Palatine bone** – has horizontal and vertical process, forms floor and lateral wall of the nose.

#### Structures passing through the foramina

Foramen rotundum- maxillary nerve

Foramen ovale- mandibular nerve

Foramen spinosum- middle meningeal artery and vein, meningeal branch of mandibular nerve

Internal acoustic meatus- contains- facial and vestibulocochlear nerves, labyrinthine artery

Jugular foramen- glossopharyngeal, vagus, accessory nerves, jugular bulb, inferior petrosal and sigmoid sinuses.

Hypoglossal canal- hypoglossal nerve

Foramen magnum- accessory nerve, medial posterior spinal arter.

574/727

## 7. Bacteraemia

**Bacteria:**

Aerobes -streptococci, staphylococcus aureus, Klebsiella; Anaerobes.

**Symptoms:**

1. Sudden onset swelling in the preauricular region-unilateral
2. High grade fever with chills
3. Dysphagia / odynophagia
4. Facial weakness

**Signs:**

1. Patient is febrile and toxic
2. Parotid is swollen and tender, hard with no fluctuation

**LEMIERRE'S SYNDROME:**

It is septic thrombosis of the internal jugular vein as a complication of quinsy or parapharyngeal abscess, caused by anaerobic fusobacterium necrophorum, which are normal commensals in the throat. Other bacteria including anaerobic streptococci are also present.

It can also occur in a previously healthy child with simple pharyngitis.

It is a serious illness and can lead to septicemia and septic emboli.

**Symptoms:**

- a. Fever – intermittent, high grade, rigors,
- b. Lateral neck pain, neck stiffness, headache

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565

- c. Neck swelling- due to enlarged lymph nodes
- d. Severe lethargy

**Signs:**

- a. Swelling and tenderness in the neck
- b. signs of shock and meningitis

**Investigation:**

CECT -Neck – shows opacity of Internal jugular vein

**Treatment:**

IV ampicillin with sulbactam  
IV metronidazole  
Anticoagulants- Enoxaparin

**NECROTISING FASCITIS****Definition:**

It is cellulitis of the neck involving the subcutaneous tissue superficial neck space.

It is rapidly progressive and necrotising infection seen in immunocompromised patients caused by GABHS and other bacteria.

**Symptoms:**

1. Severe neck pain
2. Numbness of the skin
3. Fever

**Signs:**

1. crepitus
2. central zone of vesiculation, intermediate zone of ecchymosis and outer zone erythema
3. Signs of hypocalcemia, dehydration

**Diagnosis:**

MRI neck- shows gas bubbles in the soft tissue

**Treatment:****Medical:**

1. Fluid and electrolyte balance
2. IV antibiotics – Ceftriaxone and Metronidazole
3. Hyperbaric oxygen
4. Immunotherapy

**Surgical:**

1. Aspiration of pus
2. Debridement of all necrotic tissues is the key to recovery. Followed by skin grafting.

**Complications:**

1. Toxic shock syndrome
2. Necrotising mediastinitis.

**CERVICOFACIAL ACTINOMYCOSIS:  
(LUMPY JAW)****Definition:**

It is a rare, chronic, suppurative, granulomatous infectious disease of face and neck, caused by Actinomyces which are gram positive non-acid fast, anaerobic bacteria, present in the oral cavity as commensals.

This disease is difficult to diagnose, masquerades as many head and neck diseases, less than 10% are diagnosed correctly.

Actinomyces invades the subcutaneous tissue when mucosal barrier is broken.

**Incidence:**

More common in women than men-3:1  
Age- 20-50 years

**Etiology:**

- a) Dental caries
- b) Dental or oral surgery
- c) Poor dental hygiene
- d) Periodontal disease
- e) Radiotherapy to neck

**symptoms:**

1. Painless swelling in the submandibular or perimandibular region
2. Reddish or bluish discoloration of the skin
3. Difficulty in chewing and opening the mouth

**Signs:**

- a) Tender/ nontender woody hard nodules around the angle of the mandible, becoming abscesses and start to form sinuses opening into cheek or submandibular area
- b) Yellow sulfur granules are seen draining out of sinuses.
- c) Trismus
- d) Fever – variable
- e) No cervical lymphadenopathy

**Investigations:**

- a) Smear for culture
- b) Sulfur granules – for actinimycetes.

**Treatment:****Medical**

- a) Inj Penicillin or Cap Amoxycillin or cap doxycycline or cap clindamycin for long term
- b) Inj/ cap cephalosporins

**Surgical**

- a) Incision and drainage of abscesses
- b) Excision of sinus tracts

**SKULL BASE SYNDROMES:**

Malignant and inflammatory lesions affecting the skull base and the cranial nerves which are leaving the skull through various foramina produce syndromes depending on the symptoms produced depending on the location of the lesions.

Causes and symptoms are described in brief as below.

**SUPERIOR ORBITAL FISSURE SYNDROME:****Etiology:**

- a) Meningioma affecting sphenoid wing
- b) Meningitis
- c) sinusitis
- d) Trauma – zygo
- e) Idiopathic

590/727

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566

**Clinical features:**

- a) Ptosis
- b) Proptosis
- c) Ophthalmoplegia
- d) Dilated and fixed pupil
- e) Loss of sensation in forehead

**Etiology**

- Glomus jugulare
- Vestibular schwannoma

**Clinical features:**

9,10,11 and 12 CN palsy

**FOSTER KENNEDY SYNDROME****Etiology:**

- a) Frontal lobe tumours
- b) Meningioma from olfactory groove cribriform plate

**Clinical features:**

- a) Optic nerve atrophy- ipsilateral
- b) Contralateral papilloedema

**VILLARET SYNDROME  
(RETROPHARYNGEAL SPACE SYNDROME)****Etiology**

Jugular vein thrombosis

**Clinical features:**

- 9,10,11 and 12 CN palsy
- Horner syndrome
- 7<sup>th</sup> CN palsy



**ANSWERS:**

Q1) A-3,B-4,C-1

Q2) A-2,B-3,C-1

Q3) A-4,B-3

**KEYPOINTS:**

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568

1. Retropharyngeal space is divided into 2 lateral compartments called "**Spaces of Gillette**" by a midline raphe. Each compartment contains a node called "**Nodes of Rouvier**".
2. Danger space [ Alar space] is between the Retropharyngeal space and Prevertebral space. It extends from skull base to diaphragm.
3. Trismus in lateral pharyngeal space infection is due to spasm of the medial pterygoids. In general, trismus can occur due to spasm of any of the muscles of deglutition- masseter, medial and lateral pterygoids and temporalis.
4. Quinsy is collection of pus in peritonsillar space which is between the tonsils and the superior constrictor muscle. Tonsil alone gets pushed medially in quinsy whereas in parapharyngeal space abscess, both the tonsil and the lateral wall of pharynx get pushed medially.
5. CT Scan head and neck with contrast is an important investigation for some deep neck space infections like Ludwig's angina or lateral pharyngeal space infection.
6. Lemierre's syndrome can occur in a previously healthy child or as a complication of quinsy or parapharyngeal abscess. It is a serious, life threatening disease caused by anaerobic fusobacterium necrophorum, a normal commensal in the throat.

**CONFLICT IS THE PRIMARY ENGINE OF CREATIVITY AND INNOVATION.—RANOLD HEIFETZ**

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593/727



569

**CHAPTER 59:**

1. **NECK MASSES**
2. **NECK LYMPH NODES**
3. **NECK TRAUMA**

**Core competency**

**EN 2.7:** Demonstrate the correct technique of examination of neck including elicitation of laryngeal crepitus.

**EN 4.31:** Describe the clinical features, investigations and principles of management of trauma to the neck

**CLASSIFICATION OF NECK MASSES****CLASSIFICATION BASED ON SITE OF LESION**

Neck masses are divided into 1. Midline masses 2. Lateral masses

**MIDLINE NECK MASSES:**

1. Submental lymph node

4. Cervical rib

**C. Occipital triangle**

1. Lymphadenopathy
  - a. Inflammatory
  - b. Neoplastic
  - c. Metastatic



- Vertigo
- Headache
- Diplopia
- Facial palsy

#### GRADENIGO SYNDROME

See the chapter on CSOM – complications

#### COLLET SICARD SYNDROME

- Cholesteatoma
- Neurofibroma
- Carcinoma nasopharynx
- Jugular vein thrombosis

#### Clinical features:

- 9<sup>th</sup> CN palsy- loss of gag reflex, loss of soft palate sensation, dysphagia
- 10<sup>th</sup> CN palsy- hoarse voice, weak cough, dysphagia, dysarthria, nasal regurgitation

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567

- 11<sup>th</sup> CN palsy- weakness of trapezius, sternocleidomastoid

- 12<sup>th</sup> CN palsy- deviation of tongue, dysphagia

#### CASE STUDY 1.

Q1) An image of the oropharynx is shown here of a patient with trismus, hot potato voice, pain and difficulty in swallowing.



A) The probable diagnosis?

1. Parapharyngeal abscess
2. Lymphoma tonsil
3. Quinsy\*\*
4. Tonsillar abscess

B) Etiology of this case;

1. De novo
2. Acute tonsillitis
3. Intratonsillar abscess
4. All of the above\*\*

C) Treatment includes all except;

1. Abscess tonsillectomy\*\*
2. IV antibiotics, IV fluids, analgesics
3. Tonsillectomy after 6 weeks
4. Incision and drainage

#### CASE STUDY 2

Q2) A 3 years old child was brought to emergency with history of sudden onset, marked throat pain and difficulty in swallowing for both solids and liquids, fever with rigors and chills, neck pain and tilting to one side since 12 hours. Child had a penetrating injury to postpharyngeal wall, when he was running with a sharp pencil in the mouth and fell down on face 3 days back. On examination child was toxic and irritable, having inspiratory stridor, there was bulging in the posterior

pharyngeal wall. X-ray neck lateral view showed increased prevertebral thickening with gas shadow.

A) Diagnosis of this case is;

1. Acute prevertebral abscess
2. Acute retropharyngeal abscess\*\*
3. Acute retropharyngeal cellulitis
4. Acute retropharyngeal hematoma

B) Investigations to be done are all except;

1. Ultrasound neck
2. CECT neck
3. Aspiration of pus for culture and sensitivity
4. Throat swab for culture and sensitivity\*\*

C) Next step in management is;

1. External incision and drainage through carotid sheath
2. External incision and drainage below the mandible
3. Intraoral incision and drainage\*\*
4. Transpalatal incision and drainage

D) Complications include all except;

1. Pneumothorax\*\*
2. Jugular vein thrombosis
3. Carotid artery rupture
4. Cervical spine osteomyelitis

#### CASE STUDY 3

Q3) A 30 years old female patient developed fever with chin swelling and trismus following sepsis in right lower molar tooth. On examination, there was tenderness and induration in the submandibular region with oedema of the floor of the mouth.

A) Most probable diagnosis is

1. Intraoral abscess
2. Parapharyngeal abscess
3. Dental abscess
4. Ludwig's angina\*\*

B) Treatment includes all except;

1. IV antibiotics
2. Incision and drainage
3. High dose steroids\*\*
4. Tracheostomy SOS

#### Answers:

Q1) A-3,B-4,C-1

Q2) A-2,B-3,C-1

Q3) A-4,B-3

#### KEYPOINTS:

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568

1. Retropharyngeal space is divided into 2 lateral compartments called "Spaces of Gillette" by a midline raphe. Each compartment contains a node called "Nodes of Rouvier"
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6. Lemierre's syndrome can occur in a previously healthy child or as a complication of quinsy or parapharyngeal abscess. It is a serious, life threatening disease caused by anaerobic fusobacterium necrophorum, a normal commensal in the throat.

antibiotic therapy. It is done before I&D.

**Treatment:**

1. **Peritonsillitis** is cellulitis and is treated conservatively with antibiotics and does not require surgical procedure of incision and drainage.
2. **Peritonsillar abscess:**
  - a) Hospitalisation
  - b) I.V fluids- 5% Dextrose, DNS
  - c) IM Inj diclofenac 75mg or IV paracetamol 1G TID



Fig 58-21: Aspiration of quinsy

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564

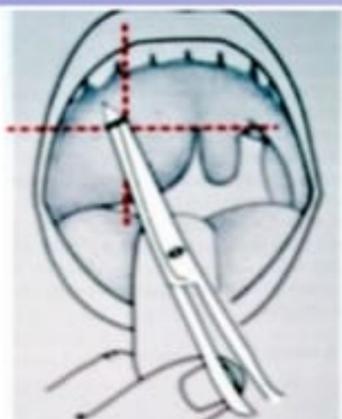


Fig 58-22: Point of incision in quinsy

**Complications:**

1. Parapharyngeal abscess
2. Laryngeal oedema
3. Septicaemia
4. Endocarditis
5. Nephritis
6. Brain abscess
7. Pneumonitis
8. Lung abscess
9. Jugular vein thrombosis (Lemierre's syndrome)
10. Carotid artery rupture

**PAROTID SPACE INFECTION**

**Definition:**

It is infection of the parotid space.

**Incidence:**

It is seen in new born, premature infants, immunocompromised children and adults, elderly debilitated individuals.

**Etiology:**

1. Via Stenson's duct - infection spreading from oral cavity
2. Suppuration of parotid lymph nodes
3. Otitis externa spreading through foramen of Huschke and Fissures of Santorini.
4. Dehydration
5. Post-operative
6. Stones and tumours obstructing the ducts
7. Bacteraemia

**Bacteria:**

Aerobes -streptococci, staphylococcus aureus, Klebsiella; Anerobes.

**Symptoms:**

1. Sudden onset swelling in the preauricular region-unilateral
2. High grade fever with chills
3. Dysphagia / odynophagia
4. Facial weakness

**Signs:**

1. Patient is febrile and toxic
2. Parotid is swollen and tender, hard with no fluctuation

3. Stenson's duct opening is reddish, and pus is seen on pressing the parotid gland.
4. Cervical lymphadenitis
5. Facial nerve palsy- as complication



Fig 58-23: Parotid space abscess (Courtesy: Dr Noorali Bharwani, Surgeon, Canada)

**Investigations:**

1. USG parotid gland
2. USG guided aspiration / FNAC and pus for culture and sensitivity.
3. C T Scan parotid gland

**Treatment:**

**Medical**

- a. IV fluids - 5% glucose, N saline, Ringer lactate
- b. IV antibiotics
- c. Improve oral hygiene

**Surgical**

Incision and drainage under LA/ GA

Skin incision - Blair's incision: Deep fascia and the gland - multiple incisions done parallel to facial nerve branches through the fascia. Blunt dissection is done to evacuate the pus. Drainage tube inserted.

**Complications:**

1. Spontaneous rupture into mouth or external auditory canal
2. Rupture onto skin with fistula formation
3. Spread to parapharyngeal or retropharyngeal space.

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It is a serious illness and can lead to septicemia and septic emboli.

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- b. Lateral neck pain

589/727

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- c. Neck swelling- due to enlarged lymph nodes
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**Signs:**

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**Investigation:**

CECT - Neck - shows opacity of Internal jugular vein

**Treatment:**

IV ampicillin with sulbactam  
IV metronidazole  
Anticoagulants- Enoxaparin

**NECROTISING FASCITIS**

**Definition:**

It is cellulitis of the neck involving the subcutaneous tissue superficial neck space.

It is rapidly progressive and necrotising infection seen in immunocompromised patients caused by

**Definition:**

It is a rare, chronic, suppurative, granulomatous infectious disease of face and neck, caused by Actinomyces which are gram positive non-acid fast, anaerobic bacteria, present in the oral cavity as commensals.

This disease is difficult to diagnose, masquerades as many head and neck diseases, less than 10% are diagnosed correctly.

Actinomycis invades the subcutaneous tissue when mucosal barrier is broken.

**Incidence:**

More common in women than men-3:1  
Age- 20-50 years

**Etiology:**

- a) Dental caries
- b) Dental or oral surgery
- c) Poor dental hygiene



upto subperiosteal space.  
 c) For temporal space infection, external horizontal incision above the zygomatic arch

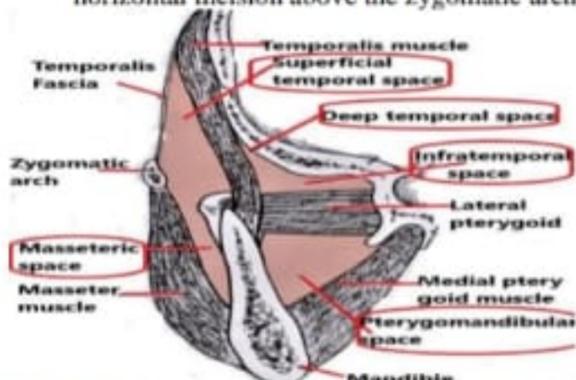


Fig 58-18: Superficial, deep and infra temporal space, Masticator space and pterygomandibular space

**Peritonsillar abscess**

**Pathogenesis:**

There are 2 theories

1. **Infection of the weber's gland:** a collection of 25-30 mucous salivary glands situated in the supratonsillar fossa in the soft palate. It spreads to peritonsillar space.
2. **Starts as abscess in the crypta magna:** and its mouth gets closed thus forming Intratonsillar abscess, which then ruptures and spreads to peritonsillar space to become quinsy.

Refer to chapter 39 – pathogenesis of tonsillitis.

**Aetiology:**

1. De Novo
2. Acute Tonsillitis
3. Intratonsillar abscess

**Bacteriology:**

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Streptococci, staph aureus and anaerobic organisms. Both aerobes and anerobes may be present.

**Symptoms:**

**General:**

1. Fever with chills and rigors
2. Body aches , malaise
3. Headache
4. Foetid breath
5. Nausea
6. Constipation

**Local:**

7. Severe sore throat- unilateral
8. Odynophagia- severe
9. Hot potato voice- muffled and thick speech
10. Ipsilateral severe earache – via 9<sup>th</sup> CN
11. Inability to open the mouth
12. Dribbling of saliva

**Signs:**

1. **Tonsil is pushed medially.** [ in contrast to parapharyngeal space abscess -entire lateral wall and tonsils are pushed medially]
2. Congested and edematous anterior pillar and uvula. Uvula deviated to the opposite side.
3. Bulging of the soft palate above the tonsil
4. JD node is enlarged and tender.
5. Torticollis -neck tilted to abscess side



Fig 58-20: Left peritonsillar abscess

**Investigations:**

1. CBP- TLC,DLC
2. Blood- FBS/RBS, Blood urea, serum creatinine- to rule out diabetes and renal disease.
3. Pus for culture and sensitivity for proper antibiotic therapy. It is done before I&D.

**Treatment:**

1. **Peritonsillitis** is cellulitis and is treated conservatively with antibiotics and does not require surgical procedure of incision and drainage.
2. **Peritonsillar abscess:**
  - a) Hospitalisation
  - b) I.V fluids- 5% Dextrose, DNS
  - c) IM Inj diclofenac 75mg or IV paracetamol 1G TID

- d) IV Amoxyclav or Ceftriaxone or Ciprofloxacin
- e) IV Metronidazole 500 mg x TID x 5 days
- f) Oral antiseptic gargles

**Surgery:**

**1. Incision & Drainage :**

- 10% Lignocaine is sprayed over the tonsil and palate on the affected side and after 10 min
- I & D is done by using quinsy forceps by any of the 2 methods-
  - a. stab incision at the point of maximum pointing or
  - b. at the junction of a vertical line drawn at the level of anterior pillar margin and a horizontal line at the level of the base of the uvula.
- Quinsy forceps is a misnomer, as it is not a forceps but it is like a scissors, as the outer edges of the forceps blades are sharp.
- If quinsy forceps is not available, no. 11-scalpel blade is also used, with its base covered with plaster, leaving the tip open for stab incision.

**Contraindications for I & D:**

- a) Suspected malignancy
- b) Vascular malformations

2. **Needle aspiration :** Alternatively, abscess can be aspirated using a wide bore needle and 10 cc syringe. This avoids I & D.

3. **Interval tonsillectomy** is done after 6-8 weeks. This is an absolute indication for tonsillectomy.

4. **Abscess or Hot tonsillectomy** is obsolete now and it is only of historical importance.



Fig 58-21: Aspiration of quinsy

588/727

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3. Stenson's duct opening is reddish, and pus is seen on pressing the parotid gland.
4. Cervical lymphadenitis
5. Facial nerve palsy- as complication



**PRETRACHEAL SPACE ABSCESS****Etiology:**

Perforation of the anterior oesophageal wall by endoscopic instrumentation, foreign body or trauma.

**Symptoms:**

Dysphagia, odynophagia, pain, fever, hoarseness and stridor.

**Treatment:**

Antibiotics



Fig 58-17 b: Buccal space infection – swelling

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562

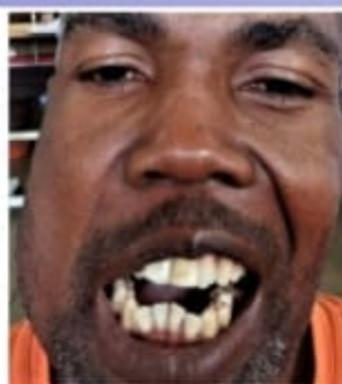


Fig 58-17 c : Buccal space infection –note trismus (Courtesy Dr Deena Singh, Director, ENT hospital, Mauritius)

**MASTICATOR SPACE ABSCESS:****Etiology:**

Main cause is dental infections involving 2<sup>nd</sup> and 3<sup>rd</sup> molar teeth

**Symptoms:**

1. Inability to open mouth
2. Severe pain and swelling over ramus of the mandible.
3. Difficulty and pain on swallowing

**Signs:**

1. Trismus- due to spasm of medial pterygoid and masseter muscle
2. Inability to depress the tongue
3. Induration of the floor of the mouth.

**Treatment**

1. Medical –I.V antibiotics- for 5-7 days

**2. Surgical:**

- a) **For masseteric and pterygomandibular spaces-** intraoral incision and drainage lateral to retromolar trigone. Blunt dissection is done medial and lateral to ramus of the mandible.
- b) **For masseteric space infection,** external incision below and behind the angle of the mandible is done and blunt dissection is done upto subperiosteal space.
- c) **For temporal space infection,** external horizontal incision above the zygomatic arch

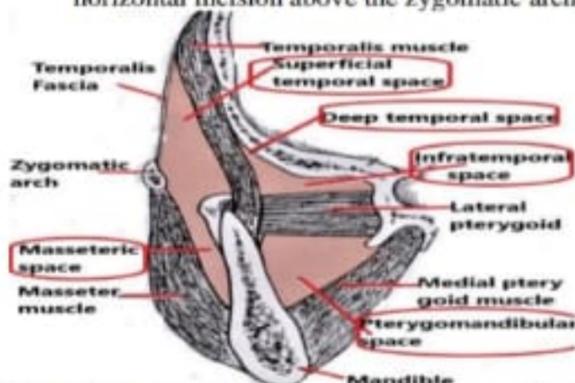


Fig 58-18: Superficial, deep and infra temporal space, Masticator space and pterygomandibular space

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Fig 58-19: Masticator space abscess [ note trismus]

**Complications:**

1. Osteomyelitis of the mandible
2. Spread of infection to buccinator space, temporal space, parotid space and rarely to parapharyngeal space.

**PERITONSILLAR ABSCESS: [ QUINSY] PERITONSILLITIS**

Quinsy is a common ENT emergency and can cause serious complications if not well treated in time.

**Def:** It is collection of pus in the peritonsillar space which is between the tonsils and the superior constrictor muscle.

- It affects adults and rare in children.
- It is usually unilateral but rarely bilateral.
- Sometimes it is recurrent and second attack can occur.
- Quinsy is an absolute indication for tonsillectomy.

Peritonsillitis is cellulitis of this space and it is prelude to quinsy.

**Non-core competency**

AN36.4: Describe the anatomical basis of peritonsillar abscess

**Pathogenesis:****There are 2 theories**

1. **Infection of the weber's gland:** a collection of 25-30 mucous salivary glands situated in the supratonsillar fossa in the soft palate. It spreads to peritonsillar space.
2. **Starts as abscess in the crypta magna:** and its mouth gets closed thus forming Intratonsillar abscess, which then ruptures and spreads to peritonsillar space to become quinsy.

Refer to chapter 39 – pathogenesis of tonsillitis.

**Aetiology:**

1. De Novo
2. Acute Tonsillitis
3. Intratonsillar abs

**Bacteriology:**

587/727

Streptococci, staph aureus and anaerobic organisms. Both aerobes and anerobes may be present.

**Symptoms:****General:**

1. Fever with chills and rigors
2. Body aches, malaise
3. Headache
4. Foetid breath
5. Nausea
6. Constipation

**Local:**

7. Severe sore throat- unilateral
8. Odynophagia- severe
9. Hot potato voice- muffled and thick speech
10. Ipsilateral severe earache – via 9<sup>th</sup> CN
11. Inability to open the mouth

- d) IV Amoxycylav or Ceftriaxone or Ciprofloxacin
- e) IV Metronidazole 500 mg x TID x 5 days
- f) Oral antiseptic gargles

**Surgery:****1. Incision & Drainage :**

- 10% Lignocaine is sprayed over the tonsil and palate on the affected side and after 10 min
- I & D is done by using quinsy forceps by any of the 2 methods-
  - a. stab incision at the point of maximum pointing or
  - b. at the junction of a vertical line drawn at the level of anterior pillar margin and a horizontal line at the level of the base of the uvula.

563

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more useful drainage under ultrasound guidance.

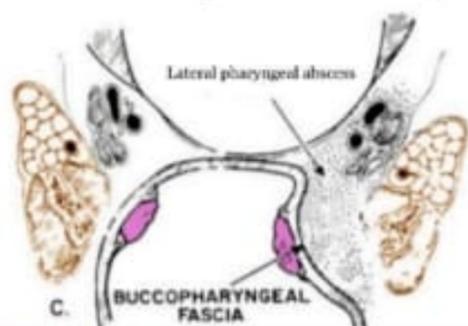


Fig 58-14: Parapharyngeal abscess(left)

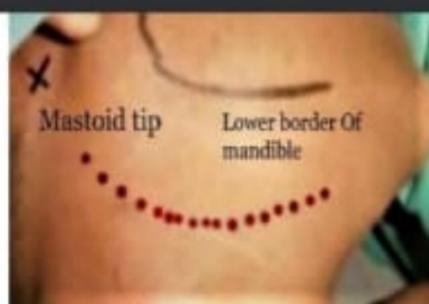


Fig 58-16 a: Modified apron Incision for LPA;

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Fig 58-16 b : Hockey stick incision in the neck for a large LPA: (Courtesy: Dr Jagadish Tubachi , Sampige clinic, Hubli, Karnataka,India)

**SURGICAL**

1. Incision and drainage under G.A
  - a. **Intraoral approach**- longitudinal incision on the pharyngeal wall. Repeated after 12-24 hours if required. It is contraindicated in multi space involvement and if abscess is lateral to great vessels of the neck.
  - b. **Extraoral approach** – 2 types of incision are used:
    - i. Hockey stick incision- used for extensive parapharyngeal abscess
    - ii. Modified apron incision- used for parapharyngeal abscess and ludwig’s angina cases. blunt dissection is done along the inner surface of the medial pterygoid muscle upto styloid process and abscess is drained.
2. **Image guided percutaneous aspiration** using ultrasound or CT scan- is an alternative to I&D as it is more safer.
3. **Tracheostomy** is mandatory if trismus prevents intubation.

**Complications:**

1. Laryngeal oedema causing stridor
2. Internal jugular vein thrombosis. [ Lemierre’s syndrome]
3. Spread to Retropharyngeal space
4. Carotid artery aneurysm
5. Carotid blow out

**PRETRACHEAL SPACE ABSCESS**

**Etiology:**  
Perforation of the anterior oesophageal wall by endoscopic instrumentation, foreign body or trauma.  
**Symptoms:**  
Dysphagia, odynophagia, pain, fever, hoarseness and stridor.  
**Treatment:**  
Antibiotics

**BUCCAL SPACE ABSCESS**

**Etiology:**  
**Dental** – premolars and molars -whose teeth roots are above and below the insertion of the buccinator muscle in upper and lower jaw respectively.

- Symptoms:**
1. Painful swelling in the cheek
  2. Fever
  3. Odynophagia
  4. Trismus

**Sign:**  
Dome shaped swelling extending from angle of mouth to angle of mandible, from zygomatic arch to lower border of mandible in the cheek.

- Treatment:**  
Incision and drainage -
1. Intraoral- horizontal incision in the buccal mucosa in premolar and molar region
  2. Extraoral – incision is done below the border of mandible

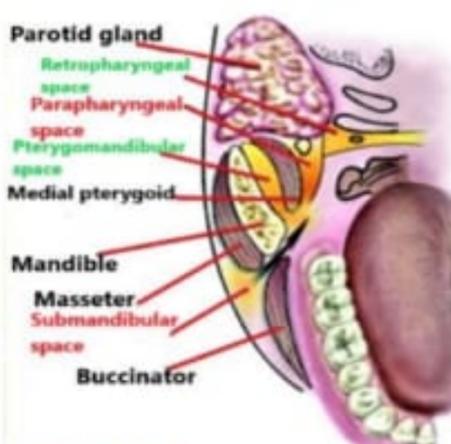


Fig 58-17 a : Buccal space infection:

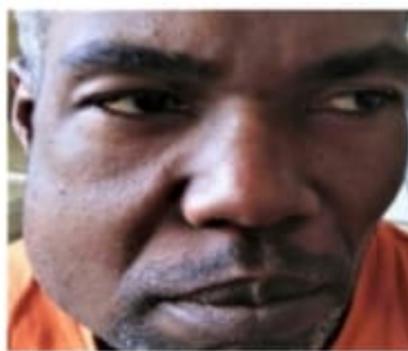


Fig 58-17 b: Buccal space infection – swelling

586/727

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Fig 58-17 c : Buccal space infection –note trismus (Courtesy Dr Deena singh, Director, ENT hospital, Mauritius)



Fig 58-19: Masticator space abscess [ note trismus]

**Complications:**



- b) Iatrogenic –
- LA injection done for tonsillectomy,
  - Mandibular nerve block for dental procedures.

**SYMPTOMS:**

**COMMON TO BOTH COMPARTMENTS:**

2. Drooping of the eyelid-Horner's syndrome
3. Deviation of the tongue to opposite side on protrusion -12<sup>th</sup> CN palsy
4. Numbness in the throat -9<sup>th</sup> CN palsy
5. Hoarseness of voice -10<sup>th</sup> CN palsy
6. Nasal regurgitation due to palatal palsy
7. Weakness of the shoulder due to 11<sup>th</sup> CN palsy.

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560

8. Minimum trismus and no tonsil medialisation.

**Signs:**

1. Throat: bulging in the lateral pharyngeal wall, behind the post pillar of the tonsil.
2. Neck stiffness
3. Neck swelling in large abscess
4. Paralysis of 9,10,11 and 12<sup>th</sup> CN and sympathetic chain.

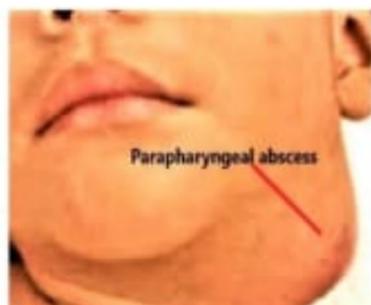


Fig 58-13 b : Parapharyngeal space abscess



Fig 58-13c: Parapharyngeal abscess [right]

**Investigations:**

- 1 X-Ray Neck-lat view soft tissue- swelling of the lateral pharyngeal space is visible
- 2 CT scan Neck with contrast-for extent of the lesion
- 3 MRA Magnetic Resonance Angiography for internal carotid artery aneurysm and IJV thrombosis
- 4 Ultrasound Neck- safe, portable, no radiation, less traumatic, no sedation needed in children-more useful drainage under ultrasound guidance.

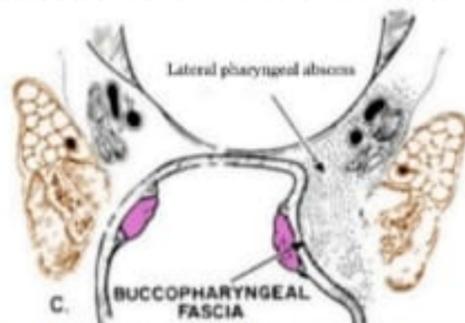


Fig 58-14: Parapharyngeal abscess(left)



Fig 58-15 a: Parapharyngeal abscess –CT scan Head and Neck-axial view



Fig 58-15 b : C T Scan Head and Neck- coronal view -Parapharyngeal space abscess

**TREATMENT:**

Admission in ICU for monitoring and intensive therapy; High dependency intensive care is needed.

**MEDICAL:**

- 1 IV amoxicillin -clavulanic acid 150 mg/Kg /day
- 2 IV Imipenam 500 mg 6 hrly
- 3 IV metronidazole 500 mg 8 hourly
- 4 IV Gentamycin 80 mg 8 hourly
- 5 IV Dextrose 5%, DNS , Ringer lactate- to correct dehydration and to correct electrolyte imbalance

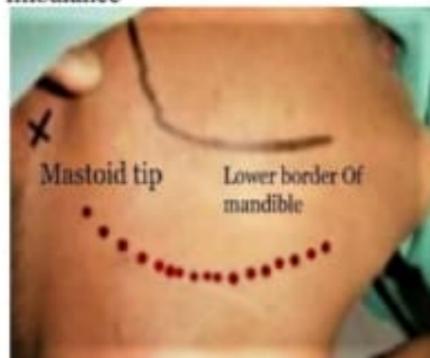


Fig 58-16 a: Modified apron Incision for LPA;

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585/727

561



Fig 58-16 b : Hockey stick incision in the neck for a large LPA: (Courtesy: Dr Jagadish Tubachi , Sampige clinic, Hubli, Karnataka,India)

**SURGICAL**

1. Incision and drainage under G.A
  - a. **Intraoral approach-** longitudinal incision on the pharyngeal wall. Repeated after 12-24 hours if required. It is contraindicated in multi space involvement and if abscess is lateral to great vessels of the neck.

**BUCCAL SPACE ABSCESS**

**Etiology:**

**Dental** – premolars and molars -whose teeth roots are above and below the insertion of the buccinator muscle in upper and lower jaw respectively.

**Symptoms:**

1. Painful swelling in the cheek
2. Fever
3. Odynophagia
4. Trismus

**Sign:**

Dome shaped swelling extending from angle of mouth to angle of mandible, from zygomatic arch to lower border of mandible in the cheek.

**Treatment:**

Incision and drainage -

1. Intraoral- horizontal incision in the buccal mucosa in premolar and molar region
2. Extraoral – incision is done below the border of mandible

Parotid gland

Fig 58-11c ; X-ray Neck lateral view: Acute RPA

### ABSCESS: (PREVERTEBRAL SPACE ABSCESS)

It is abscess situated between the prevertebral layer and alar layer of deep fascia of neck.

#### Etiology:

1. TB of the cervical spine
2. TB lymphadenitis [of retropharyngeal node- which disappears by age of 5]

#### Symptoms:

1. Discomfort in the throat- insidious onset
2. Dysphagia – mild
3. Fever low grade, evening time
4. Swelling in the neck.
5. Cough with expectoration [if pulmonary TB is present]
6. Loss of appetite and weight

#### Signs:

1. Upper deep cervical -level 2- lymphadenopathy- matted nodes
2. Fluctuant swelling in the posterior pharyngeal wall-
  - a) midline if it is due to involvement of caries cervical spine vertebra,
  - b) paramedian if it is due to tuberculosis of retropharyngeal node.

#### Investigations:

1. X-Ray cervical spine – AP & Lat views
2. X-Ray chest -PA view – to rule out pulmonary TB
3. Sputum for AFB
4. Mantoux test

#### Treatment:

1. Incision and drainage- along anterior border if the abscess is lower and along posterior border of the SCM if the abscess is at a higher level.
2. ATT-Anti tubercular treatment – full course.
3. Tracheostomy- for stridor.

### PARAPHARYNGEAL ABSCESS:

Also called Lateral pharyngeal space abscess

Etiology: [ TEAT - I T ] (remember- tweet it)

1. Tonsils- 60% cases of abscess are due to tonsil lesions
  - a) post tonsillectomy
  - b) complication of quinsy
  - c) acute and chronic tonsillitis
2. Ear -mastoiditis with Bezold abscess and petrositis can spread to lateral pharyngeal space.
3. Adenoiditis
4. Teeth - Dental abscess- lower last molar tooth [ seen in 35% ]
5. Infection can also spread from parotid space/ retropharyngeal space and submaxillary space
6. Trauma:
  - a) penetrating injuries of neck
  - b) Iatrogenic –
    - LA injection done for tonsillectomy,
    - Mandibular nerve block for dental procedures.

#### SYMPTOMS:

#### COMMON TO BOTH COMPARTMENTS:

1. Fever, malaise first symptoms
2. Ptyalism- excessive salivation / drooling of saliva
3. Sorethroat
4. Severe odynophagia / dysphagia
5. Torticollis due to spasm of prevertebral muscles.
6. Symptoms and signs of toxemia

#### Additional symptoms and signs of each compartment:

#### A. ANTERIOR COMPARTMENT INFECTION

##### Symptoms:

1. Inability to open mouth
2. Swelling behind the angle of the jaw

##### Signs:

1. Trismus- mainly due to spasm of medial pterygoid which lies laterally to the space. [ Trismus can also occur in other conditions, due to spasm of any of the muscles of deglutition- i.e, masseter, medial and lateral pterygoid and temporalis]
2. Swelling in the retromolar region
3. Tonsil and entire lateral wall is displaced medially. ( In quinsy, only tonsil is pushed medially.)
4. Hot, tender mass behind the angle of the mandible



Fig 58-13 a: Parapharyngeal abscess  
Note swelling in the lateral pharyngeal wall ;

#### B. POSTERIOR COMPARTMENT INFECTION

##### Symptoms:

1. Swelling in the parotid region- parotid pushed laterally
2. Drooping of the eyelid-Horner's syndrome
3. Deviation of the tongue to opposite side on protrusion -12<sup>th</sup> CN palsy
4. Numbness in the throat -9<sup>th</sup> CN palsy
5. Hoarseness of voice -10<sup>th</sup> CN palsy
6. Nasal regurgitation due to palatal palsy
7. Weakness of the shoulder due to 11<sup>th</sup> CN palsy.

584/727

8. Minimum trismus and no tonsil medialisation.

#### Signs:

1. Throat: bulging in the lateral pharyngeal wall, behind the post pillar of the tonsil.
2. Neck stiffness
3. Neck swelling in large abscess
4. Paralysis of 9,10,11 and 12<sup>th</sup> CN and sympathetic chain.



Fig 58-13 b: Parapharyngeal space abscess

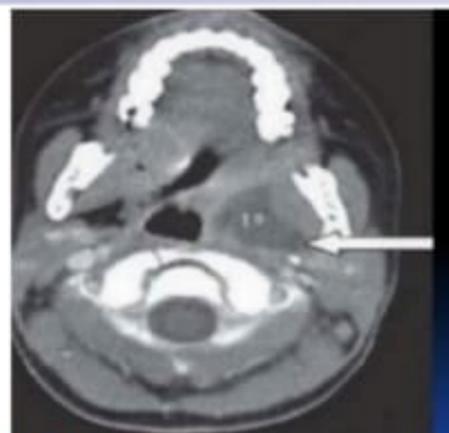


Fig 58-15 a: Parapharyngeal abscess –CT scan Head and Neck-axial view





**Fig 58-10 b:** Ludwig's angina; Note tracheostomy done for stridor.

**RETROPHARYNGEAL ABSCESS:**  
**2 Forms- ACUTE AND CHRONIC**  
**ACUTE RETROPHARYNGEAL ABSCESS:**

It is suppuration of retropharyngeal lymph nodes ( Henle's node/ Rouviere node) in children or due to penetrating injuries in adults. It is common in children below 3 years. Nodes of Rouvier disappear by 5 years age and hence it occurs only in young children..



**Fig 58-11 a :** Acute retropharyngeal Abscess

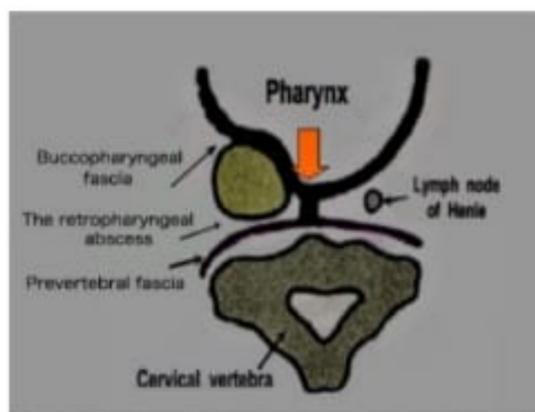
**Signs of complications:**

- Jugular vein thrombophlebitis- induration and tenderness along anterior border of Sternocleidomastoid (SCM)
- Vocal cord palsy- hoarse voice

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558

- Carotid artery rupture- bleeding from ear, nose or mouth,



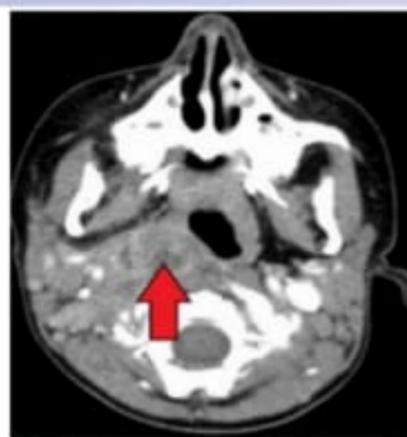
**Fig 58-11 b:** Acute RPA (Courtesy Dr Simon, SUMS, South Wales,UK)

**Investigations:**

1. X-Ray Neck lateral view- soft tissue-increased prevertebral thickness with presence of gas shadow.  
 Radiological criteria are-
  - a) Soft tissue thickness is more than half the width of the corresponding cervical vertebra,
  - b) Presence of gas shadow and
  - c) Straightening of cervical spine. [ loss of lordosis]
2. Ultrasound Neck- advantages:
  - a) Safe, portable,
  - b) No radiation,
  - c) Less traumatic,
  - d) No sedation needed in children-
  - e) Useful for drainage under ultrasound guidance.
3. CT Scan Neck with contrast:
  - a) Ideal investigation
  - b) Useful in distinguishing cellulitis from abscess.



**Fig 58-11c :** X-ray Neck lateral view: Acute RPA



**Fig 58-12:** CT Scan skull -axial view-Acute RPA

**Treatment:**

1. **Surgical:** Intraoral Incision and drainage of the abscess is done under no anaesthesia in infants and done under GA in older children. In infants, baby is wrapped and held upright. Mouth gag is applied. Child is kept supine with head low. Vertical incision is done on the most fluctuant area of the abscess on the posterior pharyngeal wall. Abscess incised with a guarded knife. Sinus forceps inserted into it and opened to break the loculi. Baby is then kept with face turned down to allow pus to escape from mouth. Pharynx needs to be packed after intubation, if done under GA, to prevent aspiration. Care should be taken when intubation is attempted as it may rupture the abscess and cause aspiration.

**1. Criteria for intraoral I&D –**

- a) Abscess should be medial to great vessels
- b) Abscess should be confined

If lateral space is involved, cervical approach is used Tracheostomy is done , before I & D ,in case of stridor and to secure the airway.

2. Antibiotics and others as described under Ludwig's angina.

**Complications:**

1. Rupture of the abscess- asphyxia or pneumonia
2. Jugular vein thrombosis
3. Carotid artery rupture
4. Mediastinitis
5. Purulent pericarditis
6. Cervical spine osteomyelitis and erosion of cervical spine causing subluxation and spinal injury.

**CHRONIC RETROPHARYNGEAL ABSCESS: (PREVERTEBRAL)**

583/727

It is abscess situated between the prevertebral layer and alar layer of deep fascia of neck.

**Etiology:**

1. TB of the cervical spine
2. TB lymphadenitis [of retropharyngeal node- which disappears by age of 5]

**Symptoms:**

1. Discomfort in the throat- insidious onset
2. Dysphagia – mild
3. Fever low grade, evening time
4. Swelling in the neck.
5. Cough with expectoration [if pulmonary TB is present]
6. Loss of appetite and weight

**Signs:**

1. Fever, malaise first symptoms
2. Ptyalism- excessive salivation / drooling of saliva
3. Sorethroat
4. Severe odynophagia / dysphagia
5. Torticollis due to spasm of prevertebral muscles.
6. Symptoms and signs of toxemia

**Additional symptoms and signs of each compartment:**

559

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Fig 58-9 b: Ludwig's angina- left side

**Bacteriology:** both aerobes and anaerobes are present.

- Aerobes – streptococcus viridans [41%], staphylococcus aureus [27%], staph albus [21%] H.influenza, E.coli, Pseudomonas.
- Anaerobes- bacteroides.

**Symptoms:**

1. Odynophagia and dysphagia for solids and liquids
2. Inability to open the mouth
3. Fever with chills and rigors
4. Swelling and pain in the submandibular region.
5. Difficulty in breathing.- due to laryngeal oedema
6. Drooling of saliva – due to severe trismus
7. Hoarseness of voice – due to vocal cord oedema

**Signs:**

3. Does not involve salivary glands
4. Does not spread by lymphatics, but by continuity.

**DD:**

1. Angioneurotic oedema
2. Sublingual hematoma
3. Lingual carcinoma

**Treatment:**

1. Hospital admission in intensive surgical care unit.
2. Inj IV Ceftriaxone 1 Gm x 2 x 5 days- for gram positive cocci
3. Inj IV Gentamycin 80 mg x 2x5 days- for gram negative bacilli
4. Inj IV Metronidazole 500 mg x 3 x 5 days- for anaerobes

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5. IV 5% Dextrose and Dextrose saline- for hydration and nutrition
6. Watch for respiratory distress – Tracheostomy SOS
7. Incision and drainage:
  - a) Intra-oral if the abscess is in sublingual space
  - b) Extra oral- if the abscess is in the submaxillary/submental space- transverse incision below the mandible , parallel to mandible is made. Pus may not be found; small quantity of serosanguinous fluid can be drained.

**Premature incision** in an area of cellulitis may actually **worsen the situation** by breaking down the natural defences thus hastening spread of infection.

**Complications:**

1. Mediastinitis- mortality 40% . Patient has increasing dyspnoea, chest pain. Chest X-Ray shows widened mediastinum.
2. Extension to retro and lateral pharyngeal spaces
3. Laryngeal oedema- stridor
4. Septicaemia
5. Aspiration Pneumonia
6. Septicaemia
7. Internal jugular vein thrombosis
8. Carotid artery rupture – mortality 20- 40%. Most cases- internal carotid artery involved.



Fig 58-10 b: Ludwig's angina; Note tracheostomy done for stridor.

**RETROPHARYNGEAL ABSCESS:**

**2 Forms- ACUTE AND CHRONIC ACUTE RETROPHARYNGEAL ABSCESS:**

It is suppuration of retropharyngeal lymph nodes ( Henle's node/ Rouviere node) in children or due to penetrating injuries in adults.

It is common in children below 3 years. Nodes of Rouvier disappear by 5 years age and hence it occurs only in young children..

**Etiology:**

1. Secondary to adenoiditis, sinusitis, rhinitis
2. Petrositis sec to CSOM extends to this space, complication of mastoid abscess
3. Extension from other neck spaces.
4. Penetrating injuries of posterior pharyngeal wall, cervical oesophagus and due to foreign body ingestion (fish bone)
5. Pharyngeal trauma due to intubation, ryle's tube insertion, endoscopy

**Symptoms:**

- Dysphagia – sudden onset and marked; feeding difficulties due to obstruction of food passage.
- Odynophagia
- Sorethroat
- Fever with rigors and chills
- Respiratory distress- Stridor due to obstruction of air passage.
- Cough - croupy type
- Neck pain, stiffness and head tilting to side
- Nose block

**Signs:**

- Patient is toxic and irritable
- "Hot potato voice"
- Inspiratory stridor
- Torticollis- painful and decreased range of motion of neck.
- **Tracheal rock sign- Pain on pressing trachea**
- Bulging in the posterior pharyngeal wall – paramedian, only on one side.
- Palatal bulge
- Laryngoscopy - pooling of saliva in pyriform fossa.
- Cervical lymphadenitis- unilateral and tender nodes



Fig 58-11 a : Ac

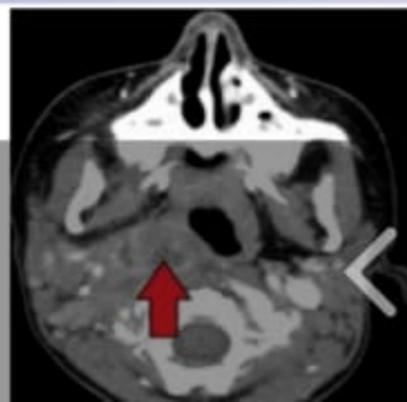
582/727

**Signs of complication**

- Jugular vein thrombosis and tenderness along anterior border of Sternocleidomastoid (SCM)
- Vocal cord palsy- hoarse voice

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- Carotid artery rupture- bleeding from ear, nose or mouth,



11. Arteriogram- if carotid artery / jugular vein involvement

#### Management in general:

1. Top priority is ensuring airway
2. Due to oedema of the tissues, tracheal displacement, trismus, cervical spine rigidity, endotracheal intubation can be very difficult. Tracheostomy is needed urgently for respiratory distress.
3. Maintenance of fluids and electrolyte balance
4. Management of diabetes, if present
5. IV antibiotics- to cover aerobes and anaerobes, drug resistant bacteria.

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...ness- DM in 10%, AIDS in 5% and HIV positive in 5% cases.

#### Etiology:

##### 1. Dental infections:

- most common cause is odontogenic-75-90%, lower second and third molar teeth infection is the common cause;
  - roots of the upper premolars are in the sublingual space and lower molars roots extend to submaxillary space.
2. Submandibular cervical lymphadenitis
  3. Injuries of oral mucosa
  4. Fractures of the mandible.
  5. Dental extraction.
  6. URTI

556

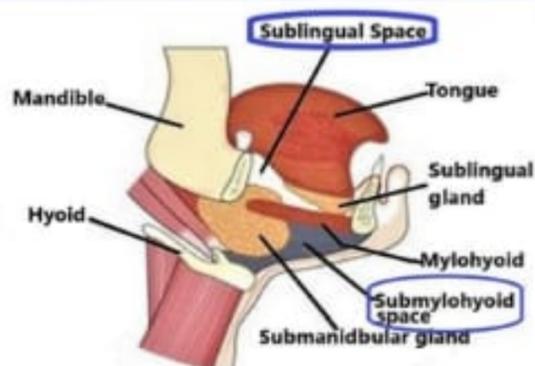


Fig 58-8- Submandibular space



Fig 58-9a: Trismus in Ludwig's angina



Fig 58-9 b: Ludwig's angina- left side

**Bacteriology:** both aerobes and anaerobes are present.

- Aerobes – streptococcus viridans [41%], staphylococcus aureus[ 27%], staph albus [21%] H.influenza, E.coli, Pseudomonas.
- Anaerobes- bacteroides.

#### Symptoms:

1. Odynophagia and dysphagia for solids and liquids
2. Inability to open the mouth
3. Fever with chills and rigors
4. Swelling and pain in the submandibular region.
5. Difficulty in breathing.- due to laryngeal oedema
6. Drooling of saliva – due to severe trismus
7. Hoarseness of voice – due to vocal cord oedema

#### Signs:

5. IV 5% Dextrose and Dextrose saline- for hydration and nutrition
6. Watch for respiratory distress – Tracheostomy SOS
7. Incision and drainage:
  - a) Intra-oral if the abscess is in sublingual space
  - b) Extra oral- if the abscess is in the submaxillary/submental space- transverse incision below the mandible , parallel to mandible is made. Pus may not be found; small quantity of serosanguinous fluid can be drained.

**Premature incision** in an area of cellulitis may actually **worsen the situation** by breaking down the natural defences thus hastening spread of infection.

1. Induration of the area.[ woody hard feel]. Swelling is not fluctuant.
2. Trismus
3. Stridor-due to laryngeal oedema
4. Cyanosis- due to asphyxia
5. Tongue pushed up and backwards- by floor of the mouth oedema
6. Oedema of the floor of the mouth
7. IDL- laryngeal oedema



Fig 58-10a: Ludwig's angina; Note severe trismus

#### Investigations:

##### Blood:

1. Blood- CBP

##### Radiology:

2. X-Ray Neck – AP & lat views
3. CT Scan Head & Neck- plain and contrast- for evidence of extent of abscess and other spaces involvement
4. CT scan of chest, if mediastinum is involved.
5. Ultrasound Neck- safe, portable, no radiation, less traumatic, no sedation needed in children- more useful drainage under ultrasound guidance.

#### Grodynsky and Holyoke's criteria:

There are four criteria described for the diagnosis of Ludwig's angina

1. Bilateral cellulitis and not an abscess
2. Produces gangrene with very little pus
3. Does not involve salivary glands
4. Does not spread by lymphatics, but by continuity.

#### DD:

1. Angioneurotic oedema
2. Sublingual hematoma
3. Lingual carcinoma

#### Treatment:

1. Hospital admission in intensive surgical care unit.
2. Inj IV Ceftriaxone + Metronidazole + Clindamycin + Vancomycin (if positive cocci)
3. Inj IV Gentamycin + Clindamycin (if negative bacilli)
4. Inj IV Metronidazole + Clindamycin (if anaerobes)

581/727

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557

5. IV 5% Dextrose and Dextrose saline- for hydration and nutrition
6. Watch for respiratory distress – Tracheostomy SOS
7. Incision and drainage:
  - a) Intra-oral if the abscess is in sublingual space
  - b) Extra oral- if the abscess is in the submaxillary/submental space- transverse incision below the mandible , parallel to mandible is made. Pus may not be found; small quantity of serosanguinous fluid can be drained.

**Premature incision** in an area of cellulitis may actually **worsen the situation** by breaking down the natural defences thus hastening spread of infection.

#### Etiology:

1. Secondary to adenoiditis, sinusitis, rhinitis
2. Petrositis sec to CSOM extends to this space, complication of mastoid abscess
3. Extension from other neck spaces.
4. Penetrating injuries of posterior pharyngeal wall, cervical oesophagus and due to foreign body ingestion (fish bone)
5. Pharyngeal trauma due to intubation, ryle's tube insertion, endoscopy

#### Symptoms:

- Dysphagia – sudden onset and marked; feeding difficulties due to obstruction of food passage.
- Odynophagia
- Sorethroat

advanced surgical techniques have brought down the complications rate.

#### Challenges in deep neck infections:

- Deep neck spaces are inaccessible and need to cross important neurovascular structures.
- Deep neck spaces are intercommunicative, so easily spread from one space to other, even to outside neck- mediastinum and upto coccyx.
- Deep neck space infections cause thrombosis of great vessels in the neck, affect nerves and bones.
- Difficult to locate the abscesses.

- e) Iatrogenic trauma
- Instrumentation- endoscopy
  - feeding tube insertion
  - endotracheal tube insertion
  - head and neck surgery
  - dental procedures
  - Injections for anaesthetic infiltrations

Additional causes for Pretracheal space infection include,

- Perforation of anterior oesophageal wall by,
- Foreign body oesophagus,
  - Trauma to neck
  - Endoscopic instrumentation

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555

Incidence of different spaces infections is as follows.

1. Peritonsillar infections (49%)
2. Retropharyngeal infections (22%)
3. Submandibular infections (14%)
4. Buccal infections (11%)
5. Parapharyngeal space infections (2%)
  - In children - 73 %.
  - In adults - 7 % cases.

#### Bacteria:

- Aerobes are present in 65% and anaerobes in 35% cases.
- Anaerobes are normal commensal flora. They contain many virulent factors and toxins which are responsible for tissue necrosis. Presence of gas in the abscess visible on X-Ray and putrid odour in the pus are indications of anaerobes.

#### Predisposing factors:

1. Immunodeficiency states due to,
  - a. Chemotherapy for malignancy
  - b. Transplant patients on immunotherapy
  - c. Diabetes mellitus
  - d. HIV

#### Investigations in general:

##### Blood:

1. CBC, clotting profile
2. RBS, RFT

##### Microbiology:

3. Blood cultures
4. Pus from abscess for culture

##### Radiology:

5. X-Ray Neck -lateral view
6. Orthopantomogram-to rule out dental causes.
7. Chest -X-ray for mediastinum, lungs
8. **CT scan with contrast- is the gold standard** – it suggests location, boundaries, loculations and closeness to important nerves and vessels of the neck.
9. **MRI not much useful**
10. Ultrasound- useful as a guide for fine needle aspiration – FNAC
11. Arteriogram- if carotid artery / jugular vein involvement

#### Management in general:

1. Top priority is ensuring airway
2. Due to oedema of the tissues, tracheal displacement, trismus, cervical spine rigidity, endotracheal intubation can be very difficult. Tracheostomy is needed urgently for respiratory distress.
3. Maintenance of fluids and electrolyte balance
4. Management of diabetes, if present
5. IV antibiotics- to cover aerobes and anaerobes, drug resistant bacteria.

6. Incision and drainage – is standard dictum.
7. Needle aspiration

**Antibiotic therapy in general: is based on the source of infection and immune status.**

#### 1. Oral or odontogenic source

- a) I V Amoxicillin +clavulanic acid-1.2G BD or TID
- b) I V Metronidazole-500 mg -TID
- c) I V Clindamycin 600mg -TID

#### 2. Rhinogenic or Otogenic source

- a) I V Ceftriaxone 1 G, OD/ BD
- b) I V Metronidazole
- c) I V Ciprofloxacin 400mg -BD
- d) I V Clindamycin

#### 3. Immunocompromised state:

- a) IV Cefepime-2 G -BD
- b) I V Metronidazole
- c) I V Imipenam 500 mg -QID
- d) I V Meropenem 1 G / QID

#### LUDWIG'S ANGINA: [ Wilhelm von Ludwig 1836]

Ludwig's angina refers to bilateral submandibular space infection.

- It is a serious ,rapidly progressive, life threatening ENT emergency due to bacterial infection of the submandibular space, bilaterally.
- It is named after German physician- Von Ludwig. It is an acute severe diffuse cellulitis which rapidly spreads and does not produce frank pus.
- It easily spreads to lateral and retropharyngeal spaces thus encircling the airway, needing emergency tracheostomy.
- Early diagnosis and emergency treatment planning are essential to save the lives of patients.
- Before the antibiotic era, the mortality was 50%, now it is reduced markedly to 5 %. Nearly 33% cases have associated systemic illness- DM in 18% , AIDS in 9% and HIV positive in 5% cases.

#### Etiology:

##### 1. Dental infections:

- most common cause is odontogenic-75-90%, lower second and third molar teeth infection is the common cause;
- roots of the upper premolars are in the sublingual space and lower molars roots extend to submaxillary space.

##### 2. Submandibular cervicofacial abscess

##### 3. Injuries of oral mucosa

##### 4. Fractures of the mandible

##### 5. Dental extraction

##### 6. URTI

580/727

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556

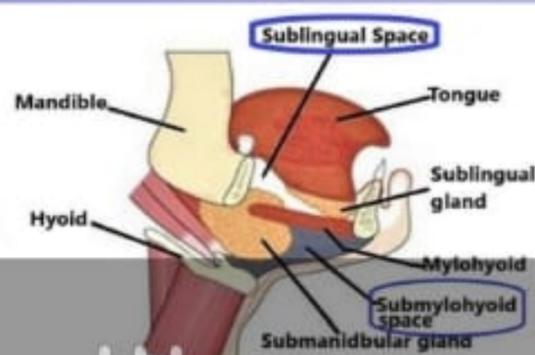
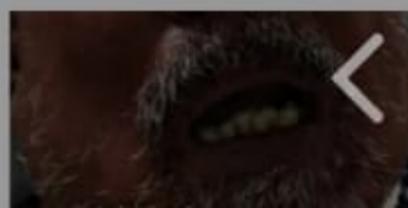


Fig 58-8- Submandibular space

1. Induration of the area.[ woody hard feel]. Swelling is not fluctuant.
2. Trismus
3. Stridor-due to laryngeal oedema
4. Cyanosis- due to asphyxia
5. Tongue pushed up and backwards- by floor of the mouth oedema
6. Oedema of the floor of the mouth
7. IDL- laryngeal oedema



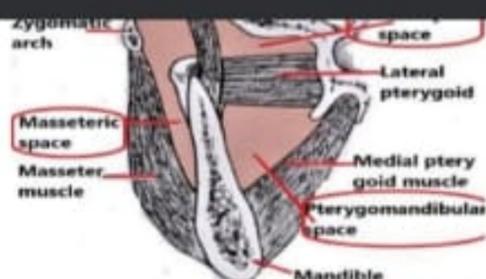


Fig 58-7: Masticator space

It is divided into 3 spaces

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of the mandible and the deep fasciae.

**Boundaries:**

Anterior: Anterior belly of digastric.  
Posterior: Internal pterygoid muscle

**SUBMANDIBULAR SPACE:**

It lies between the mucosa of the floor of the mouth above and the deep cervical fascia which extends between the hyoid bone and mandible below.

➤ It is divided into 2 compartments by the mylohyoid muscle-

554

- Sublingual space above the muscle
- Submylohyoid and Submental space below the muscle.

Submental space contains- sublingual salivary gland, hypoglossal nerve and Wharton duct

**CAROTID SPACE:**

It is a paired, tubular space lying on either side of the neck within the carotid sheath. It extends from skull base to root of the neck. It is true space only below the level of carotid bifurcation.

In the suprahyoid portion of the neck, it is part of Post styloid compartment of parapharyngeal space.

It is formed by all the three layers of deep cervical fascia.

**Boundaries:**

Medial: visceral space.

Anterolateral: Sternocleidomastoid muscle.

Posterior: Prevertebral space.

**Contents:**

It contains carotid artery, internal jugular vein, vagus (10<sup>th</sup> CN). Ansa cervicalis lies embedded in the anterior portion of the carotid sheath. Cervical sympathetic plexus lies embedded in the posterior portion of the carotid sheath.

Superiorly, the space contains 9<sup>th</sup>, 10<sup>th</sup>, 11<sup>th</sup> and the 12<sup>th</sup> cranial nerves and cervical sympathetic plexus. Within the carotid space, carotid artery is medial, IJV

Internal Jugular vein is lateral and Vagus nerve is posterior to both the vessels.

It is resistant to spread of infection longitudinally due to scanty areolar tissue, yet the infection spreads from above downwards to mediastinum and hence called- Lincoln's Highway.

**PRETRACHEAL SPACE**

It lies between trachea and the visceral layer of deep cervical fascia.

**Boundaries:**

- It extends from the hyoid bone to the upper border of aortic arch and fibrous pericardium in superior mediastinum. It is limited superiorly by the attachments of the infrahyoid muscles to the thyroid cartilage and the hyoid bone.

**Contents:**

- It contains larynx, trachea, cervical oesophagus, Recurrent laryngeal nerves, part of sympathetic trunk, thyroid gland, parathyroid glands and delphian node.
- Attachment of oesophagus laterally to prevertebral fascia separates the Pretracheal space from Retrovisceral space. Hence Pretracheal space lies anterior to oesophagus and Retropharyngeal space lies posterior to it.

**DEEP NECK SPACE INFECTIONS:**

Deep neck space infections most commonly arise from a septic focus of the mandibular teeth, deep cervical nodes, parotid glands, tonsils, middle ear or paranasal sinuses.

These infections often have rapid onset and can progress to life threatening complications.

Single space infection incidence is 63% and multi space is 37%.

In the earlier days, mortality and morbidity were very high.

Now modern antibiotics, diagnostic tools like CT scan, MRI, availability of intensive care and advanced surgical techniques have brought down the complications rate.

**Challenges in deep neck infections:**

- Deep neck spaces are inaccessible and need to cross important neurovascular structures.
- Deep neck spaces are intercommunicative, so easily spread from one space to other, even to outside neck- mediastinum and upto coccyx.
- Deep neck space infections cause thrombosis of great vessels in the neck, affect nerves and bones.
- Difficult to locate the abscesses.

**Etiology:**

- Idiopathic in 20-50% cases.
- Teeth and tonsils are two important sources of infection -dental infections, tonsillitis post tonsillectomy
- Spread from one space to the other, from mastoiditis/ petrositis.
- Trauma
  - penetrating trauma
  - injury to oral mucosa
  - fracture mandible
  - Foreign body pharynx
  - Iatrogenic trauma
    - Instrumentation- endoscopy
    - feeding tube insertion
    - endotracheal tube insertion
    - head and neck surgery
    - dental procedures
    - Injections for anaesthetic infiltrations

Additional causes for Pretracheal space infection include,

Perforation of anterior oesophageal wall by,

- Foreign body oesophagus,
- Trauma to neck
- Endoscopic in-

579/727

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555

Incidence of different spaces infections is as follows.

- Peritonsillar infections (49%)
- Retropharyngeal infections (22%)
- Submandibular infections (14%)
- Buccal infections (11%)
- Parapharyngeal space infections (2%)
  - In children - 73 %.
  - In adults -7 % cases.

**Bacteria:**

- Aerobes are present in 65% and anaerobes in 35% cases.
- Anaerobes are normal commensal flora. They contain many virulent factors and toxins which are responsible for tissue necrosis. Presence of gas in the abscess visible on X-Ray and putrid odour in the pus are indications of anaerobes.

- Incision and drainage - is standard dictum.
- Needle aspiration

Antibiotic therapy in general: is based on the source of infection and immune status.

**1. Oral or odontogenic source**

- I V Amoxicillin +clavulanic acid-1.2G BD or TID
- I V Metronidazole-500 mg -TID
- I V Clindamycin 600mg -TID

**2. Rhinogenic or Orogenic source**

- I V Ceftriaxone 1 G, OD/ BD
- I V Metronidazole
- I V Ciprofloxacin 400mg -BD
- I V Clindamycin

**Immunocompromised state:**

- IV Cefepime-2 G -BD
- I V Metronidazole
- I V Imipenam 500 mg -QID



**Fig 58-5:** Retropharyngeal space, Danger space, Prevertebral space. (Courtesy Dr Simon, Asso Prof, SUMS, South Wales, UK)

This space infection can spread to mediastinum.

#### PREVERTEBRAL SPACE:

It lies between the vertebral bodies with longus colli muscles posteriorly and prevertebral fascia anteriorly.

It extends from the skull base to insertion of psoas muscles to lumbar spine / coccyx.

It contains prevertebral muscles. Infections in this space occur by hematogenous spread, injury to trachea or oesophagus, osteomyelitis of vertebrae and Discitis.

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553

Dense fibrous attachments between the prevertebral fascia and the deep cervical muscles limit the prevertebral space infections.

#### DANGER SPACE [ALAR SPACE]:

The Danger space is between the retropharyngeal space and prevertebral space, between the alar and prevertebral fascia.

It extends from the skull base through the posterior mediastinum upto diaphragm beyond the level of true RPS.

It is dangerous because it extends upto diaphragm and infection of this space leads to mediastinitis, purulent pericarditis and cardiac tamponade - potentially fatal diseases.

Laterally, it is limited by the fusion of the alar and prevertebral fascia.

#### BUCCAL SPACE

It is the space between the skin and the buccinator muscle.

##### Boundaries:

- Anterior- corner of the mouth
- Posterior- masseter muscle, pterygomandibular raphe
- Superior- Maxilla, infraorbital space
- Inferior- Lower border of mandible

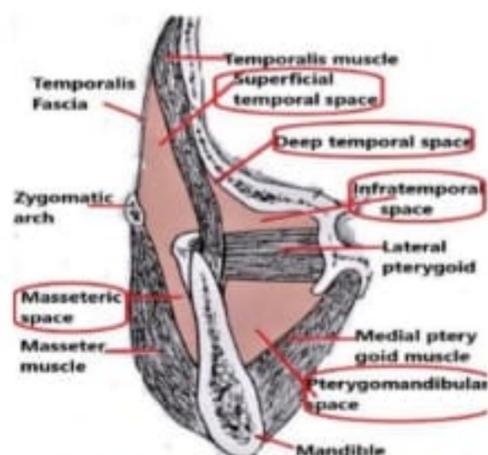
##### Contents:

- Buccal pad of fat
- Stenson's duct
- Facial artery and vein

#### MASTICATOR SPACE:

It is the space between the superficial cervical fascia covering temporalis and masseter muscles laterally and medial and lateral pterygoid muscles medially.

- It extends from skull base to lower border of mandible.
- It communicates with parotid space and parapharyngeal space



**Fig 58-7:** Masticator space  
It is divided into 3 spaces

1. Masseteric space.
2. Temporal space- subdivided into superficial temporal, deep temporal and infratemporal spaces.
3. Pterygomandibular space.

##### Contents:

- Masseter and temporalis muscle
- Medial and lateral pterygoid muscles
- Maxillary artery and its inferior alveolar branch
- Inferior alveolar nerve
- Ramus of mandible

#### PERITONSILLAR SPACE:

It is between the tonsils and the superior constrictor muscle.

#### PAROTID SPACE

Superficial layer of deep cervical fascia divides into two laminae to cover the parotid glands. The fascia is inseparable from the parotid gland as it is attached by septae. Due to this, the gland can not be shelled out with clear fascial boundaries.

##### Boundaries:

- Superior – attached to mastoid process and external auditory canal.
- Inferior – inferior mandibular margin
- Anterior- Masticator space
- Medial – it is incomplete and the space continues with parapharyngeal space.

Fascial layer is very thick superficially. It is thin or deficient on deep side in many people.

##### Contents:

- a) Parotid glands
- b) Parotid lymph nodes
- c) Facial nerve
- d) External carotid artery – part
- e) Auriculotemporal nerve
- f) Superficial temporal artery
- g) Retromandibular vein.

#### SPACE OF THE BODY OF THE MANDIBLE:

The superficial layer of DCF divides into two layers at the lower border of the mandible, the outer layer is attached to outer cortex and the inner layer is attached to mylohyoid line on the mandible.

This is a potential space between the lingual cortex of the mandible and the deep fascia.

##### Boundaries:

Anterior: Anterior belly of digastric.  
Posterior: Internal pterygoid muscle

#### SUBMANDIBULAR SPACE:

It lies between the mucosa of the floor of the mouth above and the deep cervical fascia below. It is bounded anteriorly by the hyoid bone and posteriorly by the mylohyoid muscle.

- It is divided into sublingual and submylohyoid spaces.

578/727

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554

- a) Sublingual space above the muscle
- b) Submylohyoid and Submental space below the muscle.

Submental space contains- sublingual salivary gland, hypoglossal nerve and Wharton duct

#### CAROTID SPACE:

It is a paired, tubular space lying on either side of the neck within the carotid sheath. It extends from skull base to root of the neck. It is true space only below the level of carotid bifurcation.

In the suprahyoid portion of the neck, it is part of Post styloid compartment of parapharyngeal space. It is formed by all the three layers of deep cervical fascia.

##### Boundaries:

Medial: visceral space.

Internal Jugular vein is lateral and Vagus nerve is posterior to both the vessels.

It is resistant to spread of infection longitudinally due to scanty areolar tissue, yet the infection spreads from above downwards to mediastinum and hence called- Lincoln's Highway.

#### PRETRACHEAL SPACE

It lies between trachea and the visceral layer of deep cervical fascia.

##### Boundaries:

- It extends from the hyoid bone to the upper border of aortic arch and fibrous pericardium in superior mediastinum. It is limited superiorly by the attachments of the infrahyoid muscles to the thyroid cartilage and the hyoid bone.

##### Contents:



**PARAPHARYNGEAL SPACE ( PPS):[ Also called Lateral pharyngeal space (LPS ) or Pterygomaxillary space or Pharyngomaxillary space]**

It is pyramidal in shape, a potential space between the pharynx medially, mandible/ parotid gland/ medial pterygoid muscle laterally and prevertebral fascia posteriorly; extending from skull base above to the hyoid bone below.

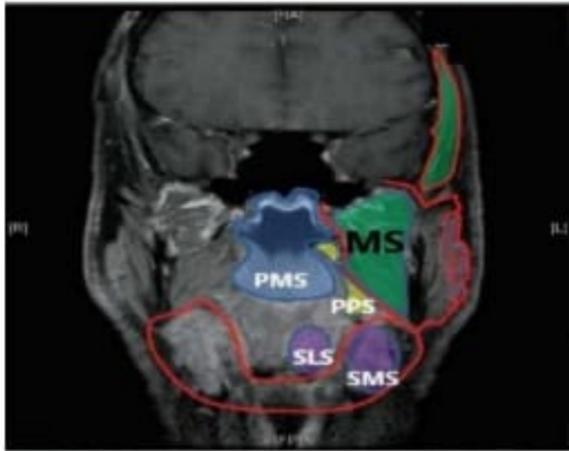
It is divided into 2 compartments by the styloid process and the stylohyoid ligament- **pre styloid and post styloid.**

1. **Pre-styloid compartment** lies between the lateral pharyngeal wall and the parotid gland. It contains maxillary artery, lymph nodes and fat.
2. **Post styloid compartment** lies between the lateral pharyngeal wall and the parotid gland. It contains common/ internal carotid artery, internal jugular vein, cervical sympathetic plexus and 9, 10, 11 and 12 cranial nerves.

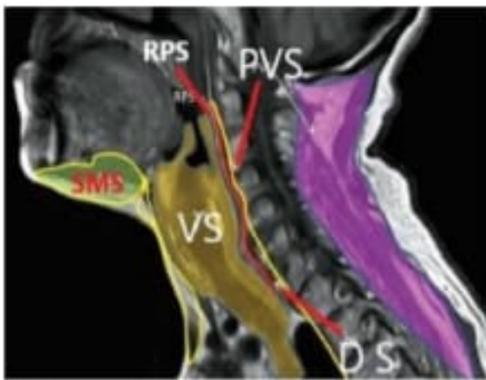
PPS communicates with other spaces-

- a) retropharyngeal space
- b) submandibular space
- c) parotid space
- d) carotid space
- e) visceral spaces

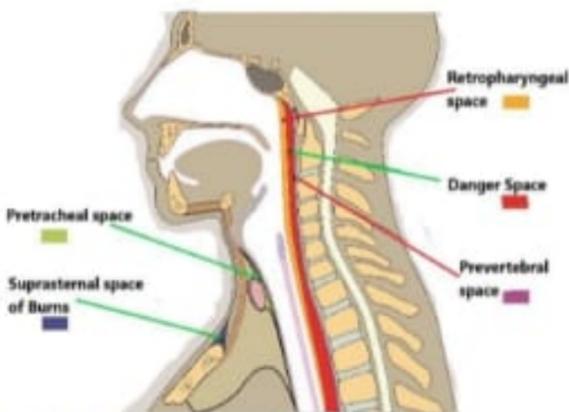
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**Fig 58-3:** MRI Head and Neck-coronal section showing suprahyoid fascial spaces; SLS-Sublingual space( **medial purple**) SMS-Submandibular space (**lateral purple**); (Courtesy: [www.entokey.com](http://www.entokey.com))

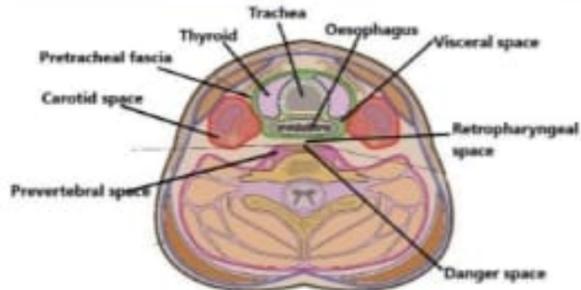


**Fig 58-4:** MRI head and neck-Sagittal section showing infra hyoid neck spaces: Note RPS ends at T3 level. DS -Danger space continues down to mediastinum.



**Fig 58-5:** Retropharyngeal space, Danger space, Prevertebral space.(Courtesy Dr Simon, Asso Prof, SUMS, South Wales, UK)

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**Fig 58-6:** Deep neck spaces.(Courtesy Dr Simon, Asso Prof, Swansea UMS, South Wales, UK)

**RETROPHARYNGEAL SPACE ( R P S) [also called SPACE OF GILLETTE]:**

It is anterior to prevertebral muscles and immediately posterior to pharynx, oesophagus, larynx and trachea.

It is bound anteriorly by buccopharyngeal fascia, laterally by the carotid sheath and posteriorly by the alar fascia and prevertebral fascia.

It has **two components**- suprahyoid and infrahyoid. Suprahyoid part has lymph nodes and fat and infrahyoid part has only fat.

It is **divided into two spaces** by alar fascia –

- a. "True retropharyngeal space" anteriorly- and
- b. " Danger space (alar space)" behind.

"True retropharyngeal space" extends from the skull base to the mediastinum till bifurcation of trachea-T2 vertebral level. Though it is named "retropharyngeal" it is to be noted that this space lies behind oesophagus also- upto T2 vertebral level, sometimes upto T6 vertebral level.

This space is divided into two lateral compartments (Spaces of Gillette) by a midline fibrous raphe. Each lateral compartment contains a chain of retropharyngeal nodes (Nodes of Rouvier) which disappear at 3-4 years age. These nodes drain the adenoids, posterior ethmoid sinuses, nasopharynx and posterior part of nasal cavities.

This space infection can spread to mediastinum.

**PREVERTEBRAL SPACE:**

It lies between the vertebral bodies with longus colli muscles posteriorly and prevertebral fascia anteriorly.

It extends from the skull base to insertion of psoas muscles to lumbar spine / coccvx.

It contains prevertebral space occur by the trachea or oesophagus and Discitis.

577/727

Dense fibrous attachments between the prevertebral fascia and the deep cervical muscles limit the prevertebral space infections.

**DANGER SPACE [ALAR SPACE]:**

The Danger space is between the retropharyngeal space and prevertebral space, between the alar and prevertebral fascia.

It extends from the skull base through the posterior mediastinum upto diaphragm beyond the level of true RPS.

It is dangerous because it extends upto diaphragm and infection of this space leads to mediastinitis, purulent pericarditis and cardiac tamponade - potentially fatal diseases.

Laterally, it is limited by the fusion of the alar and

1. Masseteric space.
2. Temporal space- subdivided into superficial temporal, deep temporal and infratemporal spaces.
3. Pterygomandibular space.

**Contents:**

- Masseter and temporalis muscle
- Medial and lateral pterygoid muscles
- Maxillary artery and its inferior alveolar branch
- Inferior alveolar nerve
- Ramus of mandible

**PERITONSILLAR SPACE:**

It is between the tonsils and the superior constrictor muscle.



- The **superficial investing layer** covers the muscles- SCM, trapezius, strap muscles of neck and two glands- parotid and submandibular salivary glands and encloses two spaces- supraclavicular space and suprasternal space of BURNS.

**Investing layer** is like a tube in the neck, attached above- to skull, anteriorly to the hyoid bone, below to the clavicle and sternum, posteriorly to ligamentum nuchae.

- The middle **layer** has two divisions- muscular layer and visceral layer. It is attached above to the hyoid, below to the pericardium.

**Visceral layer has three parts-**

- Buccopharyngeal fascia
- Pretracheal fascia
- Retropharyngeal fascia

Visceral layer covers thyroid gland, pharynx, larynx, oesophagus and trachea.

- The **deep layer splits into 2 layers- prevertebral and alar layers.**

head and neck region.

Hence, the head and neck space infections can be dangerous and fatal.

### CLINICAL IMPORTANCE OF DEEP NECK SPACES:

- They cover vital neurovascular structures, airway and food passages, thyroid and parathyroid glands and infections in these spaces can lead to fatal complications- Jugular vein thrombosis, airway obstruction and asphyxia, mediastinitis, pericarditis, septic shock and lung abscess.
- Understanding the anatomy of these spaces and their interconnections help in predicting tumour spread and planning surgical approach.
- CT scan and MRI Neck are crucial in delineation of disease extension within neck spaces.

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551

### CLASSIFICATION OF DEEP NECK SPACES:

Deep neck spaces are divided in relation to the hyoid- into three groups viz, Supra hyoid, Infra hyoid and Along entire length of neck.

#### 1. Entire length of neck spaces:

- Retropharyngeal space
- Danger space- between alar fascia and prevertebral fascia- extends from skull base to diaphragm.
- Prevertebral space
- Carotid sheath space [ Lincoln's highway]

#### 2. Suprahyoid spaces:

- Submandibular space- divided into-submental, sublingual and submylohyoid space.
- Parapharyngeal space- Prestyloid and post styloid compartments
- Peritonsillar space
- Masticator space- contains 5 spaces ( see fig 58-7 below)
- Parotid space
- Buccal space

#### 3. Infrahyoid spaces:

- Visceral space
- Suprasternal space of Burns

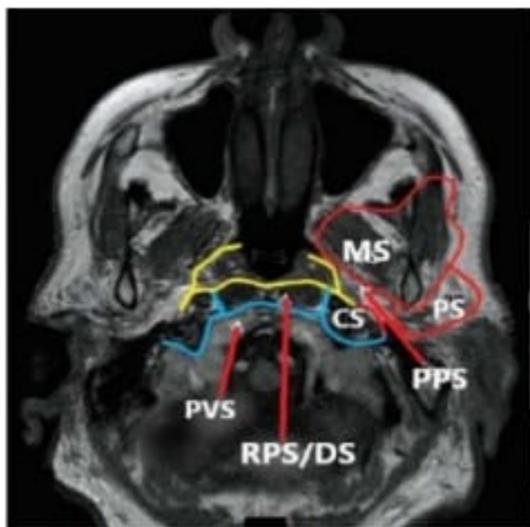


Fig 58-1a : MRI Neck-axial section-at nasopharynx level- (Courtesy: [www.entokey.com](http://www.entokey.com))

### PARAPHARYNGEAL SPACE ( PPS):[ Also called Lateral pharyngeal space ( LPS ) or Pterygomaxillary space or Pharyngomaxillary space]

It is pyramidal in shape, a potential space between the pharynx medially, mandible/ parotid gland/ medial pterygoid muscle laterally and prevertebral fascia posteriorly; extending from skull base above to the hyoid bone below.

It is divided into 2 compartments by the styloid process and the stylohyoid ligament- **pre styloid and post styloid.**

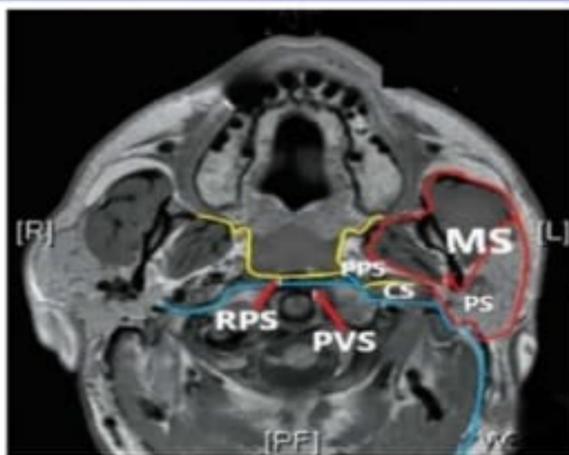


Fig 58-1b : MRI Neck -axial section-at oropharynx level ; 3 layers of Deep cervical fascia (DCF)- Red-superficial ;Yellow-middle ;Blue-deep. MS-masticator space;PS-Parotid space;PMS-Pharyngeal mucosa space; CS- Carotid space; PPS-Parapharyngeal space; RPS- Retropharyngeal space; DS-Danger space; PVS-Prevertebral space.

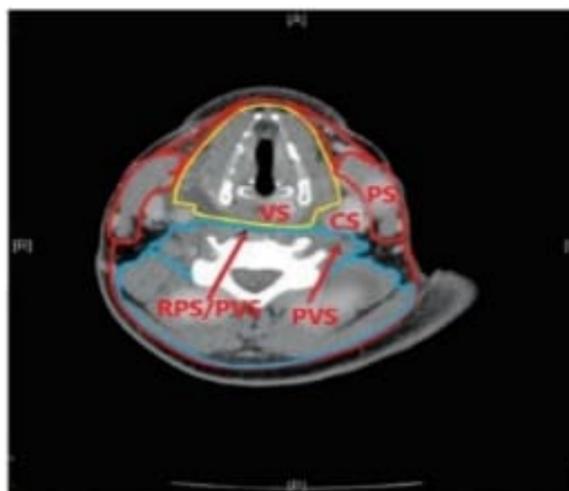


Fig 58-2: MRI Neck-axial section of infrahyoid spaces; 3 layers of DCF- colour code as above; VS-Visceral space. (Courtesy: [www.entokey.com](http://www.entokey.com))

- Prestyloid compartment** is related medially to tonsils and laterally to medial pterygoid muscle and this contains maxillary artery, lymph nodes and fat.
- Post styloid compartment** lies between the lateral pharyngeal wall and the parotid gland. It contains common internal jugular vein, internal jugular plexus and 9, 10, 11, 12 cranial nerves. PPS communicates with:
  - retropharyngeal space
  - submandibular space
  - parotid space
  - carotid space
  - visceral spaces

576/727

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552

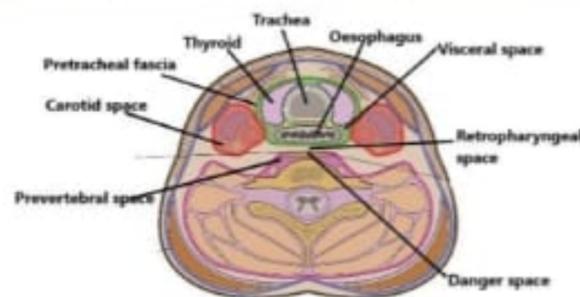
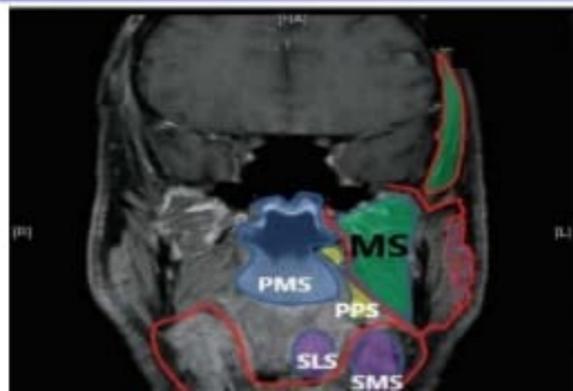


Fig 58-6: Deep neck spaces.(Courtesy Dr Simon, Assoc Prof, Guyana LIME, South Wales, UK)

**CLASSIFICATION OF DEEP NECK SPACES:**

Deep neck spaces are divided in relation to the hyoid-into three groups viz, Supra hyoid, Infra hyoid and Along entire length of neck.

**1. Entire length of neck spaces:**

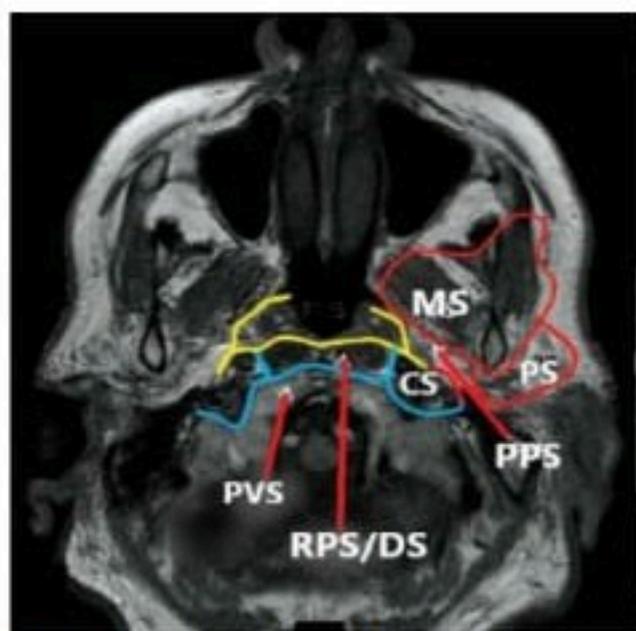
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- Buccal space

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- Visceral space
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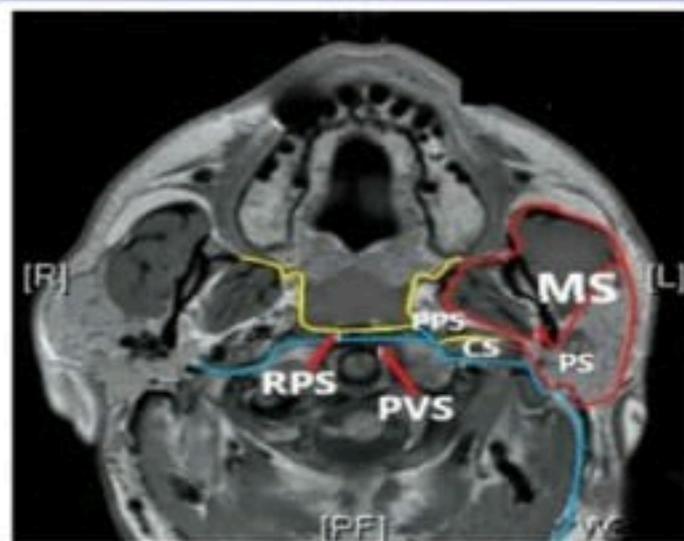


**Fig 58-1a** : MRI Neck-axial section-at nasopharynx level- (Courtesy: [www.entokey.com](http://www.entokey.com))

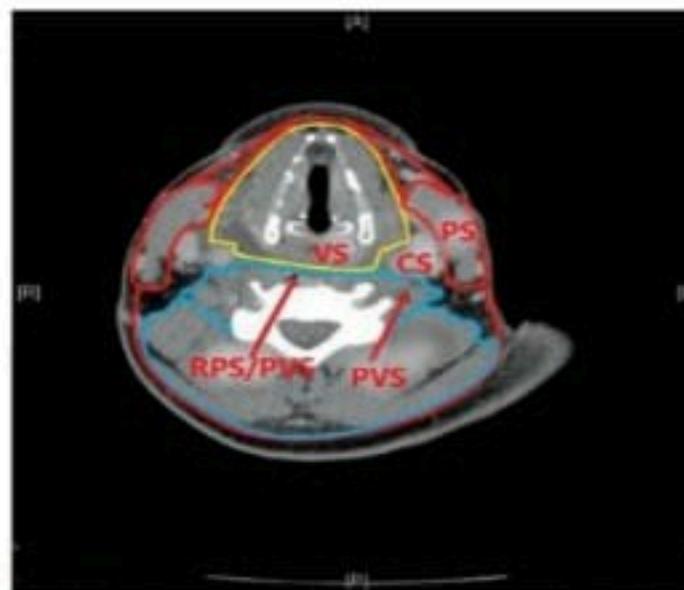
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- PPS communicates with
- retropharyngeal space
  - submandibular space
  - parotid space
  - carotid space
  - visceral spaces

576/727



Hence pituitary lesions are easily approachable by nasal endoscope. It has four foramina – optic, rotundum, ovale and spinosum.

**Temporal bone** - has four parts- squamous, petrous, mastoid and tympanic. Squamous part forms roof of EAC. Petrous part forms roof of middle ear, anteriorly it has canal for tensor tympani and eustachian tube, and foramina for greater and lesser superficial petrosal nerves, posteriorly it has internal auditory canal, sulci for sigmoid

vestibulocochlear nerves, labyrinthine artery  
Jugular foramen- glossopharyngeal, vagus, accessory nerves, jugular bulb, inferior petrosal and sigmoid sinuses.  
Hypoglossal canal- hypoglossal nerve  
Foramen magnum- vertebral arteries, spinal accessory nerve, medulla and meninges, anterior and posterior spinal arteries

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550

#### ACUTE ABSCESSSES IN RELATION TO PHARYNX:

- Peritonsillar abscess
- Lateral pharyngeal abscess
- Acute Retropharyngeal abscess
- Ludwig's angina
- Parotid space abscess
- Masticator space abscess

#### CHRONIC ABSCESS IN RELATION TO PHARYNX

- Chronic retropharyngeal abscess  
( Also called Prevertebral abscess)

#### ANATOMY OF HEAD & NECK SPACES:

##### Definition:

The fascial spaces in head and neck are potential spaces between different layers of deep fascia, filled with connective tissue and bound by anatomical barriers -bone, muscle or fascial layers.( Moore-1975)

##### Applied anatomy: Fascial compartments of the neck:

Neck spaces lie between the layers of cervical fascia.  
➤ Cervical fascia is in two layers- superficial ( Colle's fascia) and deep layer.

1. **Superficial fascia** covers platysma and muscles of facial expression.

Infections in this space are drained with an incision in langer's lines.

2. **Deep fascia** is subdivided into -3 layers- superficial, middle and deep.

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**Prevertebral layer** lies immediately adjacent to the vertebral bodies and covers deep muscles of the neck.

It is attached above to the skull base, below to the fascia of the thoracic rib cage, anteriorly to the vertebral bodies and posteriorly to the ligamentum nuchae.

**Alar layer** is anterior to prevertebral layer.

- Prevertebral space extends along the entire length of the spine upto coccyx.
- Alar space extends upto diaphragm.

**All three layers contribute to carotid sheath.**

- Carotid sheath space contains carotid artery, internal jugular vein, vagus nerve and sympathetic plexus. It is called **Lincoln's Highway** as the infection spread fast along this sheath.

These spaces communicate even across the midline and through which infections easily spread in the head and neck region.

Hence, the head and neck space infections can be dangerous and fatal.

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575/727

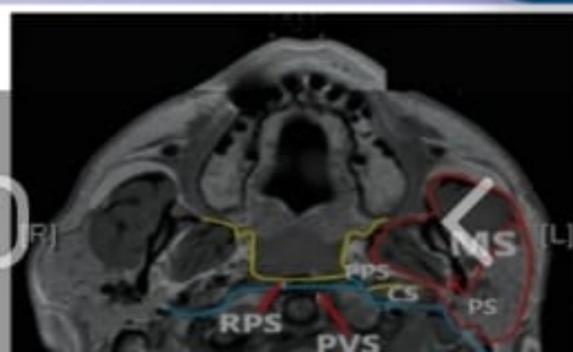
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- Understanding their interconnections helps in diagnosis, spread and planning of treatment.
- CT scan and MRI Neck are crucial in delineation of disease extension within neck spaces.

575/727

**1. NECK MASSES**  
**2. NECK LYMPH NODES**  
**3. NECK TRAUMA**

**Core competency**

**EN 2.7:** Demonstrate the correct technique of examination of neck including elicitation of laryngeal crepitus.

**EN 4.31:** Describe the clinical features, investigations and principles of management of trauma to the neck

**CLASSIFICATION OF NECK MASSES**

**CLASSIFICATION BASED ON SITE OF LESION**

Neck masses are divided into 1. Midline masses 2. Lateral masses

**MIDLINE NECK MASSES:**

1. Submental lymph node
2. Delphian node
3. Dermoid cyst
4. Ludwig's angina
5. Thyroglossal duct cyst
6. Thymic cyst
7. Subhyoid bursitis
8. Aberrant thyroid
9. Delphian node enlargement
10. Laryngeal malignancy
11. Suprasternal dermoid
12. Suprasternal lymphadenopathy

**LATERAL NECK MASSES**

**A. Anterior triangle**

1. Submandibular sialadenitis and tumours
2. Submandibular lymphadenopathy
  - a. Inflammatory - epidermoid cyst
  - b. Neoplastic
  - c. Metastatic - lymphadenopathy
3. Plunging ranula
4. Cervical lymphadenopathy /lymphadenitis
  - a. Nonspecific
  - b. Tubercular
  - c. Non-tubercular -mycobacterial
5. Branchial cyst
6. Thyroid tumours/ goitre
7. Carotid body tumour
8. Parotid tail tumour
9. Parapharyngeal tumour / abscess
10. Laryngocoele
11. Pharyngeal pouch
12. Sternomastoid tumour

**B. Supraclavicular triangle**

1. Metastatic nodes from Breast, Lungs, GI tract, Kidney, Ovary / Testis
2. Cystic hygroma
3. Subclavian aneurysm

4. Cervical rib

**C. Occipital triangle**

1. Lymphadenopathy
  - a. Inflammatory
  - b. Neoplastic
  - c. Metastatic
2. Epidermoid cysts

**CLASSIFICATION OF NECK MASSES BASED ON ETIOLOGY: ( I N C- Remember- Indian national congress)**

**Inflammatory**

1. Lymphadenopathy / lymphadenitis- bacterial / viral / fungal
2. Tuberculosis
3. Sarcoidosis
4. Sialadenitis

**Neoplastic-**

1. Primary -epidermoid carcinoma/melanoma
2. Secondary- primary in upper aero digestive tract
3. Thyroid /salivary gland/ carotid body tumours
4. Lymphoma/ angioma
5. Lipoma – most common benign lesion
6. Sarcoma

**Congenital -**

1. Branchial cysts
2. Thyroglossal cysts
3. Dermoid cysts
4. Thymic cysts
5. Haemangioma/ lymphangioma
6. Sebaceous cysts

**SUBMENTAL NODES / DELPHIAN NODES:**

These nodes are enlarged either due to inflammation or malignancy.

**SUBMENTAL NODES**

There are 2-8 nodes between the platysma and the mylohyoid muscle in the submental triangle. Lymphatics from chin, lower lip, anterior floor of mouth and

594/727

malignancy has to be ruled out in these areas, if these nodes are enlarged.

It may be rarely involved in cases of papillary carcinoma of thyroid isthmus with aggressive tumour biology.

**DELPHIAN NODE,**

Also called Prelaryngeal node. It was first described in 1948 and is named after " Oracle of Delphi" as It foretells the prognosis of thyroid cancer or laryngeal cancer due to which there is metastasis in this node.

- Delphian node ( DN) gets involved in vocal cord growths extending to anterior commissure.
- DN involved with thyroid cancer, is predictive of aggressive tumour biology and can lead to persistent or recurrent disease with extension to

Dermoid cyst is also seen in the midline above the suprasternal notch. Treatment is surgical excision under general anaesthesia.

**THYROGLOSSAL CYST:**

This is **most common congenital midline cystic anomalous neck mass** with 7% prevalence but only a few develop symptoms.

- **Carcinoma can develop** in the cyst in less than 1% cases, of which 93% are papillary type carcinoma.
- It may **contain only functioning thyroid gland**. Hence thyroid scan has to be done before the excision to rule out presence of normal thyroid tissue elsewhere.

**Incidence:**

- Both men and women are equally affected.

3. Neurofibroma of vagus nerve

**Treatment:**

1. **Surgical excision** is indicated in fit patients and those below 50 years:

**Indications:**

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576



**Fig 59-10:** Lipoma neck  
( Courtesy: [www.entokey.com](http://www.entokey.com))

**PARAPHARYNGEAL TUMOURS:**

These tumours may appear in the upper neck below the angle of the mandible and retromandibular region.

It may be seen intraorally displacing the tonsils, lateral pharyngeal wall and soft palate medially.

The common tumours are pleomorphic adenoma, others are schwannoma, neurofibroma, lipoma, hemangioma, paraganglioma and lymph node metastasis.

**Diagnosis:**

1. FNAC,
2. Biopsy,
3. CT Scan and
4. MRI Neck.

Refer to chapter 41 for more details.

**CYSTIC HYGROMA: Syn: lymphangioma (Wernher-1843)**

Hygroma is a Greek word meaning water containing tumour.

It is a benign tumour, composed of large cysts.

**Incidence:**

It is common in the neonate, early infancy and childhood. Incidence is around 1 in 6000 to 16,000 live births. No racial predominance. Occurs equally in both sexes, 50-65% occur at birth.

90% occur below 2 years.

**Etiology:** it is said to be due to one or more of the following factors.

1. It arises from obstruction of the part of the jugular lymph sac, which is sequestered from the lymphatic system during embryonic development.
2. 50% cases have chromosomal anomalies.
3. Lymphatics fail to communicate with venous system.
4. Abnormal budding of the lymphatic tissue

It is often associated with Noonan, Turner, Klinefelter, Down syndromes, Trisomy 13 and 18 anomalies and intrauterine alcohol exposure

- It appears in the supraclavicular region and extends to posterior triangle and axilla
- It may occur in the tongue and floor of the mouth.
- It involves several tissue planes, neural and vascular structures.
- It may extend to involve laryngeal or pharyngeal structures.
- It sometimes regresses spontaneously.
- It can present as OSAS- obstructive sleep apnoea syndrome- due to mass pressing on the supraglottis or paraglottic region.

**Classification based on type:**

1. Capillary
2. Cavernous
3. Cystic

**Classification based on size:**

1. Microcystic – cysts < 2 cms size
2. Macrocystic- cysts > 2 cms size
3. Mixed – cysts are of variable sizes

**Symptoms:**

- Stridor,
- feeding difficulty,
- pain and increase in size occurs if it gets infected.
- Causes difficult labour due to neck mass.

**Signs:**

- cystic, multilocular mass
- soft, spongy lump in the neck
- partially compressible and
- brilliantly translucent mass.

**Investigation:**

**Radiology:**

1. Intrauterine USG at 10<sup>th</sup> week can reveal cystic hygroma
2. Plain X-Ray Neck- shows airway compromise
3. CT scan neck- faster, but risk of high radiation. Ring like margin enhancement with sharp demarcation of cystic areas is revealed.
4. MRI neck – is the investigation of choice ; done to know the extent of the lesion
5. Fast spin MRI intrauterine – shows extent of the mass
6. USG neck -a safe and non- invasive investigation.

**Other:**

7. Alpha fetoprotein levels in amniotic fluid are elevated in pregnant woman with cystic hygroma foetus.

**Treatment:**

1. If infected- start I V antibiotics. Surgical excision done 3 months after infection is controlled.
2. Sclerosant

601/727

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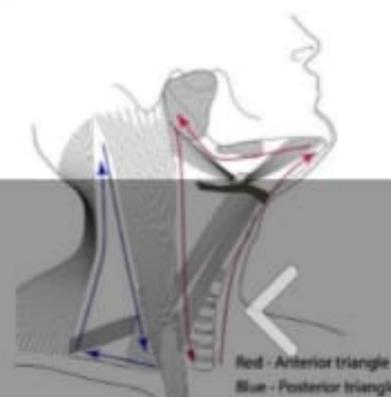
577

- a) with OK-432 ( inactive strain of group A streptococcus pyogenes)
  - b) pure ethanol
  - c) sodium tetradecyl sulphate
  - d) doxycycline – safe and effective
3. Surgical excision can be done around 2 years age. It must be done in toto in one go as repeat procedure is difficult due to fibrosis. Bipolar diathermy is used and care is taken for preservation of neural and vascular structures.

**Contraindications for surgery:**

- a) Prema an: infant
- b) Small lesion
- c) Nerves involvement -too small and difficult to identify-eg; facial nerve.

Viruses cause bilateral and gram positive bacteria cause unilateral lymphadenitis.



Red - Anterior triangle  
Blue - Posterior triangle



- ii. Anaplastic carcinoma- common in old age
- iii. Lymphoma
- iv. Metastatic carcinoma
- v. Sarcoma

#### 5. Inflammatory:

- a) Autoimmune disorders -Hashimoto's thyroiditis
- b) Granulomatous- De quervain's thyroiditis
- c) Fibrosing - Reidel's thyroiditis
- d) Infective –

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#### PALPATION – of the mass-

There are 3 methods-

- a. **Standard method:** ideal to stand behind and on each side as well of the patient. Identify each lobe while patient swallows. Feel the gland surface, any asymmetry, texture and estimate the size of the each lobe.
- b. **Lahey's method** (1926) palpating from the front. In this method, posterior surface of

586

the gland can also be palpated. Gland is pushed to one side, to feel the margins.

- c. **Crile's method:** Thumb is placed on the gland and patient is asked to swallow. Feel for nodules.

1. Check for local raise of temp, tenderness
2. Single nodule-
  - a) check for location -lobe/isthmus,
  - b) consistency of the nodule,
  - c) check rest of the gland -palpable or not
3. Whole gland is enlarged- check for
  - a) **Surface**  
smooth in Colloid goiter, Grave's disease; bosselated in multinodular goiter- MNG
  - b) **Consistency-**  
Soft in colloid goiter, Grave's disease,  
Firm in nodule may be solitary or multinodular.  
Hard in Carcinoma, Reidel's thyroid ;
  - c) **Mobility-** restricted in malignancy and chronic thyroiditis.  
Check mobility in all directions.
4. **Pressure effects-**
  - a) **Kocher's test-** slight compression on lateral lobe of thyroid gland produces stridor. Trachea becomes flabby and soft due to long standing pressure from the gland. Trachea is kept patent by the goiter itself. When the gland is excised, soft tracheal wall collapses causing airway obstruction and stridor. Temporary tracheostomy is done along with goiter excision and stoma is retained for 3 weeks, by which time, trachea regains its strength.
  - b) **Horner's syndrome;**
5. **Thrill** is felt in the upper pole of the thyroid as the superior thyroid artery is superficial near the where it enters the gland. Inferior thyroid artery is deeper.
6. **Berry's sign-**lack of pulsation on one side of thyroid gland suggests malignancy.

#### PERCUSSION-

On manubrium – resonant in normal persons, dull in retrosternal goiter

#### AUSCULTATION-

Systolic bruit is heard over upper pole of the thyroid gland in primary toxic goiter.

#### ENDOSCOPY:

**IDL ( Indirect laryngoscopy)** – to check the position and movement of vocal cords to rule out recurrent laryngeal nerve palsy.

**NECK - Measure neck circumference to monitor the growth of the mass.**

#### SIMPLE GOITER

It is diffuse hyperplasia of the gland, due to persistent growth stimulation.

It occurs in children as endemic goiters, in puberty as sporadic case.

It is soft and large , causes discomfort in the neck.

There is no correlation between size and function. A person with goiter can be euthyroid or hypothyroid or hyperthyroid.

Once stimulation ceases, goiter reduces in size, only to occur during stress as in pregnancy.

If the stimulation is fluctuating, there will be some active and some inactive lobules.

Active lobules undergo necrosis due to haemorrhage and necrotic lobules coalesce to form inactive lobules -leading to formation of colloid goiter.

Continual repetition leads to Nodular goiter.

#### Symptoms:

- Painless mass in the anterior neck in the thyroid region
- Tightness in the throat
- Coughing
- Difficulty in swallowing
- Difficulty in breathing

#### Signs:

- Smooth mass
- Firm palpable nodules

#### Investigations:

##### Blood:

1. Thyroid function tests – to rule out toxicity
2. Thyroid antibodies against Thyroperoxidase and Thyroglobulin to rule out thyroiditis

##### Radiology:

3. Neck and Chest X-Ray- PA and lateral views- for tracheal deviation, retrosternal extension
4. USG Neck – to assess malignancy, lymphadenopathy
5. CT Scan neck

##### Pathology:

6. FNAC- to rule out carcinoma, lymphoma, thyroiditis, colloid nodules
7. US guided FNAC

##### Complications:

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1. Tracheal obstruction- biphasic stridor
2. Secondary thyrotoxicosis
3. Carcinoma

#### Treatment:

1. Asymptomatic- no treatment
2. Surgery-

#### Indications

- a. Cosmetic
- b. Stridor
- c. Anxiety
- d. Retrosternal extension

#### Types of surgery –

- a. Total thyroidectomy – with thyroxine replacement
- b. Subtotal thyroidectomy
- c. Total lobectomy

#### MULTI NODULAR GOITRE

##### Definition:

It is a diffuse, da it growth with structurally and functionally altered thyroid follicles presenting as multiple nodules in thyroid. It is a slowly

Persistent TSH stimulation, leads to diffuse hyperplasia of the gland. Later with fluctuation of TSH levels, mixed areas of active and inactive lobules develop. Active lobules become more vascular and hyperplastic. Haemorrhage occurs in the lobule, causing central necrosis. Necrotic nodules coalesce to form nodules filled with either iodine free colloid or a mass of new but inactive follicles. Center of the nodule is inactive and only the margin is active. Many nodules are formed, ultimately resulting in multinodular goiter.

##### Pathology:

##### Gross:

Thyroid gland is multilobulated. Cut section shows irregular nodules containing gelatinous colloid. Areas of haemorrhage, fibrosis, calcification and cystic changes are seen in older lesions.

##### Microscopy:

Follicles of varying size with areas of haemorrhage, hemosiderin -laden macrophages and calcification are seen.

##### Symptoms:

611/727



5. Dysmorphogenesis – familial, autosomal recessive condition, with deficiency of peroxidase or dehalogenase.

**Pathogenesis:**

- c. Anti-TPO ( Thyroperoxidase) and Anti-TG( Thyroglobulin) antibodies. ( Autoimmunity may co-exist with goiter)
2. Radiological :

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588

- a. USG Neck and USG guided FNAC- High resolution USG identifies impalpable nodules, number, nature and vascularity of nodule.
- b. X-Ray Neck –AP and Lateral views- shows ring calcification, position and compression of trachea.
- c. Radio-isotope  $I^{131}$  scan – useful to check gland activity in the nodules.
- d. CT scan /MRI Neck and chest- for retrosternal goiter.
3. Pathology:
- a. FNAC- from most dominant and suspicious nodule

**Treatment:**

Most of the MNG are asymptomatic and do not require surgery.

- a. **Medical** – in early stages- thyroxine 0.15 to 0.2 mg daily for a few months- hyperplastic nodule may regress. Post-operative thyroxine is given to prevent recurrence.
- b. **Surgical** – Total thyroidectomy if entire gland is involved. Subtotal thyroidectomy if gland involved is less. Eight grams of thyroid tissue is left in each lobe. Partial thyroidectomy- depends on tissue involved. Now this procedure is obsolete. Retrosternal goiter is an indication for surgery.
- c. **Prevention:** Correcting Iodine deficiency by giving Iodine rich diet- Iodised salt, eggs, sea food and milk. Avoid use of goitrogens.

**Complications of MNG:**

- a. Secondary thyrotoxicosis ( 30%)
- b. Follicular carcinoma thyroid (10%)
- c. Haemorrhage in a nodule
- d. Tracheal compression, calcification
- e. Cosmetic problem.

**Complications of surgery:**

- a. Bleeding
- b. Infection
- c. RLN palsy and loss of voice
- d. Hypocalcemia
- e. Life long need of thyroxine.

**RETROSTERNAL GOITER:**

**Definition:** more than 50% of the goiter is below the suprasternal notch.

If intrathoracic extension reaches upto 4<sup>th</sup> thoracic vertebra, more than 2 cms in anterior mediastinum or if it requires mediastinal dissection, it is said to be major intrathoracic extension.

It arises from lower pole of the gland.  
May be asymptomatic.

**It is of 3 types-**

- a. **nodular,**
- b. **toxic and**
- c. **malignant.**

It can produce RLN palsy- unilateral or bilateral.

**Symptoms:**

- cough
- dyspnoea at night on lying down or neck extended
- noisy breathing

**Signs:**

- congested veins in the neck, face and upper chest wall.
- lower border of the mass is not seen or felt
- positive pemberton sign-see above
- dull note on manubrium sterni on percussion
- expiratory stridor- it is dangerous as it can not be relieved by tracheostomy or intubation

**Investigations:**

1. Chest and Thoracic inlet X-ray- PA view and lateral views
2. Ultrasound scanning – to rule out metastatic nodes
3. Barium swallow -shows oesophageal indentation
4. CT scan / MRI and PET scan chest and neck – shows the extent of goiter, for assessment of known malignancy.
5. Thyroid function tests-  $T_3, T_4$  and TSH levels
6. Lung function tests
7. RAI -radioactive iodine  $I^{131}$  or  $^{99m}Tc$  scan study

**Treatment:**

1. Excision via cervical approach and sternotomy if needed.
2. Even asymptomatic goiter needs excision.
3. Radioiodine therapy is not suggested in this condition

**LINGUAL THYROID**

It is an ectopic thyroid gland and it is a developmental anomaly, in which thyroid gland grows at the base of the tongue. It may be only functioning thyroid tissue.

- It is common in females- 4:1, appears in teenage, coinciding with puberty and also seen during pregnancy. Incidence- 1 in 1,00,000.
- It can be asymptomatic. 70% cases present with hypothyroidism. 10% as cretins.

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589

- It can become nodular, toxic or malignant. Follicular carcinoma is most common. Papillary carcinoma is very rare.

**Symptoms:**

- Swelling in the tongue
- Dysphagia for solids
- Bleeding from mouth
- Snoring and sleep disturbance – apnoeic attacks during sleep
- Change in voice
- Foreign body sensation

**Signs:**

- Pink or strawberry like round mass in the base of the tongue
- Hot potato voice
- Tracheal rings are bare.

**Investigations:**

- Radioisotope study- most important in confirming the function of the gland and absence of thyroid in the neck.
- Ultrasonography neck- to confirm absence of thyroid gland in the neck.
- MR<sup>i</sup> neck
- FNAC and biopsy.
- Thyroid function tests.

**Differential diagnosis:**

- Lingual tonsil
- Carcinoma tongue base

**ETIOLOGY:**

1. Grave's disease-( also called Basedow disease or primary thyrotoxicosis) seen in young females 5:1, it is due to autoantibodies against receptors. Incidence 1 in 1000.
2. Toxic multi nodular goiter- secondary thyrotoxicosis or Plummer disease- 20%
3. Toxic, autonomous nodule( Goetsch disease)- 5%
4. Functioning thyroid cancer / metastasis
5. Excess thyroxine intake- Thyrotoxicosis factitial- taking L-thyroxine more than normal
6. T-3 thyrotoxicosis
7. De Quervain's thyroiditis or Autoimmune Thyroiditis
8. Jod Basedow thyrotoxicosis- due to intake of large doses of iodides. [Jod means iodine in German].

613/727

**EYE SIGNS IN THYROTOXICOSIS:**

1. **Von Graefe's sign:** Lid lag sign- inability of upper eye lid to keep pace with downward movement of the eye ball, while following the examiner's finger. **Second sign to appear.**
2. **Dalrymple's sign-** upper eyelid retraction with visible upper sclera



artery is deeper.

6. **Berry's sign**-lack of pulsation on one side of thyroid gland suggests malignancy.

#### PERCUSSION-

On manubrium – resonant in normal persons, dull in retrosternal goiter

#### AUSCULTATION-

Systolic bruit is heard over upper pole of the thyroid gland in primary toxic goiter.

#### ENDOSCOPY:

3. Neck and Chest X-Ray- PA and lateral views- for tracheal deviation, retrosternal extension
4. USG Neck – to assess malignancy, lymphadenopathy
5. CT Scan neck

#### Pathology:

6. FNAC- to rule out carcinoma, lymphoma, thyroiditis, colloid nodules
7. US guided FNAC

#### Complications:

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587

1. Tracheal obstruction- biphasic stridor
2. Secondary thyrotoxicosis
3. Carcinoma

#### Treatment:

1. Asymptomatic- no treatment
2. Surgery-

#### Indications

- a. Cosmetic
- b. Stridor
- c. Anxiety
- d. Retrosternal extension

#### Types of surgery –

- a. Total thyroidectomy – with thyroxine replacement
- b. Subtotal thyroidectomy
- c. Total lobectomy

### MULTINODULAR GOITRE

#### Definition:

It is a discordant growth with structurally and functionally altered thyroid follicles presenting as multiple nodules in thyroid. It is a slowly progressive disease over many years. It can weigh upto 2 kgs. Mostly Euthyroid, but can be toxic or non toxic.

Toxic multinodular goiter is called **Plummer syndrome**. In this syndrome, a hyperfunctioning nodule develops within a long standing goiter resulting in Hyperthyroidism.

#### Incidence:

- It is more common in middle aged women (10:1)
- 13-17% have carcinoma, of which papillary carcinoma is commonest type ( Bisi et al). National cancer survey in USA found an incidence of 40 per 1 million.

#### Etiology:

**Chronic low grade intermittent stimulus leads to thyroid hyperplasia.**

1. Fluctuating TSH levels
2. Iodine deficiency – Endemic, increased demand during pregnancy, puberty
3. Goitrogens- cabbage, cauliflower, cassava root, iodides, sulfonamides, PAS
4. Hereditary
5. Dyshormonogenesis – familial, autosomal recessive condition, with deficiency of peroxidase or dehalogenase.

#### Pathogenesis:

Persistent TSH stimulation, leads to diffuse hyperplasia of the gland. Later with fluctuation of TSH levels, mixed areas of active and inactive lobules develop. Active lobules become more vascular and hyperplastic. Haemorrhage occurs in the lobule, causing central necrosis. Necrotic nodules coalesce to form nodules filled with either iodine free colloid or a mass of new but inactive follicles. Center of the nodule is inactive and only the margin is active. Many nodules are formed, ultimately resulting in multinodular goiter.

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#### Gross:

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#### Microscopy:

Follicles of varying size with areas of haemorrhage, hemosiderin -laden macrophages and calcification are seen.

#### Symptoms:

1. Mass in the neck- in thyroid region; slowly growing; enlargement in pregnancy
2. Sudden, transient pain or increase in size (due to bleeding into the nodule)
3. Cosmetic effects
4. Pressure effects- dyspnoea, dysphagia, prominent veins in the neck
5. Symptoms of hypothyroidism
6. Recent increase in size suggests malignancy or haemorrhage.

#### Signs:

1. Firm, nodular, non tender mass in the thyroid region moving with deglutition
2. IDL- occult RLN palsy, past undiagnosed palsy may be noted.
3. Hard in consistency due to calcification
4. Soft in consistency due to necrosis
5. Pemberton's sign- positive
6. Kocher's test – positive – due to compression of trachea

#### Investigations:

1. Blood –
  - a. T3,T4,TSH
  - b. Serum calcium
  - c. Anti-TPO ( Thyroperoxidase) and Anti-TG( Thyroglobulin) antibodies. ( Autoimmunity may co-exist with goiter)
2. Radiological :

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- a. USG Neck and USG guided FNAC- High resolution USG identifies impalpable nodules, number, nature and vascularity of nodule.
- b. X-Ray Neck –AP and Lateral views- shows ring calcification, position and compression of trachea.
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Most of the MNG are asymptomatic and do not require surgery.

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It arises from lower pole

May be asymptomatic.

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- a. nodular,
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- c. malignant.

It can produce RLN palsy- unilateral or bilateral.

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- cough
- dyspnoea at night on lying down or neck extended
- noisy breathing

#### Signs:

- congested veins in the neck, face and upper chest wall.
- lower border of the mass is not seen or felt
- positive pemberton sign-see above
- dull note on manubrium sterni on percussion
- expiratory stridor- it is dangerous as it can not be relieved by tracheostomy or intubation

#### Investigations:

1. Chest and Thoracic inlet X-ray- PA view and

612/727



medially, sternothyroid muscle insertion superiorly and upper pole of thyroid with superior thyroid vessels laterally.

### PHYSIOLOGY:

Thyroid gland follicular cells produce Thyroxine. This fact was discovered by Prof Kocher, who got Noble prize for this discovery. Parafollicular cells produce calcitonin which controls calcium metabolism.

### CLASSIFICATION OF THYROID SWELLINGS.

Any thyroid swelling irrespective of the etiology, is called Goiter. It is classified as follows.

#### 1. Physiological

- Puberty
- Pregnancy
- Lactation

2. **Non -Toxic-** can be diffuse or nodules – can be single or multiple, commonly seen in women of 20-30 years age. The causes of such goitre include,

##### a) Endemic-

- Iodine deficiency
- Iodine excess
- Dietary goitrogens – cabbage

##### b) Sporadic –

- Goitrogens – anti thyroid drugs
- Iodine deficiency
- Compensatory hypertrophy following thyroidectomy
- Dyshormonogenesis.

#### 3. Toxic -

- Primary (Grave's disease)
- Secondary – Toxic multinodular goiter

#### 4. Neoplasm –

- Benign – Adenoma
- Malignant- 3 types- papillary, follicular and well differentiated carcinoma
  - Medullary carcinoma
  - Anaplastic carcinoma- common in old age
  - Lymphoma
  - Metastatic carcinoma
  - Sarcoma

#### 5. Inflammatory:

- Autoimmune disorders -Hashimoto's thyroiditis
- Granulomatous- De quervain's thyroiditis
- Fibrosing - Reidel's thyroiditis
- Infective –

- Acute - bacterial ,
- Subacute - viral,
- Chronic - TB, Syphilis
- Others- Amyloidosis

### DIAGNOSIS:

#### CASE HISTORY:

- Swelling - duration, onset, site, progression
- Pain -duration, site, character, radiation
- Pressure symptoms- dyspnoea, dysphagia, hoarseness of voice
- Features of hyperthyroidism – see the table below
- Features of hypothyroidism – see the table below

### CLINICAL EXAMINATION

#### INSPECTION:

- Number of swellings, site, size, shape, borders (with respect to sternocleidomastoid and suprasternal notch) surface- smooth, nodular, bosselated ( many protruberances), skin over the swelling - redness, edema, scars, sinuses, fistula and dilated veins, pulsations over the swelling, movement on deglutition and tongue protrusion
- Trail's sign-** prominence of sternal head of SCM muscle due to tracheal shift to same side
- Pizzillo's method** – keep the hands on the back of the head, and push back against clasped hands, thyroid becomes more prominent
- Pemberton sign** – patient is asked to raise both arms over the head, touching the ears and maintain for 2-3 min. If neck, face veins become dilated and prominent- sign is positive, it is seen in retrosternal goiter. The mass compresses superior vena cava. Stridor or dysphagia also occur due to compression of trachea and oesophagus respectively.

#### PALPATION – of the mass-

There are 3 methods-

- Standard method:** ideal to stand behind and on each side as well of the patient. Identify each lobe while patient swallows. Feel the gland surface, any asymmetry, texture and estimate the size of the each lobe.
- Lahey's method** (1926) palpating from the front. In this method, posterior surface of

the gland can also be palpated. Gland is pushed to one side, to feel the margins.

- Crile's method:** Thumb is placed on the gland and patient is asked to swallow. Feel for nodules.

- Check for local raise of temp, tenderness
- Single nodule-
  - check for location -lobe/isthmus,
  - consistency of the nodule,
  - check rest of the gland -palpable or not
- Whole gland is enlarged- check for
  - Surface**  
smooth in Colloid goiter, Grave's disease; bosselated in multinodular goiter- MNG
  - Consistency-**  
Soft in colloid goiter, Grave's disease, Firm in nodule may be solitary or multinodular.  
Hard in Carcinoma, Reidel's thyroid ;
  - Mobility-** restricted in malignancy and chronic thyroiditis.  
Check mobility in all directions.
- Pressure effects-**
  - Kocher's test-** slight compression on lateral lobe of thyroid gland produces stridor. Trachea becomes flabby and soft due to long standing pressure from the gland. Trachea is kept patent by the goiter itself. When the gland is excised,

**IDL ( Indirect laryngoscopy)** – to check the position and movement of vocal cords to rule out recurrent laryngeal nerve palsy.

#### NECK - Measure neck circumference to assess the growth of the mass

### SIMPLE GOITER

It is diffuse hyperplasia, persistent growth stimulation.

It occurs in children as endemic goiters, in puberty as sporadic case.

It is soft and large, causes discomfort in the neck.

There is no correlation between size and function. A person with goiter can be euthyroid or hypothyroid or hyperthyroid.

Once stimulation ceases, goiter reduces in size, only to occur during stress as in pregnancy.

If the stimulation is fluctuating, there will be some active and some inactive lobules.

Active lobules undergo necrosis due to haemorrhage and necrotic lobules coalesce to form inactive lobules -leading to formation of colloid goiter.

Continual repetition leads to Nodular goiter.

#### Symptoms:

- Painless mass in the anterior neck in the thyroid region
- Tightness in the throat
- Coughing
- Difficulty in swallowing

610/727



## DEVELOPMENT:

- It is endodermal in origin.
- It develops from thyroglossal duct which extends from foramen cecum in the tongue

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Fig 60-1: Note the pyramidal lobe of thyroid gland

- There are 3 veins- superior, middle and inferior- first two drain into internal jugular

584

vein and the last one drains into innominate vein.

- Superior artery and vein run together like a happy married couple,
- Inferior thyroid vessels run independent of each other like divorced couple and
- Middle thyroid vein is single like a bachelor. It has no accompanying artery.
- Rarely in 10% cases, there is another single artery – Thyroid ima which arises from the aortic arch or the innominate artery and runs upwards to reach the thyroid gland at the lower border of isthmus.
- Rarely, there is fourth thyroid vein ( of Kocher) present between middle and inferior thyroid veins.

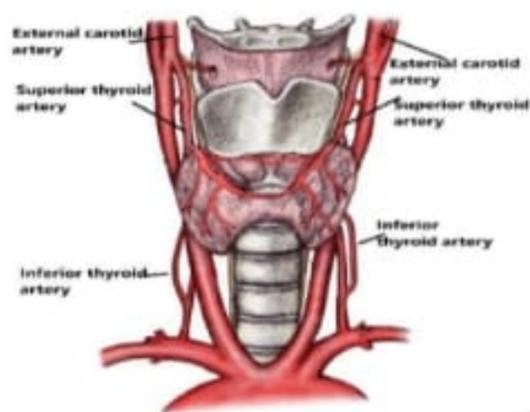


Fig 60-2a : Arteries of the thyroid gland.(Courtesy: [www.entokey.com](http://www.entokey.com))

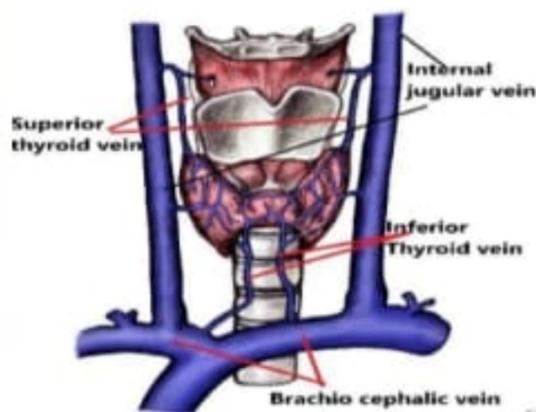


Fig 60-2 b : Veins of the thyroid gland.(Courtesy: [www.entokey.com](http://www.entokey.com))

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## Lymphatic drainage:

Subcapsular lymphatic plexus drains mainly into “Delphian” and paratracheal nodes. From there it drains to deep cervical and mediastinal nodes.

Lymphatic channels accompany the blood vessels.

- Superior channels drain into upper deep cervical nodes directly or through delphian node,
- Inferior channels drain into delphian node and paratracheal nodes.
- Some channels go to retropharyngeal and retro-oesophageal nodes.

## Nerve supply:

- Parasympathetic fibers, from vagus via laryngeal nerves.
- Sympathetic fibers arise from superior, middle and inferior cervical sympathetic ganglia and these fibers accompany the blood vessels.

They mainly act on the blood vessels to control the perfusion rate.

## Applied anatomy:

- a) There is dense capillary plexus of vessels under the true capsule and hence excision of the gland must include true capsule, else there will be heavy bleeding from the gland tissue proper.
- b) RLN passes deep to the Berry's ligament and the inferior thyroid vessels cross the RLN close to the lower border of Berry's ligament. Clamping of blood vessels in this area for control of bleeding during thyroidectomy can damage the RLN and is an important cause of RLN palsy in thyroidectomy cases.
- c) RLN lies in **Behr's triangle**, boundaries of which are-carotid artery laterally, inferior thyroid artery superiorly and tracheoesophageal groove medially.
- d) Right RLN is more prone to damage as it is more in anterior and lateral position and not protected in the tracheo-oesophageal [ TE] groove.
- e) External branch of SLN lies in **Joll's triangle**, deep to upper pole of thyroid gland. It runs sometimes close to superior vascular pedicle and can be injured while ligating the upper pole of the gland. **Boundaries of Joll's triangle** are cervical midline

medially, sternothyroid muscle insertion superiorly and upper pole of thyroid with superior thyroid vessels laterally.

## PHYSIOLOGY:

Thyroid gland follicular cells produce Thyroxine. This fact was discovered by Prof Kocher, who got Noble prize for this discovery. Parafollicular cells produce calcitonin which controls calcium metabolism.

## CLASSIFICATION OF THYROID SWELLINGS.

Any thyroid swelling irrespective of the etiology, is called Goiter. It is classified as follows.

### 1. Physiological

- a) Puberty
- b) Pregnancy
- c) Lactation

2. **Non -Toxic**- can be diffuse or nodules – can be single or multiple, commonly seen in women of 20-30 years age. The causes of such goitre include,

#### a) Endemic-

- i. Iodine deficiency
- ii. Iodine excess
- iii. Dietary goitrogens – cabbage

#### b) Sporadic –

- i. Goitrogens – anti thyroid drugs
- ii. Iodine deficiency
- iii. Compensatory hypertrophy following thyroidectomy

- a. Acute - bacterial ,
- b. Subacute - viral,
- c. Chronic - TB, Syphilis
- e) Others- Amyloidosis

## DIAGNOSIS:

### CASE HISTORY:

1. Swelling - duration
2. Pain -duration, site,
3. Pressure symptoms- dyspnoea, dysphagia, hoarseness of voice
4. Features of hyperthyroidism – see the table below
5. Features of hypothyroidism – see the table below

## CLINICAL EXAMINATION

### INSPECTION:

1. Number of swellings, site, size, shape, borders (with respect to sternocleidomastoid and suprasternal notch) surface- smooth, nodular, bosselated ( many protruberances), skin over the swelling - redness, edema, scars, sinuses, fistula and dilated veins, pulsations over the swelling, movement on deglutition and tongue protrusion
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3. **Pizzillo's method** – keep the hands on the back of the head, and push back against clasped hands, thyroid becomes more

585

609/727

THYROID DISEASES

Core competency

EN 1.1: Describe the anatomy & physiology of ear, nose, throat, head and neck.

EN 1.2: Describe the pathophysiology of common diseases in ENT

ANATOMY OF THYROID GLANDS

The thyroid gland (**Greek- shield like**) is the largest endocrine gland in the body, situated in the anterior neck.

- It extends from the middle of the thyroid cartilage to the level of 6<sup>th</sup> tracheal ring.
- It is butterfly in shape and it has two lobes. The lobes are pyramidal in shape and mobile.
- They are situated one on each side of the trachea under the strap muscles of the neck, connected by isthmus. The isthmus is placed across 2<sup>nd</sup> to 4<sup>th</sup> tracheal ring. The isthmus is attached to the trachea.
- The thyroid gland is attached to the trachea by suspensory ligament of Berry, which is a condensation of deep fascia.
- Lobule is the functional unit, and each lobule is supplied by an arteriole.
- Each lobule consists of 25-40 follicles, lined by cuboidal epithelium.
- It moves with deglutition because of this attachment, but it does not move on protrusion of the tongue.
- The gland is not visible outside unless it is enlarged, when it is called Goitre [ Latin-gutter-throat].
- It has two capsule sheaths-an inner true capsule and an outer false capsule. False capsule is formed by pretracheal fascia which is a part of deep cervical fascia. True capsule is a condensation of connective tissue covering the gland.

DEVELOPMENT:

- It is endodermal in origin.
- It develops from thyroglossal duct which extends from foramen cecum in the tongue

and drops down to the middle of the neck. End of the duct bifurcates to form two lobes and some times, a portion of the tip forms pyramidal lobe. This duct disappears once thyroid gland is formed. The descent and gland formation is complete by 7<sup>th</sup> week and the gland start functioning by 3<sup>rd</sup> month of fetal life.

- Some times this duct does not descend and the thyroid is seen in the base of the tongue as Lingual thyroid.
- In 30% cases, there is another congenital anomaly in which, another lobe called pyramidal lobe, extends from the isthmus upwards.

**Blood supply:** It is highly vascular organ. Blood supply is very rich and it flows at the rate of 5ml/g/min.

- There are 2 arteries- namely superior and inferior thyroid arteries, branches of external carotid artery and thyrocervical trunk respectively. Both are paired arteries one on each side.

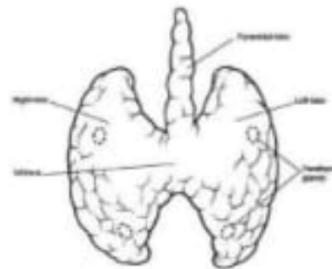


Fig 60-1: Note the pyramidal lobe of thyroid gland

- There are 3 veins- superior, middle and inferior- first two drain into internal jugular

608/727

vein and the last one drains into innominate vein.

- Superior artery and vein run together like a happy married couple,
- Inferior thyroid vessels run independent of each other like divorced couple and
- Middle thyroid vein is single like a bachelor. It has no accompanying artery.
- Rarely in 10% cases, there is another single artery – Thyroid ima which arises from the aortic arch or the innominate artery and runs upwards to reach the thyroid gland at the lower border of isthmus.
- Rarely, there is fourth thyroid vein ( of Kocher) present between middle and inferior thyroid veins.



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- Parasympathetic fibers, from vagus via laryngeal nerves.
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They mainly act on the blood vessels to control the perfusion rate.

midline neck swelling in thyroid region since 6 months. O/E- a swelling of size 3 cm diameter seen in midline of neck, cystic in consistency, smooth

& deglutition.

1) What is the diagnosis:

a) Dermoid cyst

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582

- b) Thyroglossal cyst\*\*  
 c) Cystic metastatic lymph node  
 d) Epidermoid cyst  
 2) Treatment of choice;

- a) Anti thyroid drugs  
 b) Antibiotics  
 c) Chemotherapy  
 d) Sistrunk operation\*\*

**Answers:**

QA) 1- b , 2-d

**KEY POINTS**

1. Delphian node gets involved in vocal cord growths involving anterior commissure.
2. Delphian node is called "sentinel node" of carcinoma thyroid. Delphian node if involved in thyroid cancer, it is predictive of aggressive nature of the growth.
3. Thyroglossal cysts move with both deglutition and tongue protrusion unlike thyroid swellings which move only with deglutition.
4. Ultrasound neck is the investigation of choice and sistrunk operation is the treatment of choice in thyroglossal cyst.
5. Sudden attacks of fainting and fall attacks occur on turning the neck in carotid body tumour. It is called "carotid body syncope"
6. MRI angiography neck shows splaying of internal and external carotid arteries. It is called "Lyre's sign"
7. Ranula is produced only in sublingual salivary gland.

**BE SLOW TO CRITICIZE AND FAST TO APPRECIATE.**

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607/727



583

**CHAPTER 60**

**THYROID DISEASES**

**Core competency**

**EN 1.1:** Describe the anatomy & physiology of ear, nose, throat, head and neck.

**EN 1.2:** Describe the pathophysiology of common diseases in ENT

**ANATOMY OF THYROID GLANDS**

The thyroid gland (**Greek- shield like**) is the largest endocrine gland in the body, situated in the anterior neck

and drops down to the middle of the neck. End of the duct bifurcates to form two lobes and some times, a portion of the tip forms



**1. Based on structures injured**

- Laryngotracheal (airway)(4-12%)
- Pharyngo-esophageal (digestive) (5-15%)
- Vascular (IJV 9%, CA-7%)
- Neurological system( 3-8%)

**2. Based on mechanism of trauma**

- Blunt trauma**
  - MVA – Motor vehicle accidents
  - Sports injury
  - Strangulation
  - Blows
- Penetrating injuries** (5-10%)
  - Stab injury-Knife, Blades, Glass
  - Projectile –

d. Tracheal deviation

e. Subcutaneous emphysema

f. Sucking wound

**2. Vascular**

- Haematoma
- Persistent bleeding
- Absent carotid pulse, decreased upper extremity pulse,
- Bruit / thrill
- Hypovolemic shock –unresponsive to volume expanders
- Change of sensorium
- Neurologic deficit
- Widened mediastinum

**3. Pharynx / oesophagus**

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581

- Subcutaneous emphysema
- Hematemesis
- Dysphagia
- Odynophagia
- Tachycardia

**4. Neurological**

- Hemiplegia
- Quadriplegia
- Coma
- Cranial nerve deficit
- Change of sensorium
- Stroke

Laryngotracheal injuries are less common ,but carry high mortality rates.

It is divided into – supraglottic, glottic and sub glottis.

**Aetiology:****External trauma**

- Motor vehicle accidents
- Assault
- Strangulation
- Near hanging
- Clotheline trauma

**Internal trauma**

- Iatrogenic-bronchoscopy, intubation, percutaneous tracheostomy

**Classification of injuries(Schafer)****Acute laryngeal trauma is divided into 5 types**

- Minor** endolaryngeal haematoma or laceration without detectable fracture
- Oedema**, hematoma, minor mucosal disruption without exposed cartilage, nondisplaced fracture noted on CT
- Massive** oedema, mucosal tear, exposed cartilage, cord immobility, displaced fracture
- Same as group 3**, with more than two fracture lines or massive trauma to laryngeal mucosa
- Complete** laryngotracheal separation

**Supraglottic injuries:** Thyroid ala horizontal fractures, posterior displacement of epiglottis, cricoarytenoid dislocation,

**Glottic injuries:** Thyroid cartilage fractures-cruciate type

**Subglottic injuries:** Injury to cricoarytenoid joint, RLN palsy, cricothyroid joint dislocation

**Hyoid bone:** Fracture in the center.

**CASE STUDY 1**

QA ) A 15 year old male patient reported with midline neck swelling in thyroid region since 6 months. O/E- a swelling of size 3 cm diameter seen in midline of neck, cystic in consistency, smooth

**EVALUATION AND INITIAL MANAGEMENT:**

Assessment includes taking AMPLE history and ABCDE evaluation.

**AMPLE history includes;**

- Allergies
- Medications
- Past medical history
- Last oral intake
- Events leading to trauma

**ABCDE includes;**

- ABC** – Establish **airway**, check for **breathing, circulation-** control bleeding. Avoid extension of neck till cervical spine injury is ruled out.  
**Disability-** Glasgow coma scale, facial palsy  
**Exposure** of whole body for evaluation/ environmental control ( to prevent thermal injury)
- Head end elevated for minor injuries.
- Palpate thyroid cartilage for tenderness, look for loss of thyroid prominence, subcutaneous emphysema, ecchymoses.

**Investigations**

- Blood for CBC, cross matching, RBS, RFT, ABG
- Chest X-Ray- inspiratory / expiratory films.
- X-Ray cervical spine to rule out fractures.
- X-Ray neck soft tissue –AP and lateral
- Arteriograms / CT angiography
- Carotid ultrasound
- MRI / MRA
- Direct laryngoscopy, Rigid bronchoscopy, rigid oesophagoscopy
- Flexible oesophagoscopy

**Indications for Mandatory management.**

- Massive bleeding
- Expanding haematoma
- Haemodynamic instability
- Haemomediastinum
- Haemothorax
- Major haemoptysis
- Brachial plexus injury – repaired within 24-72 hours

**Indications for selective exploration:**

- Stable and non-life threatening injuries

606/727

surface, nontender, moves with protrusion of tongue & deglutition.

1) What is the diagnosis:

- Dermoid cyst

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- Thyroglossal cyst\*\*
  - Cystic metastatic lymph node
  - Epidermoid cyst
- 2) Treatment of choice;

- Anti thyroid drugs
- Antibiotics
- Chemotherapy
- Sistrunk operation\*\*

4. Biopsy: reveals tubercular granuloma with Langerhans giant cells.
5. Biopsy material sent for culture and sensitivity- mainly in multi drug resistant bacilli.
6. Chest X-ray- to rule out pulmonary TB.

**Treatment:****A. For lymphadenitis:**

It includes multi drug regimen. Total duration of treatment is 6 months. Response is seen in 3-4 months. Response is quicker in children.

Initial phase: 4 drugs for 2 months



**Fig 59-15:** Hodgkin's lymphoma- front view and side view.

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580



**Fig 59-14:** Upper deep cervical metastatic nodes with diagnosis of supraglottic carcinoma (Courtesy: Dr Deena Singh, Director, ENT hospital Mauritius)

**NECK TRAUMA**

Neck has complex network of neurovascular and muscular structures supported by various fascial planes. In the neck, multiple vital structures are vulnerable to injury in a small anatomic area and are unprotected by bone, unlike brain and ears.

Neck trauma accounts for 5-10% of all serious traumatic injuries. 10% of neck wounds lead to respiratory compromise and may lead to sudden airway obstruction resulting in mortality as much as 33%. Missed traumatic neck injuries lead to mortality of more than 15%.

Transcervical injuries across the midline of neck will cause vascular or aerodigestive injuries in 70-100% cases.

**Death in major head and neck trauma:** It can be,

1. within seconds to minutes
2. within minutes to hours (Golden hour)
3. within days to weeks

Associated injuries in chest, spine, abdomen and pelvis, needs to be assessed and managed

**Incidence:**

1. It is more common in men than women.
2. It is more common in young adults and adolescents

**Classification of neck injuries:****1. Based on structures injured**

- a. Laryngotracheal (airway)(4-12%)
- b. Pharyngo-esophageal (digestive) (5-15%)
- c. Vascular (IJV 9%, CA-7%)
- d. Neurological system( 3-8%)

**2. Based on mechanism of trauma**

- a. Blunt trauma
  - MVA – Motor vehicle accidents
  - Sports injury
  - Strangulation
  - Blows
- b. Penetrating injuries (5-10%)
  - Stab injury-Knife, Blades, Glass
  - Projectile –

- i. Hand gun (low velocity),
- ii. Rifle (high velocity)
- iii. Shotgun (impact depends on distance)

**3. Based on site of injury**

- a. Internal – mucosal
- b. External

**4. Based on zones in the neck (Roon & Christensen's classification)**

- a. Zone 1-from sternum to cricoid.
- b. Zone 2- from cricoid to angle of mandible
- c. Zone 3 – from angle of mandible to skull base.

**Contents in each zone.****Zone 1**

This zone has highest morbidity and mortality rates.

- a. Great vessels- Subclavian vessels, brachiocephalic veins, common carotid arteries, jugular veins ,Aortic arch
- b. Oesophagus, Trachea, Lung apices , thoracic duct, spinal cord

**Zone 2**

common site of carotid injury

- a. Carotid and vertebral arteries, jugular veins,
- b. Base of the tongue, Pharynx, larynx, spinal cord
- c. Phrenic, vagus, hypoglossal nerve

**Zone 3**

Vascular and cranial nerve injuries are common.

- a. Distal carotid arteries, vertebral arteries, jugular veins
- b. Parotid and submandibular salivary glands
- c. Major cranial nerves-9,10,11 & 12<sup>th</sup>
- d. Pharynx, spinal cord

**Clinical features: are classified as below:****1. Airway**

- a. Stridor
- b. Hoarseness of voice
- c. Hemoptysis
- d. Tracheal deviation
- e. Subcutaneous emphysema
- f. Sucking wound

**2. Vascular**

- a. Haematoma
- b. Persistent bleeding
- c. Absent carotid pulse, decreased up
- d.
- e. 605/727
- f. Change
- g. Neurologic deficit
- h. Widened mediastinum

**3. Pharynx / oesophagus**

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- a. Subcutaneous emphysema
- b. Hematemesis
- c. Dysphagia
- d. Odynophagia
- e. Tachycardia

**4. Neurological**

- a. Hemiplegia
- b. Quadriplegia

**EVALUATION AND INITIAL MANAGEMENT:**

Assessment includes taking AMPLE history and ABCDE evaluation.

**AMPLE history includes;**

- Allergies
- Medications
- Past medical history
- Last oral intake

microscopy.

- b) Potential risk of seeing malignant cells in the tract.
  - c) Can not distinguish between lymphomas.
2. **Biopsy:** can be done bedside, in OT or on endoscopy.
- Excision biopsy yields better results.

with persistent discharging sinus opening. Also can form an ulcer with an undermined edge.

**Route of entry:**

Bacteria usually enter through the tonsils or hematogenous route.

**Types of clinical manifestation:**

**There are 4 types-**

1. Acute

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2. Caseating
3. Hyperplastic
4. Atrophic

**Acute type:**

Seen in infants and children below 5 years. Child is febrile. Nodes are painful, tender. Skin over the swelling is red and edematous.

**Caseating type:**

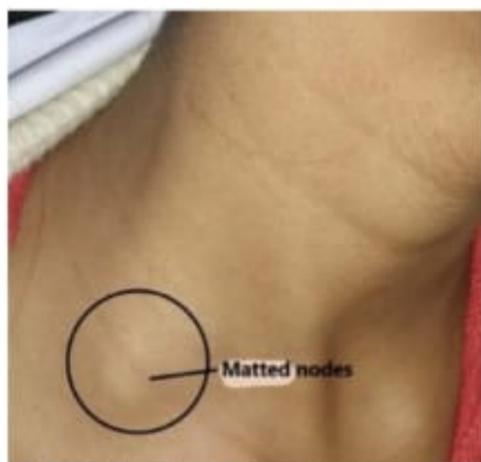
Most common type, seen in young adults. Patient is anaemic, malnourished with low grade fever, anorexia and weight loss. On examination, multiple, enlarged, matted nodes, with areas of softening due to caseation are seen.

**Hyperplastic type:**

Seen in patients with good resistance. Patients have enlarged, fleshy, elastic, freely mobile nodes, with least caseation and matting. Nodes get calcified and appear on X-Ray

**Atrophic type:**

Seen in elderly, nodes are small soon burst with caseation.



**Fig 59-13:** TB lymphadenitis- right supraclavicular triangle

**Investigations:**

1. Mantoux test- negative test excludes tuberculosis and positive test has no value.
2. Blood- ESR elevated, serum albumin is low, gamma globulin is elevated
3. FNAC of a lymph node – AFB can be seen in smears of the aspirate fluid.
4. Biopsy: reveals tubercular granuloma with Langerhans giant cells.
5. Biopsy material sent for culture and sensitivity- mainly in multi drug resistant bacilli.
6. Chest X-ray- to rule out pulmonary TB.

**Treatment:**

**A. For lymphadenitis:**

It includes multi drug regimen. Total duration of treatment is 6 months. Response is seen in 3-4 months. Response is quicker in children.

Initial phase: 4 drugs for 2 months

1. Cap Rifampicin 600 mg OD
2. Tab Isoniazid 300 mg OD
3. Tab Ethambutol 1 Gm OD
4. Tab Pyrazinamide 1.5 Gm OD

Follow up phase: 2 drugs for 4 months

1. Cap Rifampicin 600 mg OD
2. Tab Isoniazid 300 mg OD.

**B. For cold abscess:**

- Zig zag aspiration with a wide bore needle in non dependent area is done to prevent sinus formation. It can be repeated as necessary. Streptomycin is instilled into the abscess cavity after aspiration.
- Incision and drainage- incision is placed in a nondependent area and after the drainage, it is closed without inserting any drain.

**C. For medically failed cases and for sinus/ fistula:**

- Surgical excision is the treatment of choice

**METASTATIC LYMPH NODES:**

Upper deep cervical nodes are enlarged in malignancies of pharynx, oral cavity, nose and PNS. Carcinoma of nasopharynx can also spread to accessory lymph nodes in the posterior triangle. Sometimes the nodes are present but no primary growth is visible. It is called occult primary. Usually the site is in tonsil, tongue base, fossa of Rosenmuller or pyriform fossa.

- Supraclavicular nodes enlarge from primary growths in breast, lung, stomach, kidney, ovary and testis.
- Lymphomas arise from tonsils and cervical nodes are enlarged, besides, nodes in the axilla, groin and abdomen. Spleen and liver may also be enlarged.
- In 80-90% cases of Hodgkin's lymphoma painless, nontender, rubbery cervical lymph nodes are commonly seen



**Fig 59-15:** Hodgkin's lymphoma- front view and side view.

604/727

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580



**Fig 59-14:** Upper deep cervical metastatic nodes with diagnosis of supraglottic carcinoma (Courtesy: Dr Deena Singh, Director, ENT hospital Mauritius)

- i. Hand gun (low velocity),
- ii. Rifle (high velocity)
- iii. Shotgun (impact depends on distance)

**3. Based on site of injury**

- a. Internal – mucosal
- b. External

**4. Based on zones in the neck (Roos & Christensen's classification)**

- a. Zone 1- from sternum to cricoid.
- b. Zone 2- from cricoid to angle of mandible

**CERVICAL LYMPHADENITIS:****Definition:**

Lymphadenitis is defined as infective inflammation of lymph nodes.

It refers to nodes that are abnormal in either size, consistency or number.

It is defined as one or more enlarged and tender lymph nodes of the neck.

It is common in 1<sup>st</sup> decade of life, due to upper respiratory tract infections.

2. Subacute- cat-scratch disease
3. Chronic- Tuberculosis, syphilis

**Diagnosis:****1. History:**

- Localising symptoms suggest local illness - infection or neoplasm in a specific site
- Constitutional symptoms like fever, fatigue, weight loss suggest systemic illness like tuberculosis, lymphoma etc

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578

- Epidemiological clues suggest etiology towards occupational exposure, travel or high risk behaviour
- History of taking medications- like phenytoin which cause specific lymphadenopathy. Sulpha or cephalosporins may cause serum sickness like syndrome with lymphadenopathy.

**2. Location of nodes:**

- Upper deep cervical nodes suggest lesions in pharynx, nose, sinuses, tonsils
- Supraclavicular nodes suggest malignancy in 90% patients aged above 40 years v/s 25% patients below 40 years. Right side node can suggest carcinoma lungs, oesophagus or mediastinum. Left side node can suggest carcinoma testes, ovary, kidneys, pancreas, stomach or prostate.

**3. Characteristics of nodes:**

- Nodes lasting less than 2 weeks or more than one year with no increase in size are unlikely to be neoplastic and rules out low grade lymphoma.
- Matted nodes may suggest tuberculosis, sarcoidosis or metastatic carcinoma.
- Fixed nodes, hard nodes and fast growing nodes suggest malignancy.
- Rubbery nodes suggest -lymphoma, soft nodes- infection, fluctuant nodes - suppuration.
- Pain in a node suggests inflammation, haemorrhage in a malignant node.
- Size of node-less than 1 cm size had no cancer, 1 sq cm to 2.25 sq cm 8% had cancer, more than 2.25 sq.cm 38% had cancer.
- Progression of node- some times lymphoma nodes regress temporarily. One must keep a watch for recurrence.

**4. Investigations:****Pathology:****1. FNAC- safe, convenient and economical.**

- It can differentiate - infective, reactive, neoplastic and metastatic causes,
- can get material for culture, immunologic or genetic studies.
- It has high sensitivity -93% and specificity 99%.

**Limitations:**

- Inadequate tissue sample for special studies- cytogenetics, flow cytometry, electron microscopy.
  - Potential risk of seeing malignant cells in the tract.
  - Can not distinguish between lymphomas.
- Biopsy:** can be done bedside, in OT or on endoscopy.
    - Excision biopsy yields better results.

- Biopsy avoided during viral fevers, as it suggests false positive malignancy.
- Largest and most abnormal node must be excised for biopsy and not the most accessible node.

**Blood :**

- CBC- for glandular fever, leukaemia
- LFT and RFT for underlying systemic disease
- VDRL, HIV for syphilis, AIDS respectively

**Radiology:**

- USG neck** -can give the extent of the nodes, used as a guide for taking FNA in non palpable nodes.
- X-Ray chest** - shows
  - spotty calcification in tuberculosis,
  - enlarged mediastinal nodes or
  - primary occult tumour of the lungs.
- CT scan chest and abdomen**- in cases of supraclavicular lymphadenopathy- to rule out carcinoma breast, testes, ovary, prostate, kidneys etc.

**Treatment:** depends on the cause

**Delphian nodes and submental nodes are described above (page 569)**

**TUBERCULAR LYMPHADENITIS: (SCROFULA)**

It is a granulomatous inflammation with formation of a tubercle, caused by Mycobacterium tuberculosis- both bovine and human strains. Sometimes caused by atypical mycobacteria especially in HIV cases.

It is the commonest form of extra pulmonary tuberculosis. It is common in children and young adults. It can occur in any age and sex.

Tubercular cervical lymphadenitis is common in India.

**Pathology:**

**There are 5 stages**

**Stage 1:** Reactive hyperplasia- glands are enlarged, mobile, firm, with mild tenderness

**Stage 2:** Periadenitis -glands get adherent to each other-called "matting", tubercle formation -

tubercles contain Langhans giant cells, caseation and lymphocytes

**Stage 3:** Cold abscess- occurs due to caseation, necrosis and destruction

**Stage 4:** Collar- stud abscess- abscess bursts into subcutaneous space

**Stage 5:** Sinus formation: abscess bursts into skin with persistent discharging sinus opening. Also can form an ulcer with an undermined edge.

**Route of entry:**

Bacteria usually enter through the tonsils or hematogenous route.

**Types of clinical manifestation:**

**There are 4 types-**

1. Acute

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579

2. Caseating
3. Hyperplastic
4. Atrophic

**Acute type:**

Seen in infants and children below 5 years. Child is febrile. Nodes are painful, tender. Skin over the swelling is red and edematous.

**Caseating type:**

Most common type, seen in young adults. Patient is anaemic, malnourished with low grade fever,

1. Cap Rifampicin 600 mg OD
  2. Tab Isoniazid 300 mg OD
  3. Tab Ethambutol 1 Gm OD
  4. Tab Pyrazinamide 1.5 Gm OD
- Follow up phase: 2 drugs for 4 months

1. Cap Rifampicin 600 mg OD
2. Tab Isoniazid 300 mg OD.

**B. For cold abscess:**

- Zig zag aspiration with a wide bore needle in non

the lymphatic system during embryonic development.

2. 50% cases have chromosomal anomalies.
3. Lymphatics fail to communicate with venous system.
4. Abnormal budding of the lymphatic tissue

#### Other:

7. Alpha fetoprotein levels in amniotic fluid are elevated in pregnant woman with cystic hygroma foetus.

#### Treatment:

1. If infected- start I V antibiotics. Surgical excision done 3 months after infection is controlled.
2. Sclerosant therapy : can be tried;

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577

- a) with OK-432 ( inactive strain of group A streptococcus pyogenes)
  - b) pure ethanol
  - c) sodium tetradecyl sulphate
  - d) doxycycline – safe and effective
3. Surgical excision can be done around 2 years age. It must be done in toto in one go as repeat procedure is difficult due to fibrosis. Bipolar diathermy is used and care is taken for preservation of neural and vascular structures.

#### Contraindications for surgery:

- a) Premature infant
- b) Small lesion
- c) Nerves involvement -too small and difficult to identify-eg; facial nerve.



**Fig 59-11:** Cystic hygroma [Courtesy: Dr. Syed Sajjad Alam, RMO, LNHMC, Karachi, Pakistan]

#### Complications of surgery:

- a) Damage to vital nerves and blood vessels in the neck
  - b) Chylothorax
  - c) Chylous fistula
  - d) Haemorrhage
4. **In emergency airway block-** wide bore needle aspiration is done to avoid tracheostomy.
  5. **Recent advance: Magnetic resonance-controlled laser induced thermotherapy** is a novel idea.

**Prognosis:** Recurrence is 5% after complete excision and 50% if it is incomplete excision. Mortality is 2-6% due to pneumonia, bronchiectasis, respiratory distress.

#### CERVICAL LYMPHADENITIS:

##### Definition:

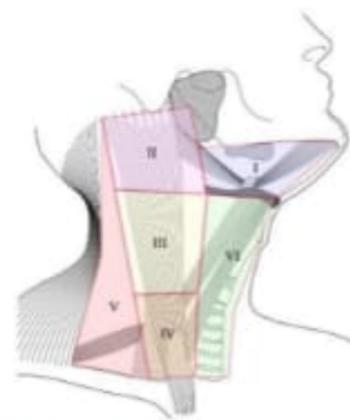
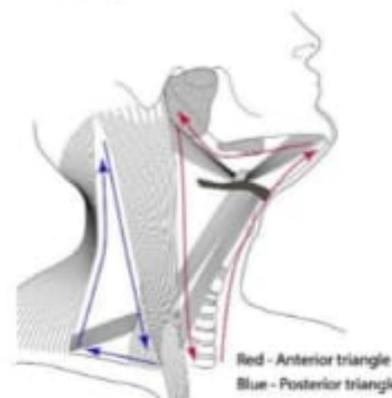
Lymphadenitis is defined as infective inflammation of lymph nodes.

It refers to nodes that are abnormal in either size, consistency or number.

It is defined as one or more enlarged and tender lymph nodes of the neck.

It is common in 1<sup>st</sup> decade of life, due to upper respiratory tract infections.

Viruses cause bilateral and gram positive bacteria cause unilateral lymphadenitis.



**Fig 59-12a, b:** Triangles of neck and cervical lymph node groups.(Courtesy Dr Simon Browning, Asso Prof., South Wales, UK)

#### Classification:

##### According to organism:

1. Bacterial –
  - a. Specific – TB, syphilis, Vincent's angina , tularaemia ( Rabbit fever- caused by francisella tularensis), brucellosis
  - b. Nonspecific- tonsillitis, pharyngitis ( caused by streptococci)
2. Viral- AIDS, infectious mononucleosis ( Epstein Barr virus), cytomegalovirus, Rubella
3. Protozoa- toxoplasmosis , leishmaniasis
4. Fungal- histoplasmosis

##### According to duration:

1. Acute- tonsillitis, dental abscess, Kawasaki disease ( seen in children below 5 years)
2. Subacute- cat-scratch disease
3. Chronic- Tuberculosis , syphilis

#### Diagnosis:

##### 1. History:

- Localising symptoms suggest local illness - infection or neoplasm in a specific site
- Constitutional symptoms like fever, fatigue, weight loss suggest systemic illness like tuberculosis, lymphoma etc

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578

- Epidemiological clues suggest etiology towards occupational exposure, travel or high risk behaviour
- History of taking medications- like phenytoin which cause specific lymphadenopathy. Sulpha or cephalosporins may cause serum sickness like syndrome with lymphadenopathy.

#### 2. Location of nodes:

- Upper deep cervical nodes suggest lesions in pharynx, nose, sinuses, tonsils
- Supraclavicular nodes suggest malignancy in

- Biopsy avoided during viral fevers, as it suggests false positive malignancy.
- Largest and most abnormal node must be excised for biopsy and not the most accessible node.

#### Blood :

- a) CBC- for glandular fever, leukaemia
- b) LFT and RFT for underlying systemic disease
- c) VDRL, HIV for syphilis, AIDS respectively

#### Radiology:

3. **USG neck** -can give the extent of the nodes, used as a guide for taking FNA in non palpable nodes

**Fig 59-6:** Lymphangioma and haemangioma  
(Courtesy: [www.entokey.com](http://www.entokey.com))

**CAROTID BODY TUMOUR:( Potato tumour; Chemodectoma)**

It is chronic, very slow growing tumour, in the lateral side of the neck in the anterior triangle,

- It presents mostly after 40 years age. Bilateral in 10% cases.

**Etiology:**

- It arises from chemoreceptor cells in the carotid body which is present at the bifurcation of the

to pressure on the carotid sinus by the mass.

**Investigations:**

**Radiology:**

- CE CT Scan –Neck
- C. T Angiogram of carotid artery
- MRI with gadolinium contrast- MRI angiography is diagnostic and shows splaying of internal and external carotid arteries and it is called- “Lyre’s sign” the extent of the tumour.

**Others:**

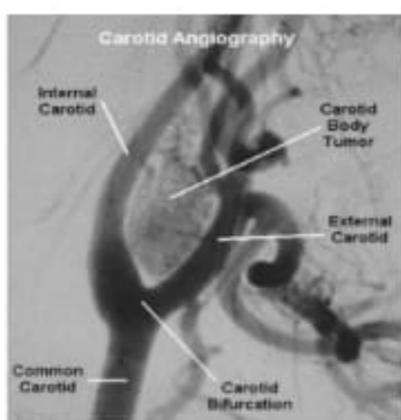
- Serum catechol amines

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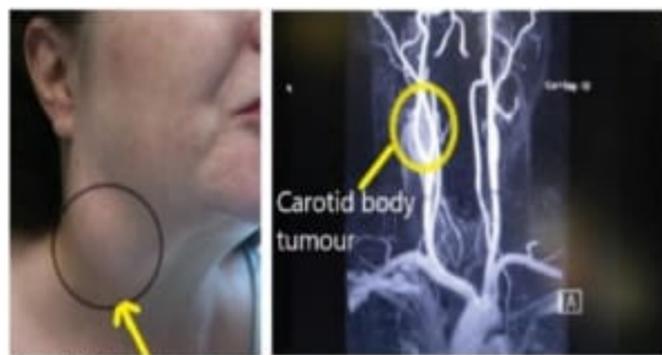
- Urine- metanephrines and VMA- vanillylmandelic acid.
- **FNAC and biopsy are absolutely contraindicated due to its vascularity.**



**Fig 59-7a:** Carotid body tumour  
(Courtesy: Dr Ghorayeb-www.houstonoto.com)



**Fig 59-7b:** Carotid Angiogram showing carotid body tumour-Lyre’s sign



**Fig 59-8a,b:** Carotid body tumour  
( Courtesy: [www.entokey.com](http://www.entokey.com))

**Differential diagnosis:**

1. Vagal paraganglioma- produces Pseudo Lyre sign. Carotid vessels are displaced anteriorly.
2. Carotid artery aneurysm
3. Neurofibroma of vagus nerve

**Treatment:**

1. **Surgical excision** is indicated in fit patients and those below 50 years:

**Indications:**

- a) Mass extending into the oropharynx causing difficulty in breathing,swallowing and phonation.

**Complications of surgery:**

- a) Bleeding
- b) Hemiplegia
- c) Injury to vagus , superior laryngeal nerve and accessory nerve

**2. Radiotherapy**

**Indications:**

- a) For those patients unfit for surgery,
- b) Patients who refuse surgery,
- c) Have a metastatic disease and
- d) Above 50 years.

**PLUNGING RANULA:**

It is due to extravasation of saliva due to **obstruction of the sublingual salivary gland duct.**

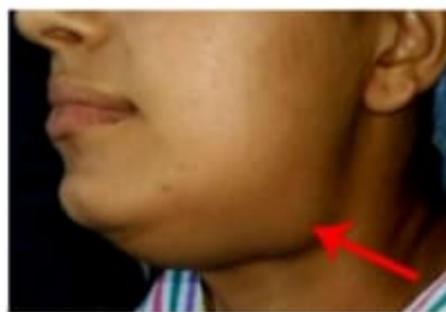
It presents in the submandibular region and also may co-exist with ranula in the floor of the mouth.

It is a pseudocyst and it is highly translucent.

**Treatment:** It is surgical and the procedure is sublingual salivary gland excision with the cyst.



**Fig 59-9a:** Ranula( Courtesy: Dr Manjit Singh, Prof &HOD,ENT, GMC ,Amritsar, India)



**Fig 59-9b:** Plunging Ranula

**LIPOMA NECK**

It is a common benign neck mass. Usually seen in adults above 35

Usually asym

It is a soft, il

**Treatment:**

600/727

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It is often associated with Noonan, Turner, Klinefelter, Down syndromes , Trisomy 13 and 18 anomalies and intrauterine alcohol exposure

- It appears in the supraclavicular region and extends to posterior triangle and axilla
- It may occur in the tongue and floor of the mouth.

- Nontender unless infected
- Fluctuant mass
- Mass overlies the sternocleidomastoid muscle
- If cyst ruptures, it presents as a sinus
- Mucoïd discharge in fistula

the tract and its tip is left to identify the internal opening in the tonsillar fossa.

#### For cyst,

1. Its bed needs to be dissected and associated fistula should be explored and excised.
2. The spinal accessory, hypoglossal and vagus nerves have to be identified and protected from injury during the dissection.
3. Cysts lying medial to carotid sheath are approached transorally.

**For 3<sup>rd</sup> and 4<sup>th</sup> arch cysts/fistulae**, there are two approaches for excision.

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574

- **External approach-** excision of the tract with endoscopic assisted cannulation. Ipsilateral hemithyroidectomy with partial resection of thyroid cartilage for 4<sup>th</sup> pouch anomaly.
- **Internal approach-** Endoscopic electric or silver nitrate cauterization

#### Complications:

- **of cyst** : if not treated in time, can get infected, rupture with scarring and sinus formation.
- **of surgery:**
  - a) damage to carotid arteries, facial nerve, hypoglossal nerve, vagus and lingual nerves.
  - b) Permanent damage to recurrent laryngeal nerve,
  - c) post operative pharyngo cutaneous fistula.
- Recurrence is also possible.

#### LYMPHANGIOMA

It is malformation of the lymphatic system. It occurs in children less than 2 years in 90% cases. It can be congenital or acquired. Congenital lesions are associated with chromosomal abnormalities such as Turner's syndrome. They can be diagnosed before birth by fetal ultrasonography. CT scan and MRI are used in diagnosis. Treatment is surgical excision.

#### HAEMANGIOMA

It is benign vascular tumour. Most common type are infantile and congenital haemangioma. Infantile type appears after birth. Congenital type appears at birth. Haemangioma involute on its own. Oral and topical betablockers, corticosteroids are effective. Laser excision is also done.



**Fig 59-6:** Lymphangioma and haemangioma (Courtesy: [www.entokey.com](http://www.entokey.com))

#### CAROTID BODY TUMOUR:( Potato tumour; Chemodectoma)

It is chronic, very slow growing tumour, in the lateral side of the neck in the anterior triangle,

- It presents mostly after 40 years age. Bilateral in 10% cases.

#### Etiology:

- It arises from chemoreceptor cells in the carotid body which is present at the bifurcation of the

common carotid artery and it is present in the tunica adventitia of the artery.

- It can occur in people living at very high altitudes due to chronic hypoxia

#### Pathophysiology:

- It is derived from neural crest and it is useful for maintaining blood levels of O<sub>2</sub>, CO<sub>2</sub> and pH. Some tumours are functional and secrete catecholamines.
- It has well developed capsule, and it is creamy, yellowish tumour with dense fibrous tissue.
- Blood supply is from external carotid artery and ascending pharyngeal artery.
- In 10% cases, it is locally malignant.
- In 20% cases, it can spread to regional lymph nodes and lungs.

#### Types:

1. Sporadic- 75%
2. Familial- 20%
3. Hyperplastic- 5%

#### Symptoms:

- Painless, very slow growing mass, in the side of the neck.
- Headache
- Neck pain
- Dysphagia
- Syncopal attacks
- Deviation of tongue ( 12<sup>th</sup> CN palsy)
- Hoarseness of voice ( RLN palsy)
- Drooping shoulder ( spinal accessory nerve palsy)

#### Signs:

- Pulsatile, firm mass, may be rubbery, compressible
- Mobile from side to side, but not vertically (**Fontaine sign**)
- Bruit is heard on the swelling.
- It extends into the parapharyngeal space and present in the oropharynx.
- Horner's syndrome – ( cervical sympathetic involvement)
- Sudden attacks of fainting and fall attacks on turning the neck-“Carotid body syncope” – due to pressure on the carotid sinus by the mass.

#### Investigations:

##### Radiology:

- CE CT Scan –Neck
- C. T Angiogram of carotid artery
- MRI with angiogram internal called- “L

##### Others:

- Serum catechol amines

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575

- Urine- metanephrines and VMA- vanillylmandelic acid.
- **FNAC and biopsy are absolutely contraindicated due to its vascularity.**



- a) Mass extending into the oropharynx causing difficulty in breathing,swallowing and phonation.

#### Complications of surgery:

- a) Bleeding
- b) Hemiplegia
- c) Injury to vagus, superior laryngeal nerve and accessory nerve

#### 2. Radiotherapy

Branchial cleft cysts form about 20% of neck masses in children

**Second branchial cleft anomalies are most common (95%).**

- It can be unilateral or bilateral.
- It is seen in all races and both sexes.
- Seen usually in late childhood or early adulthood.

**BRANCHIAL CYST:**

- c. **Type 3-** lies between the internal and external carotid arteries, extending to skull base or lateral wall of pharynx.
- d. **Type 4** – lies medial to great vessels of neck at tonsillar fossa level.

- **Cyst** manifests as smooth, soft mass, in the lateral neck anterior and deep to sternocleidomastoid (SCM) muscle. Mostly seen in 20-30 yrs age group patients. Swelling increases in size after URTI.
- **Fistula** manifests as recurrent neck infection following URTI. It is commonly seen along the anterior border of SCM.
- It has internal opening in the tonsillar fossa and external opening along the anterior border of the sternocleidomastoid muscle. The tract ascends deep to deep cervical fascia, external carotid artery, post belly of digastric, stylohyoid muscle. It runs superficial to internal carotid artery and hypoglossal nerve.

### 3. THIRD BRANCHIAL CLEFT FISTULA

- It has internal opening in the pyriform sinus and external opening in the anterior border of SCM.
- Third branchial cleft runs deep to internal and external carotid arteries and superficial to vagus and hypoglossal nerves.
- It is closely related to thyroid gland and when inflamed causes thyroiditis.

### 4. FOURTH BRANCHIAL CLEFT CYST

- It presents as lateral cervical cyst with an internal opening in the pyriform sinus.
- Seen mostly in children.
- At birth, presents as lateral neck mass or abscess with obstructive airway symptom.
- In children or adult, it manifests as recurrent lateral neck abscess and recurrent thyroiditis.

#### Symptoms:

- Painless, solitary swelling in the lateral neck
- Pain -if infected
- Fluid discharge if it is fistula

#### Signs:

- Smooth, cystic mass
- Nontender unless infected
- Fluctuant mass
- Mass overlies the sternocleidomastoid muscle
- If cyst ruptures, it presents as a sinus
- Mucoid discharge in fistula

### 2. SECOND BRANCHIAL CLEFT CYST / FISTULA

It is most common and represent 90-95% of cases. Cyst is more common than fistula.

#### Branchial cleft anomalies classification: ( Bailey)

- a. **Type 1-** lies deep to platysma but anterior to SCM muscle.
- b. **Type 2-** lies in contact with great vessels of the neck, deep to submandibular gland, antero-medial to SCM muscle.



Fig 59-5: Branchial cyst

#### Investigations:

##### Radiology:

1. USG neck – differentiates cystic and solid mass
2. Sinogram- if it is sinus
3. Fistulogram – fluoroscopic or CT fistulogram
4. CECT neck- helps in planning surgery and to identify surrounding structures. It is first choice investigation.
5. MRI -neck

##### Other:

6. FNAC to differentiate from malignant neck mass. Also helps in culture study if it is infected.

##### Diagnosis:

It is always a clinical diagnosis as the mass always appears consistently anterior to sternocleidomastoid muscle.

##### Differential diagnosis:

1. Secondaries from carcinoma tonsil, tongue base and thyroid. They can present as cystic mass.
2. Thyroglossal cyst- it moves on deglutition.

##### Treatment:

1. Medical- antibiotics- if infected
2. Sclerotherapy- with OH 432 ( picibanil)
3. Surgical –

##### For 2<sup>nd</sup> branchial cleft fistula,

1. complete excision is done by step ladder incisions. This is treatment of choice. Transverse elliptical incision is placed around the external opening over the skin fold.
2. Methylene blue dye is injected to highlight the fistula track in its entirety. Probe is passed in the tract and its tip is felt to identify the internal opening in the tonsillar fossa.

##### For cyst,

1. Its bed needs to be dissected and associated fistula shown.
2. The spiral nerves have to be identified from internal to external.
3. Cysts lying deep to the sheath are approached transorally.

**For 3<sup>rd</sup> and 4<sup>th</sup> arch cysts/fistulae**, there are two approaches for excision.

- **External approach-** excision of the tract with endoscopic assisted cannulation. Ipsilateral hemithyroidectomy with partial resection of thyroid cartilage for 4<sup>th</sup> pouch anomaly.
- **Internal approach-** Endoscopic electric or silver nitrate cauterization

#### Complications:

- **of cyst**: if not treated in time, can get infected,

common carotid artery and it is present in the tunica adventitia of the artery.

- It can occur in people living at very high altitudes due to chronic hypoxia

#### Pathophysiology:

- It is derived from neural crest and it is useful for maintaining blood levels of O<sub>2</sub>, CO<sub>2</sub> and pH. Some tumours are functional and secrete

- Epidermoid cysts
- Cystic metastatic lymph nodes
- Sub-hyoid bursitis
- Delphian node lesion
- Teratoma

develop in the cysts.

- It contains cheesy material.
- Treatment is simple excision.

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572



Fig 59-4: Epidermoid cyst

#### THYMIC CYST

Thymic cysts or solid mass develop anywhere from the angle of the mandible to the midline of the neck. It is a very rare condition. It can occur in children or adults.

It is present as neck mass anterior and deep to middle third of the sternocleidomastoid muscle. It is unilocular mass. Mass can extend into mediastinum.

#### Differential diagnosis:

Cystic hygroma is multilocular.

#### Treatment:

Surgical excision. Sternotomy is done, when the mass extends to mediastinum.

#### BRANCHIAL CLEFT CYST, SINUS AND FISTULA:

Branchial apparatus was first described by Von Baer and Branchial anomalies were first described by Von Asheroni.

Branchial cysts, fistulae and sinuses can arise from first to fourth branchial arches. Normally external auditory canal develops from first branchial arch and the other three branchial clefts obliterate in prenatal period. In prenatal stage, the second arch grows caudally and covers the second, third and fourth branchial clefts. The cervical sinus of HIS is formed by the fusion of the second arch with the fifth arch ridge. The edges of the cervical sinus of HIS gradually fuse and hence no defect is seen in normal individuals. But, persistence of this intervening ectoderm gives rise to branchial cyst. Branchial fistulae develop due to breakdown of the endoderm. Branchial cleft cysts form about 20% of neck masses in children

**Second branchial cleft anomalies are most common (95%).**

- It can be unilateral or bilateral.
- It is seen in all races and both sexes.
- Seen usually in late childhood or early adulthood.

#### BRANCHIAL CYST:

It is collection of fluid in an epithelium lined sac. Cyst is formed when part of the branchial cleft fails to fuse and close. It is lined by squamous epithelium or respiratory epithelium. 80% cases have lymphoid tissue in their wall. Cyst contains straw coloured fluid in which cholesterol crystals are found. Cheesy toothpaste like material is present in the cyst if the lining is squamous epithelium because of sebaceous glands in the lining.

**BRANCHIAL SINUS:** It is a blind ended track leading from an epithelial surface into deeper tissues (partial fistula). It occurs when groove or pouch fails to resorb.

**BRANCHIAL FISTULA:** It is not a true fistula, as it rarely has two openings. Even if both openings are present, usually a thin membrane covers the internal opening. It represents persistence of both the cleft and the corresponding pouch forming a communication that is epithelial lined. The fistula lies caudal to the structures that are derived from that particular arch and connects the skin to the foregut. It is lined by stratified squamous, columnar or ciliated epithelium.

#### 1. FIRST BRANCHIAL CLEFT CYST/ FISTULA

It is rare, and if present it is seen around the ear or below the mandible. It is common in females than males. It involves EAC or sometimes middle ear. Its course is close to superficial lobe of parotid gland.

There are 2 types.

- **Type 1-** it has ectodermal derived tissues. There is duplication of EAC immediately anterior, posterior or inferior to pinna. Its course is lateral to facial nerve.
- **Type 2-** it has both ectodermal and mesodermal derived tissues. It terminates in EAC, behind or below the mandible. It passes medial to facial nerve. It is more common than type 1.

**Symptoms-** otorrhoea, parotid swelling, unilateral facial palsy, discharge from a pit on the mandible.

- **Treatment:** Total parotidectomy in first branchial cleft cysts.

#### 2. SECOND BRANCHIAL CLEFT CYST / FISTULA

It is most common and represent 90-95% of cases. Cyst is more common than fistula.

#### Branchial cleft anomalies classification: (Bailey)

- Type 1-** lies deep to platysma but anterior to SCM muscle.
- Type 2-** lies in contact with great vessels of the neck, deep to submandibular gland, antero-medial to SCM muscle.

597/727

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573

- Type 3-** lies between the internal and external carotid arteries, extending to skull base or lateral wall of pharynx.
- Type 4** – lies medial to great vessels of neck at tonsillar fossa level.

- **Cyst** manifests as smooth, soft mass, in the lateral neck anterior and deep to sternocleidomastoid (SCM) muscle. Mostly seen in 20-30 yrs age group patients. Swelling increases in size after URTI.

- **Fistula** manifests as recurrent neck infection following URTI. It is commonly seen along the anterior border of SCM.

- It has internal opening in the tonsillar fossa and



Fig 59-5: Branchial cyst

#### Investigations:

#### Radiology:

1. USG neck – differentiates cystic and solid mass

and yielding. Sensation is felt by the watching fingers.

Investigation: 1) FNAC. 2) CT scan to know the size, shape and local extent of the swelling.



Fig 59-1: Thyroglossal cyst track (Dr Simon)

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571

#### Investigations:

- Ultrasound neck- is the investigation of choice- readily available, cheaper, noninvasive
- Blood for TFT- Thyroid function tests – to rule out ectopic thyroid tissue
- CT scan / MRI neck- not essential- to know extent of lesion
- FNAC



Fig 59-2a: Thyroglossal cyst -Hyoid level in an adult



Fig59-2b: Thyroglossal cyst hyoid level-in a child



Fig59-2c : Thyroglossal cyst Sub hyoid level- adult

#### Differential diagnosis:

- Dermoid cyst
- Epidermoid cysts
- Cystic metastatic lymph nodes
- Sub-hyoid bursitis
- Delphian node lesion
- Teratoma

#### Treatment:

- Surgery is the only treatment of choice. The procedure is Sistrunk operation. It should be excised with its tract in full, with a part of the body of the hyoid and core of the tongue tissue around the tract up to the foramen cecum.

- Ethanol sclerotherapy if patient refuses surgery

#### Complications of Sistrunk operation:

- Recurrence is 10% if the tract removal is incomplete.
- Injury to larynx/trachea
- Injury to hypoglossal nerve

#### Post-operative advice:

- Avoid lifting heavy weights for 2-6 weeks
- Rest for 1 week from school / duty

### LATERAL NECK MASSES

#### THYROID SWELLINGS

See chapter 60.



Fig59-3 :Goitre

#### EPIDERMOID CYST:

It is an inclusion cyst.

- It occurs in face, scalp, neck and back.
- It is due to entrapped epidermal elements in dermis during embryonic life, or due to traumatic or surgical implantation, or occlusion of a pilosebaceous unit.
- In Indian patients, 63% cases have melanin pigment in the cysts.
- It is common in both sexes, in 3<sup>rd</sup> to 4<sup>th</sup> decade.
- Generally, they are asymptomatic, but can get infected and inflamed, causing swelling and pain.
- Rarely, squamous cell carcinoma, melanoma can develop in the cysts.
- It contains cheesy material.
- Treatment is simple excision.

596/727

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572



Fig 59-4: Epidermoid cyst

#### THYMIC CYST

Thymic cysts or solid mass, develop anywhere from

It is collection of fluid in an epithelium lined sac. Cyst is formed when part of the branchial cleft fails to fuse and close. It is lined by squamous epithelium or respiratory epithelium. 80% cases have lymphoid tissue in their wall. Cyst contains straw coloured fluid in which cholesterol crystals are found. Cheesy toothpaste like material is present in the cyst if the lining is squamous epithelium because of sebaceous glands in the lining.

**BRANCHIAL SINUS:** It is a blind ended track leading from an epithelial surface into deeper tissues (partial fistula). It occurs when groove or pouch fails to resorb.

**BRANCHIAL FISTULA:** It is not a true fistula, as

8. Parotid tail tumour
9. Parapharyngeal tumour / abscess
10. Laryngocoele
11. Pharyngeal pouch
12. Sternomastoid tumour

#### B. Supraclavicular triangle

1. Metastatic nodes from Breast, Lungs, GI tract, Kidney, Ovary / Testis
2. Cystic hygroma
3. Subclavian aneurysm

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#### SUBMENTAL NODES / DELPHIAN NODES:

These nodes are enlarged either due to inflammation or malignancy.

#### SUBMENTAL NODES

There are 2-8 nodes between the platysma and the mylohyoid muscle in the submental triangle. Lymphatics from chin, lower lip middle part, anterior floor of mouth and tip of the tongue. Infections or

570

malignancy has to be ruled out in these areas, if these nodes are enlarged.

It may be rarely involved in cases of papillary carcinoma of thyroid isthmus with aggressive tumour biology.

#### DELPHIAN NODE,

Also called Prelaryngeal node. It was first described in 1948 and is named after "Oracle of Delphi" as it foretells the prognosis of thyroid cancer or laryngeal cancer due to which there is metastasis in this node.

- Delphian node ( DN) gets involved in vocal cord growths extending to anterior commissure.
- DN involved with thyroid cancer, is predictive of aggressive tumour biology and can lead to persistent or recurrent disease with extension to surrounding tissue, if it is not excised. It is suggested that DN is a "sentinel node" of thyroid carcinoma.
- If there is DN metastasis with thyroid isthmus or its upper third carcinoma, 79% cases will have additional level VI nodes. Also, it is associated with large tumours, extension beyond the thyroid gland and lymphovascular invasion.
- It is difficult to identify this node unless it is specifically looked for or it can get damaged or split while splitting the strap muscles to open the neck. Also, it can mimic cricoid muscle, pyramidal lobe or fatty tissue.
- If the node is left and gets enlarged, it can invade trachea and larynx, can give double chin appearance or Adam's apple appearance in females.

#### SUBLINGUAL DERMOID CYST:

It occurs at the line of embryonic fusion, due to inclusion of the epithelium beneath the surface. The cavity contains putty like desquamated material, hair follicle and sweat glands.

It is a submental swelling, arises from the floor of the mouth, and needs differentiation from ranula. It is insidious in onset, slowly progressive. It is smooth, soft, fluctuant, non-tender swelling. Skin over the swelling is pinchable. It does not move on protrusion of the tongue. Transillumination test is negative.

Paget's test is positive. Test method- fix the swelling with two fingers (watching fingers). Center of the swelling is indented with index finger of the other hand ( displacing finger). It feels soft at the center and yielding. Sensation is felt by the watching fingers.

Investigation: 1) FNAC. 2) CT scan to know the size, shape and local extent of the swelling.

Dermoid cyst is also seen in the midline above the suprasternal notch. Treatment is surgical excision under general anaesthesia.

#### THYROGLOSSAL CYST:

This is most common congenital midline cystic anomalous neck mass with 7% prevalence but only a few develop symptoms.

- Carcinoma can develop in the cyst in less than 1% cases, of which 93% are papillary type carcinoma.
- It may contain only functioning thyroid gland. Hence thyroid scan has to be done before the excision to rule out presence of normal thyroid tissue elsewhere.

#### Incidence:

- Both men and women are equally affected.
- It can appear in children or adults.
- 50% cases present before 20 years age.
- Rarely it is hereditary.

#### Embryology:

- Thyroid duct grows from foramen caecum, passes through base of tongue and descends in front or behind or through the hyoid bone to form the thyroid gland.
- Thyroglossal cyst can occur anywhere in the course of the duct. 20-25% cysts are above hyoid, 15-20% at the hyoid level, 25-65% below the hyoid level.

#### Symptoms:

- Swelling in the neck
- Pain in the swelling, if infected
- Dysphagia

#### Signs:

- Because of the attachment to the tongue, it moves with both deglutition and tongue protrusion. This is most important differentiating point from sublingual dermoid cyst.
- It is rounded and 2-4 cms in size , cystic mass.
- It may present as a draining sinus.
- Mass may be tender if infected.

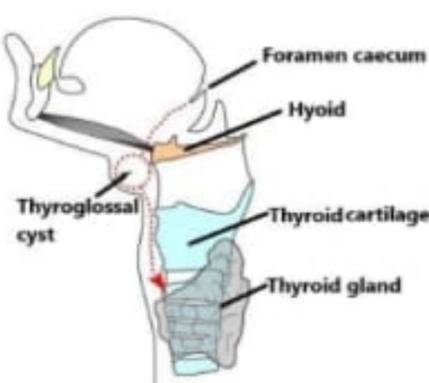


Fig 59-1: Thyroglossal duct cyst

595/727

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571

#### Investigations:

- Ultrasound neck- is the investigation of choice- readily available, cheaper, noninvasive
- Blood for TFT- Thyroid function tests – to rule out ectopic thyroid tissue
- CT scan / MRI neck- not essential- to know extent of lesion
- FNAC

#### Treatment:

- Surgery is the only treatment of choice. The procedure is Sistrunk operation. It should be excised with its tract in full, with a part of the body of the hyoid and core of the tongue tissue around the tract up to the foramen caecum.
- Ethanol sclerotherapy if patient refuses surgery

#### Complications of Sistrunk operation:

- Recurrence is 10% if the tract removal is incomplete.
- Injury to larynx/trachea
- Injury to hypoglossal nerve

#### Post-operative advice:

- Avoid lifting heavy weights for 2-6 weeks
- Rest for 1 week from school / duty



A) What is the diagnosis?

1. Thyroglossal cyst
2. Adenoma thyroid
3. Nodular cystic goiter\*\*
4. Lymphoma

3. Lobectomy
4. Hemithyroidectomy

**CASE STUDY 1**

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595

Q2) A 40 year old male with history of midline neck swelling for one and a half months, gradually increasing in size. No history of fever, difficulty in swallowing, loss of weight, DM, TB, HTN.O/E – swelling of 5cm diameter in midline of neck moves on deglutition but not on protrusion of tongue, diffuse border and on palpation cystic in middle and firm on periphery, nontender. USG neck – hypoechoic area (5x4 cm ) FNAC – plenty of pus cells, AFB, polymorphs and few lymphocytes.

A) Diagnosis is

1. Cystic thyroid nodule
2. Cold abscess\*\*
3. Thyroglossal cyst
4. Pyogenic abscess

B) Treatment options:

1. Incision and drainage from non dependent part\*\*
2. Thyroidectomy
3. ATT with antibiotics
4. Only ATT.

**CASE STUDY 3**

Q3) A 45 year old female patient presented with painful, swelling in thyroid region for 4 months, rapidly progressing in size with weight loss and dysphagia. O/E 8x6 cms mass in thyroid region seen and felt, hard in consistency, moves with deglutition but not with protrusion of tongue. HPE showed-orphan annie eye appearance of nuclei of follicular cells and psammoma bodies.

A) Diagnosis is;

1. Papillary carcinoma\*\*
2. Follicular carcinoma
3. Hurthle cell carcinoma
4. Lymphoma

B) Treatment options are:

1. Lobectomy with isthmusectomy
2. Near total thyroidectomy for both lobe diseases
3. Total thyroidectomy in high risk cases
4. All of the above\*\*.

**Answers:**

Q1) A-3, B-4, C-2

Q2) A -2, B-1

Q3) A-1,B-4

**PRAYER IS THE KEY TO HEAVEN BUT FAITH UNLOCKS THE DOOR.**

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596

620/727

**CHAPTER 61 :****HIV / AIDS in ENT****Non-core competency:**

**EN 4.53:** Describe the clinical features, investigations and principles of management of HIV manifestations in ENT.

**INTRODUCTION:**

Robert Gallo discovered that HIV virus is responsible for AIDS. HIV is still a serious problem worldwide. It is caused by a RNA retrovirus and there are two types- HIV1 and HIV 2. Type 1 is more common and more pathogenic. It infects T lymphocytes, macrophages and CNS dendritic cells. As the immune system gets compromised, body succumbs to opportunistic infections.

virus enters the body, it binds to cell membrane of T lymphocytes, viral RNA changes to DNA by the reverse transcriptase enzyme present in viral core. Viral integrase, another enzyme, helps viral DNA to integrate to host's DNA. This DNA is called provirus, and it directs the cell to produce more virus particles which enter the blood stream and attack other T lymphocytes.

There are 3 phases in AIDS illness



5. Lugol's iodine- used prior to surgery to control gland vascularity  
**B. Surgical:**

**Incidence:** common in females above 50 yrs age.  
**Family history** of other autoimmune diseases present.

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Very variable, in onset, type of goiter and function, It can be associated with papillary carcinoma and lymphoma.

**Pathology:** there is diffuse infiltration of lymphocytes

**Symptoms:** neck swelling, symptom of toxicity initially and later it can be hypothyroidism.

**Signs:** diffuse or nodular goiter, with bosselated feel

**Investigations:**

1. Anti-Thyroid antibodies against thyroid peroxidase and thyroglobulin ,present in 85% cases
2. FNAC
3. Thyroidectomy and biopsy if any compression symptoms

**Treatment:**

Thyroxine for hypofunction.

**HYPOTHYROIDISM**

Symptoms	Signs
Weight gain	Loss of hair
Cold intolerance	Puffiness of face
Coarse and sparse hair	Puffiness of hands and feet
Dry skin	Dry and coarse skin
Poor memory and lack of concentration	Bradycardia
Deafness	
Constipation	
Menorrhagia	
Fatigue and weakness	

Table 60-1: Clinical features of hypothyroidism

**CLINICAL FEATURES OF THYROTOXICOSIS:**

SYMPTOMS	SIGNS
Loss of weight inspite of increased appetite	Tremors
Heat intolerance and sweating	Warm and moist skin
Diarrhoea	Diffuse alopecia
Fatigue and weakness	Diffuse or nodular goiter
Irritability	Tachycardia
Hyperactivity	High pulse pressure
Nervousness, tremors	Exophthalmos
Palpitations	Lid retraction – in Grave’s disease only
Decreased menstrual bleeding	Periorbital oedema - in Grave’s disease only
Hair loss	Pretibial myxoedema - in Grave’s disease only

Table 60-2: Clinical features of thyrotoxicosis

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**BENIGN NEOPLASMS:**

- Adenoma is the most common type, common in middle age females, rarely turns toxic.
- It may be only functioning and autonomous nodule.
- Follicular adenoma is the common cause of a solitary nodule in children and adolescents.
- It is called cold nodule and can turn malignant in 25% cases.

**MALIGNANCY**

**PAPILLARY CARCINOMA:**

- It is the most common thyroid cancer- 70%, 7.7% per 1 lakh population.
  - Females 3 times more affected than males.
  - Age- 45 years in females, 65 years in males.
- It is seen in areas with adequate iodine intake in contrast to follicular carcinoma which occurs in low iodine intake areas.

**Causes:**

1. Childhood radiation
2. Victims of nuclear disaster
3. Family history -first degree relatives have thyroid cancer in 5-10% cases of Papillary carcinoma
4. History of thyroid cancer syndromes- Cowden disease, Gardner’s syndrome, Carney complex



616/727

Fig 60-3: Anaplastic carcinoma -thyroid ( Courtesy: [www.entokey.com](http://www.entokey.com))

**Radiological:**

4. Chest X-ray -for any pulmonary metastasis in malignant lesions.
5. Ultrasound Neck
6. CT scan and MRI Neck- to know extent of disease and retrosternal extension

**Histopathology**

7. Ultrasound guided FNAC – 100% sensitive.67% specific-
  - Orphan Annie eye appearance- nuclei of follicular cells are folded or grooved with intranuclear cytoplasm.
  - Psammoma bodies- laminated calcified bodies.

**Treatment:**

1. Lobectomy with isthmusectomy- for tumour less than 1.5 cm size
2. Total or near-total thyroidectomy for both lobe



**RETROSTERNAL GOITER:**

**Definition:** more than 50% of the goiter is below the suprasternal notch.

If intrathoracic extension reaches upto 4<sup>th</sup> thoracic vertebra, more than 2 cms in anterior mediastinum or if it requires mediastinal dissection, it is said to be major intrathoracic extension.

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It is an ectopic thyroid gland and it is a developmental anomaly, in which thyroid gland grows at the base of the tongue. It may be only functioning thyroid tissue.

- It is common in females- 4:1, appears in teenage, coinciding with puberty and also seen during pregnancy. Incidence- 1 in 1,00,000.
- It can be asymptomatic. 70% cases present with hypothyroidism. 10% as cretins.

589

- It can become nodular, toxic or malignant. Follicular carcinoma is most common. Papillary carcinoma is very rare.

**Symptoms:**

- Swelling in the tongue
- Dysphagia for solids
- Bleeding from mouth
- Snoring and sleep disturbance – apnoeic attacks during sleep
- Change in voice
- Foreign body sensation

**Signs:**

- Pink or strawberry like round mass in the base of the tongue
- Hot potato voice
- Tracheal rings are bare.

**Investigations:**

- Radioisotope study- most important in confirming the function of the gland and absence of thyroid in the neck.
- Ultrasonography neck- to confirm absence of thyroid gland in the neck.
- MRI neck
- FNAC and biopsy.
- Thyroid function tests.

**Differential diagnosis:**

- Lingual tonsil
- Carcinoma tongue base
- Lipoma, hemangioma,
- Sarcoma, salivary gland tumour

**Treatment:**

- **Medical-** L -thyroxine daily orally.
- **Surgical-**

**Indications-**

- obstructive lesions-
- bleeding
- sudden increase in size
- suspected malignancy

**Procedure:**

- Transoral approach excision by cold dissection or laser or harmonic scalpel. Mucosa is sutured with polyglatin.
- In extensive lesions or in malignancy – external approach is used with mandibulotomy and trans hyoid/suprahyoid/lateral pharyngotomy

- **Radioisotope therapy**

**THYROTOXICOSIS:**

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**ETIOLOGY:**

- Grave's disease-( also called Basedow disease or primary thyrotoxicosis) seen in young females than men, ratio- 5:1, it is due to antibodies against TSH receptors. Incidence -60%
- Toxic multi nodular goiter- also called secondary thyrotoxicosis or Plummer disease- 20%
- Toxic, autonomous nodule( Goetsch disease)- 5%
- Functioning thyroid cancer / metastasis
- Excess thyroxine intake- Thyrotoxicosis factitial- taking L-thyroxine more than normal
- T-3 thyrotoxicosis
- De Quervain's thyroiditis or Autoimmune Thyroiditis
- Jod Basedow thyrotoxicosis- due to intake of large doses of iodides. [Jod means iodine in German].

**EYE SIGNS IN THYROTOXICOSIS:**

- Von Graefe's sign: Lid lag sign-** inability of upper eye lid to keep pace with downward movement of the eye ball, while following the examiner's finger. **Second sign to appear.**
- Dalrymple's sign-** upper eyelid retraction with visible upper sclera
- Stellwag's sign-** is the **first sign to appear-** staring look- absence of normal blinking.
- Joffroy's sign-** when head is bent down, forehead wrinkling is absent. **Third sign to appear.**
- Moebius sign-** lack of convergence of eye balls. **Fourth sign to appear-** severe case
- Naffziger's sign-** protruding eye balls on looking from behind at the patient sitting with extended neck
- Jellinek's sign-** Increased pigmentation of eyelid margins
- Rosenbach's sign-** tremor of closed eyelids
- Enroth sign-** Oedema of the eye lids and conjunctiva
- Lowe's sign-** Pupil dilatation with adrenaline lotion
- Cowen's sign-** Jerky contraction of pupil on consensual light
- Gifford's sign** – difficulty in everting upper eye lid
- Knies's sign-** Unequal pupillary dilatation.

590

**THYROID DERMOPATHY:** it includes,

- Pretibial myxoedema,
- Palmar erythema,
- Facial contracture,
- Thinning of hair and pruritis.

**Pretibial myxoedema:**

It is bilateral, symmetrical, shiny, dry, red, thickened skin due to mucin like deposits in skin and subcutaneous tissues. Skin becomes cyanosed due to cold.

**THYROID ACROPACHY:** It is clubbing of fingers and toes, seen in Grave's disease

**THYROID MYOPATHY:** It is proximal muscle weakness, resembles myasthenia gravis in severe cases. Recovers with treatment of hyperthyroidism.

**Investigations for thyrotoxicosis:**

- Thyroid function tests- T3, T4 levels are very high, TSH very low. Sometimes, only T3 is high- when it is called -T3 Thyrotoxicosis.
- $I^{131}$  or  $^{99}Tc$  - Radioisotope scanning study- Former isotope causes more radiation. Latter is safe, fast and cheap

**Advantages-** high cure rate, less need for biopsy, better for women, less need for coexisting parathyroid tumour, less need for goiters.

**Disadvantages-** recurrence- 5%, hypothyroidism - 20-45%, surgical complications

**Indications:**

- Failure of medical treatment, in young patients
- Grave's disease in children
- Suspected malignancy
- Nodular toxic goiter
- Autonomous toxic nodule
- Large goiter/ intrathoracic goiter

**Procedures:**

- Total thyroidectomy
- Subtotal thyroidectomy- complete gland excised except for 5-8 gms gland near lower pole.
- Hemithyroidectomy- for autonomous nodule.

**C. Radioactive Iodine**

Patient is admitted and isolated for 7 days, to prevent radiation. freshly obtained drug is given immediately, to avoid loss of potency.

614/727



mandibulotomy and trans  
hyoid/suprahyoid/lateral pharyngotomy

- Radioisotope therapy

#### THYROTOXICOSIS:

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12. **Gifford's sign** – difficulty in everting upper eye lid
13. **Knies's sign**- Unequal pupillary dilatation.

590

**THYROID DERMOPATHY:** it includes,

- a. Pretibial myxoedema,
- b. Palmar erythema,
- c. Facial contracture,
- d. Thinning of hair and pruritis.

#### Pretibial myxoedema:

It is bilateral, symmetrical, shiny, dry, red, thickened skin due to mucin like deposits in skin and subcutaneous tissues. Skin becomes cyanosed due to cold.

**THYROID ACROPACHY:** It is clubbing of fingers and toes, seen in Grave's disease

**THYROID MYOPATHY:** It is proximal muscle weakness, resembles myasthenia gravis in severe cases. Recovers with treatment of hyperthyroidism.

#### Investigations for thyrotoxicosis:

1. Thyroid function tests- T3, T4 levels are very high, TSH very low. Sometimes, only T3 is high- when it is called -T3 Thyrotoxicosis.
2.  $I^{131}$  or  $^{99m}Tc$  - Radioisotope scanning study- Former isotope causes more radiation. Latter is safe, fast and cheap
3. TRH levels
4. Blood- TLC, DLC [ neutrophil count], TSH receptor antibody, Anti thyroglobulin antibody, Anti -TPO- (anti thyroxine peroxidase) antibody

#### Treatment:

##### A. Medical-

1. Anti thyroid drugs-
  - a) Methimazole 20-40 mg OD( more potent than carbimazole and not used in pregnancy)
  - b) Carbimazole- 20 mg TID-commonest drug used,
  - c) Propyl thiouracil- 100 mg TID ( used in pregnancy).

Treatment is given for 18 months. Relapse rate is 40%.

Side effects- agranulocytosis( sorethroat is the first symptom), severe hepatitis, polyarthritis.
2. Beta blockers- to control hyper adrenergic cardiovascular symptoms- Propranolol, Nadolol
3. Calcium channel blockers- verapamil
4. Radio active iodine.
5. Lugol's iodine- used prior to surgery to control gland vascularity

##### B. Surgical:

**Advantages-** high cure rate, provides tissue for biopsy, better for women wanting child, useful for coexisting parathyroid tumours and for retrosternal goiters.

**Disadvantages-** recurrence- 5%, hypothyroidism - 20-45%, surgical complications

#### Indications:

1. Failure of medical treatment, in young patients
2. Grave's disease in children
3. Suspected malignancy
4. Nodular toxic goiter
5. Autonomous toxic nodule
6. Large goiter/ intrathoracic goiter

#### Procedures:

1. Total thyroidectomy
2. Subtotal thyroidectomy- complete gland excised except for 5-8 gms gland near lower pole.
3. Hemithyroidectomy- for autonomous nodule.

#### C. Radioactive Iodine

Patient is admitted and isolated for 7 days, to prevent radiation. freshly obtained drug is given immediately, to avoid loss of potency. single dose 5-10 milli curie, given orally. Antithyroid drugs are given for 3 months till the RAI effect starts.

#### Advantages:

- a) Preferred as it gives 90% cure, effective, safe
- b) Avoids surgery,
- c) Avoids long term anti thyroid drugs,
- d) Single oral dose,
- e) Very few side effects.

#### Disadvantages:

- a) Permanent hypothyroidism,
- b) Worsens ophthalmopathy and dermopathy,
- c) Can induce hyperparathyroidism.

#### Contraindications:

1. Children, pregnant women, breast feeding women
2. Chronic smokers
3. Severe ophthalmopathy

#### CHRONIC LYMPHOCYTIC THYROIDITIS [ HASHIMOTO'S THYROIDITIS ]

It is an autoimmune disorder. There are antibodies to thyroglobulin and thyroid peroxidase.

**Incidence:** common in females above 50 yrs age.

**Family history** of other autoimmune diseases present.

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591

Very variable, in onset, type of goiter and function. It can be associated with papillary carcinoma and lymphoma.

**Pathology:** there is diffuse infiltration of lymphocytes

**Symptoms:** neck swelling, symptom of toxicity initially and later it can be hypothyroidism.

**Signs:** diffuse or nodular goiter, with bosselated feel

#### Investigations:

1. Anti-Thyroid antibodies against thyroid peroxidase and thyroglobulin ,present in 85% cases
2. FNAC
3. Thyroidectomy and biopsy if any compression symptoms

#### Treatment:

Thyroxine for hypofunction.

#### HYPOTHYROIDISM

Symptoms	Signs
Weight gain	Loss of hair
Cold intolerance	Puffiness of face
Coarse and sparse hair	Puffiness of hands and feet
Dry skin	Dry and coarse skin
Poor memory and lack of concentration	Bradycardia
Deafness	
Constipation	

#### GRANULOMATOUS THYROIDITIS

It is caused by virus infection. In some cases, disease, may have hypot

**Symptoms:** slow onset goiter

**Signs:** Enlarged one or b

**Investigation:** FNAC

**Treatment:** Tab Prednisolone for acute severe cases.

#### REIDEL'S THYROIDITIS

It is very rare, probably a collagen disease.

**Pathology:** thyroid follicles are replaced by fibrous tissue.

**Symptoms:** of toxicity

**Signs:** hard, fixed nodular goitre, difficult to distinguish from anaplastic carcinoma.

**Investigation:** Biopsy

**Treatment:** Tab Prednisolone in high doses and Thyroxine replacement.

615/727



Hyperactivity	High pulse pressure
Nervousness, tremors	Exophthalmos
Palpitations	Lid retraction – in Grave's disease only
Decreased menstrual bleeding	Periorbital oedema - in Grave's disease only
Hair loss	Pretibial myxoedema - in Grave's disease only

**Table 60-2:** Clinical features of thyrotoxicosis

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### BENIGN NEOPLASMS:

- Adenoma is the most common type, common in middle age females, rarely turns toxic.
- It may be only functioning and autonomous nodule.
- Follicular adenoma is the common cause of a solitary nodule in children and adolescents.
- It is called cold nodule and can turn malignant in 25% cases.

### MALIGNANCY

#### PAPILLARY CARCINOMA:

- It is the most common thyroid cancer- 70%. 7.7% per 1 lakh population.
  - Females 3 times more affected than males.
  - Age- 45 years in females, 65 years in males.
- It is seen in areas with adequate iodine intake in contrast to follicular carcinoma which occurs in low iodine intake areas.

#### Causes:

1. Childhood radiation
2. Victims of nuclear disaster
3. Family history -first degree relatives have thyroid cancer in 5-10% cases of Papillary carcinoma
4. History of thyroid cancer syndromes- Cowden disease, Gardner's syndrome, Carney complex
5. Medullary cancer thyroid syndromes
6. Hashimoto's thyroiditis

#### Symptoms:

- Rapidly growing mass in the thyroid region
- Neck masses -metastatic lymph nodes
- Hoarseness of voice – RLN involvement
- Stridor – due to pressure on trachea
- Pain in the mass
- Weight loss
- Dysphagia

#### Signs:

- Hard thyroid mass, fixed to surrounding structures
- Cervical lymphadenopathy- hard nodes

#### Investigations:

##### Blood:

1. CBC, RFT / LFT
2. TFT- for hyperthyroidism,
3. serum calcitonin – for medullary carcinoma



**Fig 60-3:** Anaplastic carcinoma -thyroid  
( Courtesy: [www.entokey.com](http://www.entokey.com))

#### Radiological:

4. Chest X-ray -for any pulmonary metastasis in malignant lesions.
5. Ultrasound Neck
6. CT scan and MRI Neck- to know extent of disease and retrosternal extension

#### Histopathology

7. Ultrasound guided FNAC – 100% sensitive, 67% specific-
  - Orphan Annie eye appearance- nuclei of follicular cells are folded or grooved with intranuclear cytoplasm.
  - Psammoma bodies- laminated calcium bodies.

#### Treatment:

1. Lobectomy with isthmusectomy- for tumour less than 1.5 cm size
2. Total or near total thyroidectomy for both lobe disease.
3. Total thyroidectomy for high risk cases.
4. Tracheal segment excision – if it is involved
5. Cervical nodes excision

#### FOLLICULAR CARCINOMA:

This growth arises from follicular cells, common in females-3:1, fifth decade

#### Symptoms:

- Swelling in the neck-thyroid region- rapidly growing

#### Signs:

- Nodule in the thyroid
- Metastatic neck nodes

#### Investigation:

- FNAC- if reported as neoplasm -to be confirmed by histopathology for malignancy and capsular invasion

#### Treatment:

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1. Lobectomy with isthmusectomy- if FNAC report is not cancer
2. Total thyroidectomy – if FNAC diagnosis is carcinoma
3. Total thyroidectomy in elderly patient with nodule bigger than 4 cms size.

#### HURTHLE CELL CARCINOMA

- Aggressive of all carcinomas.
- Presents as thyroid nodule, does not take up RAI as avidly as follicular carcinoma.
- Presents at 50 yrs age.
- FNAC is done and on HPE, if capsule is invaded, diagnosed as carcinoma

#### Treatment:

Total thyroidectomy with removal of paratracheal nodes and neck dissection.

Follow up using Technetium scan.

#### MEDULLARY CARCINOMA

- It is an aggressive tumour, seen in both sexes, in 50-60 yrs age,
- Can be sporadic or familial.

**Treatment-** Surgery, RT.

#### THYROID NODULES.

##### Definition:

It is a discrete lesion within thyroid gland that is radiologically distinct from surrounding parenchyma.

- It may be palpable or impalpable, may be functioning or non-functioning.
- It is common between 35- 60 yrs age, common in women, 6% than in men 1.5% , prevalence increases with age, radiation exposure and pregnancy.
- Nodules can be benign or malignant.

##### Benign nodules are,

1. Colloid nodule
2. Follicular adenoma
3. Hurthle cell adenoma
4. Lymphoma
5. Subacute thyroiditis- TB

##### Malignant nodules are,

1. Papillary carcinoma

617/727



- Weight loss
  - Dysphagia
- Signs:**
- Hard thyroid mass, fixed to surrounding structures
  - Cervical lymphadenopathy- hard nodes

**Investigations:****Blood:**

1. CBC, RFT / LFT
2. TFT- for hyperthyroidism,
3. serum calcitonin – for medullary carcinoma

females-3:1, fifth decade

**Symptoms:**

- Swelling in the neck-thyroid region- rapidly growing

**Signs:**

- Nodule in the thyroid
- Metastatic neck nodes

**Investigation:**

- FNAC- if reported as neoplasm -to be confirmed by histopathology for malignancy and capsular invasion

**Treatment:**

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1. Lobectomy with isthmusectomy- if FNAC report is not cancer
2. Total thyroidectomy – if FNAC diagnosis is carcinoma
3. Total thyroidectomy in elderly patient with nodule bigger than 4 cms size.

**HURTHLE CELL CARCINOMA**

- Aggressive of all carcinomas.
- Presents as thyroid nodule, does not take up RAI as avidly as follicular carcinoma.
- Presents at 50 yrs age.
- FNAC is done and on HPE, if capsule is invaded, diagnosed as carcinoma

**Treatment:**

Total thyroidectomy with removal of paratracheal nodes and neck dissection.

Follow up using Technetium scan.

**MEDULLARY CARCINOMA**

- It is an aggressive tumour, seen in both sexes, in 50-60 yrs age,
- Can be sporadic or familial.
- It arises from parafollicular C cells of thyroid.

**Symptoms-** neck mass, pain, dyspnoea, dysphagia and hoarseness of voice.**Diagnosis** is by FNAC and serum calcitonin levels are found elevated.**Treatment:**

- a. Total thyroidectomy with level 6 nodes excision, and if they are involved, complete neck dissection level II- V.
- b. If primary is more than 2 cms, ipsilateral neck dissection including level VII nodes to be done.
- c. Post-operative **follow up** is done by serum calcitonin levels.

**LYMPHOMA**

- They are B-cell Non-Hodgkin lymphoma type, females 3:1, 60-80 years age

**Symptoms:**

- Rapidly growing mass,
- Painless,
- Hoarseness, dyspnoea, stridor, dysphagia,
- Thoracic inlet obstruction.

**Signs:**

- Local invasion
- Cervical and other regions lymphadenopathy,
- Patient is hypothyroid.

**Investigation** – FNAB or isthmusectomy and IHC-immunohistochemistry studies.**Treatment-** Surgery, RT and CT.**THYROID NODULES.****Definition:**

It is a discrete lesion within thyroid gland that is radiologically distinct from surrounding parenchyma.

- It may be palpable or impalpable, may be functioning or non-functioning.
- It is common between 35- 60 yrs age, common in women, 6% than in men 1.5% , prevalence increases with age, radiation exposure and pregnancy.
- Nodules can be benign or malignant.

**Benign nodules are,**

1. Colloid nodule
2. Follicular adenoma
3. Hurthle cell adenoma
4. Lymphoma
5. Subacute thyroiditis- TB

**Malignant nodules are,**

1. Papillary carcinoma
2. Follicular carcinoma
3. Medullary carcinoma
4. Metastasis from breast/ kidney

**Nodules with suspicion of malignancy****Highly suspicious-**

1. Rapidly enlarging mass
2. Hard /firm mass
3. Fixity to underlying structures
4. VC palsy
5. Palpable lymph nodes
6. F/H of MEN 2a or 2b

**Moderately suspicious**

1. Age <20 or > 60 yrs
2. Males
3. Previous radiation to neck
4. Symptoms of compression
5. Hashimoto's thyroiditis

**Clinical assessment of a nodule**

History and findings suggestive of above factors.

**Investigations:****Blood:**

1. CBC, ESR – for infectious thyroiditis
2. TFT- most are euthyroid
3. TSH – falling levels indicate hyperfunctioning nodule
4. Serum calcitonin is elevated in medullary carcinoma

**Serology:**

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618/727

594

- Thyroid peroxidase antibodies (TPO) in patients with high TSH

**Pathology:**USG guided FNAC / FNAB – ultrasound guided - sensitivity 90% - **It is GOLD standard in diagnosis of nodule.****Radiology:**

1. USG –
  - non-invasive, inexpensive,
  - detects nonpalpable nodules,
  - differentiate solid and cystic nodules.
2. Technetium, I<sup>131</sup> and I<sup>123</sup> scans differentiate hot and cold nodules, 10% of cold nodules and 1% of hot nodules can have malignancy.
3. C<sup>125</sup> Scan useful
  - in assessing substernal extension,
  - in assessing cervical and mediastinal lymphadenopathy,

4. **Nondiagnostic nodule** on FNAC, if risk factors present- surgery
5. **Recurrent, benign ,cystic nodule** which refills quickly on 3 times , or if it is larger than 4 cms size– treatment option is surgery

**THYROID SURGERY.****Following procedures are done:**

1. Hemithyroidectomy or lobectomy
2. subtotal thyroidectomy
3. near total thyroidectomy
4. Total Thyroidectomy
5. Isthmusectomy
6. Completion thyroidectomy

**Indications:**

1. Carcinoma thyroid
2. Carcinoma – suspicion on FNAC and with risk factors
3. Compressive symptoms



- They are B-cell Non-Hodgkin lymphoma type, females 3:1, 60-80 years age

**Symptoms:**

- Rapidly growing mass,
- Painless,
- Hoarseness, dyspnoea, stridor, dysphagia,
- Thoracic inlet obstruction.

**Signs:**

- Local invasion
- Cervical and other regions lymphadenopathy,
- Patient is hypothyroid.

**Investigation** – FNAB or isthmusectomy and IHC-immunohistochemistry studies.

3. Previous radiation to neck
4. Symptoms of compression
5. Hashimoto's thyroiditis

**Clinical assessment of a nodule**

History and findings suggestive of above factors.

**Investigations:****Blood:**

1. CBC, ESR – for infectious thyroiditis
2. TFT- most are euthyroid
3. TSH – falling levels indicate hyperfunctioning nodule
4. Serum calcitonin is elevated in medullary carcinoma

**Serology:**

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USG guided FNAC / FNAB – ultrasound guided - sensitivity 90% - **It is GOLD standard in diagnosis of nodule.**

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  - differentiate solid and cystic nodules.
2. Technetium, I<sup>131</sup> and I<sup>123</sup> scans differentiate hot and cold nodules, 10% of cold nodules and 1% of hot nodules can have malignancy.
3. C T Scan useful
  - in assessing substernal extension,
  - in assessing cervical and mediastinal lymphadenopathy,
  - to evaluate relation of thyroid with adjacent structures.
4. MRI is more accurate in distinguishing recurrent or persistent thyroid tumour from fibrosis.

**MANAGEMENT OF A THYROID NODULE**

1. **Malignant nodule**, suspicious nodule- surgery
2. **Benign, solid, hot toxic nodule**- Radioactive ablation or surgery and large nontoxic nodule- Surgery
3. **Benign, solid, cold nodule** not responding to T4 suppression – surgery

4. **Nondiagnostic nodule** on FNAC, if risk factors present- surgery
5. **Recurrent, benign, cystic nodule** which refills quickly on 3 times, or if it is larger than 4 cms size– treatment option is surgery

**THYROID SURGERY.****Following procedures are done:**

1. Hemithyroidectomy or lobectomy
2. subtotal thyroidectomy
3. near total thyroidectomy
4. Total Thyroidectomy
5. Isthmusectomy
6. Completion thyroidectomy

**Indications:**

1. Carcinoma thyroid
2. Carcinoma – suspicion on FNAC and with risk factors
3. Compressive symptoms
4. Cosmetic – large goiter.

**Complications:**

1. Haematoma – to be evacuated early
2. Airway obstruction – treated by tracheostomy
3. Injury to RLN / SLN
4. Wound sepsis
5. Hypocalcaemia – due to removal of parathyroids, critical period 1-3 days after surgery, treated by IV or oral calcium
6. Pneumothorax – due to injury to pleura
7. Hypothyroidism – occurs 4-6 weeks after surgery

**CASE STUDY 1**

Q1) A 23 years old female with history of midline neck swelling since 4 months, no history of pain in the swelling, fever, trauma, dysphagia or breathing difficulty. On exam, round shaped mass of 2 cm diameter, seen in midline, moves on deglutition, but not on protrusion of tongue. On palpation, it was around 2.5 cm diameter, smooth, nontender, mobile and cystic mass. Thyroid function tests are normal.

A) What is the diagnosis?

1. Thyroglossal cyst
2. Adenoma thyroid
3. Nodular cystic goiter\*\*
4. Lymphoma

B) What are the investigations required for this case?

1. USG neck
2. Thyroid function tests.
3. FNAC
4. All of the above\*\*.

C) Treatment options of thyroid nodule are;

1. Observation only.
2. Tab Eltroxin\*\*
3. Lobectomy
4. Hemithyroidectomy

**CASE STUDY 1**

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619/727

595

Q2) A 40 year old male with history of midline neck swelling for one and a half months, gradually increasing in size. No history of fever, difficulty in swallowing, loss of weight, DM, TB, HTN.O/E – swelling of 5cm diameter in midline of neck moves on deglutition but not on protrusion of tongue, diffuse border and on palpation cystic in middle and firm on periphery, nontender. USG neck – hypoechoic area (5x4 cm ) FNAC – plenty of pus cells, AFB, polymorphs and few lymphocytes.

A) Diagnosis is

1. Cystic thyroid nodule
2. Cold abscess\*\*
3. Thyroglossal cyst
4. Pyogenic abscess

B) Treatment options:

1. Incision and drainage from non dependent

**CASE STUDY 3**

Q3) A 45 year old female patient presented with painful, swelling in thyroid region for 4 months, rapidly progressing in size with weight loss and dysphagia. O/E 8x6 cms mass in thyroid region seen and felt, hard in consistency, moves with deglutition but not with protrusion of tongue. HPE showed-orphan annie eye appearance of nuclei of follicular cells and psammoma bodies.

A) Diagnosis is;

1. Papillary carcinoma\*\*
2. Follicular carcinoma
3. Hurthle cell carcinoma
4. Lymphoma

B) Treatment options are:

1. Lobectomy with isthmusectomy

# MANUAL OF ENT, HEAD & NECK SURGERY

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**FIRST EDITION**

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**JAGADISH SUNKUM**

**MBBS (Mys) MS( ENT) PGDHM (New Delhi)**

**Formerly**

Prof & HOD, ENT , AMC and SSRMC, Mauritius  
Medical Superintendent, K.M.C,M.M.C [ AP/TS] India  
Prof & HOD,ENT, KMC,MMC,NMC (AP/TS) India  
Asso Prof & HOD,ENT,Al- Tahaddi University,Sirte,Libya  
Asst /Assoc Prof AIISH, Mysore, JSS medical college, Mysore  
ENT Specialist , MOH, Saudi Arabia  
Flt Lt Medical Officer (IAF)

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## FOREWORD

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It's a privilege to write this foreword for this book titled "Manual of ENT-Head and Neck surgery" by Jagdish Sunkum. It certainly fulfils the purpose for which it was written, that it is to give clear cut basic information about various ENT issues for the benefit of the undergraduate student and in some cases also the post graduate student. The text has been very clearly and succinctly written and this is complemented by very clear and descriptive pictures which add great value to the book.

I feel this book would be of great help to the students of ENT both under graduate and the post graduate.

### Dr. M. V. Kirtane

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## FOREWORD

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I am very happy to know that Prof Jagdish Kumar has edited a book for undergraduates in Otorhinolaryngology, Head & Neck surgery. Even a casual glance through the book will reveal the extensive effort which has gone in creating this book. Even though the author has projected this book as a book for undergraduates I'm of the opinion that it can also serve the postgraduate residents in Otolaryngology as a ready reckoner and a quick reference guide. The chapters are well laid out and at the same time comprehensive and the information is presented with clarity. Illustrations add to the allure of the book.

I thoroughly enjoyed reading the chapters of the book and in my opinion this book fulfils a long felt need for a book of this kind. I'm sure the book will go a long way in introducing the specialty to undergraduates and satiating their quest for knowledge.

I have no hesitation in commending this book in the highest terms. The book deserves a place in every medical library.

Prof. Mohan Kameswaran MS, FRCS, FAMS, DSc  
Padma Sri awardee, Dr. B. C. Roy awardee, Indo-Australian awardee.  
Managing Director, Madras ENT Research Foundation ,Chennai,  
Hon' Prof of ENT,SRM medical college & RC, Kattankullathur, Hon'y Sr Lecturer, Edgehill university,  
Lancashire, UK. Regional Secretary, International Federation of Otorhinolaryngological Societies ( IFOS)

Dear Reader,

The first edition of **Manual of ENT ,Head and Neck Surgery** written and compiled by Professor Jagdish Sunkum, is an excellent overview for medical students, general practitioners and even post-graduate residents. This is a comprehensive review of the majority of specific ENT problems which patients encounter in their daily lives. I am overwhelmed by the extensive collection of illustrations and materials which have been a valuable contribution in bringing this textbook. Those doctors who are at the primary level of medical care, the ENT problems form a large segment of the general practitioner's patient evaluation and treatment.

This textbook offers a modern guide to ENT practice, teaching medical students and junior ENT doctors. Most chapters featuring the anatomy are well illustrated and have a general review of the diseases which may affect the area. In each overview, the student will be able to identify the most common conditions since they are well highlighted. The compilation of chapters in this book will definitely provide you with knowledge and structure you require in daily practice.

The Manual of ENT, Head and Neck surgery is an excellent reference for ENT related diagnoses and procedures, whereby the author demonstrates his extensive knowledge with succinct explanation and detailed illustration.

After reading this textbook, a GP will have refreshed his knowledge of common diseases in ENT including the emergencies, a student can fly high with roaring success in the MBBS examinations besides it can be of great help to a postgraduate in MS [ENT] and D.L.O going for exam.

**Dr. Beerdarshan Singh Caussy**

MBBS,MS[Gen Surg], MMSc [Scotland] & Fellow in Neurosurgery[UK]  
Regional Health Director  
Victoria Hospital  
Consultant in Charge Neurosurgery  
Ministry of Health and Quality of Life  
Mauritius.

## COMMENTS AND REVIEWS BY PROFESSORS IN VARIOUS MEDICAL COLLEGES

Chapter 50, 51-Carcinoma Larynx and Neck dissection, Speech and voice disorders. Well written, easy to understand, with good diagrams, excellent book for undergraduates. I went through the topic. It is well written with lots of information. Topics are written in points, easy to understand and remember. **Excellent book for both undergraduate and postgraduate** students, handy book for consultants to revise.

Thank you sir., Dr Chandrakiran.C

---

Dr Mahendra Naik, Prof & HOD ENT, Maharaja Agrasena medical college, Agroha, Haryana, India  
Chapters 60,61,62-Thyroid, HIV/AIDS in ENT, Recent advances. This book meets with the requirements of the new curriculum, particularly the integration of basic sciences with clinical sciences. Applied and surgical anatomy have been given due mention. Overall a **student friendly book**, which will be **useful for undergraduates and postgraduates**

---

Dr Belaldavar, Senior consultant ,Prof & HOD, ENT ,JN medical college and Research centre, Belagavi, Karnataka, India

Chapter 42,43,44-Tumours of hypopharynx, Anatomy and physiology of Larynx, Congenital lesions of Larynx.

"The content of this text book is well charted keeping in mind, the tender understanding of the academic maturity of the undergraduate students. And also useful for the ready reference script for postgraduate students and faculty. I feel there is lot of shedding of sweat ,sparing of personal time and concern to bring such a **motivational book**. The standard by which this book has been penned suggests ,the highest acumen and experience of the author. I wish best of luck for his endeavours."

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Dr Nitin Ankle, Prof and Senior Consultant, KLE HOSP & MRC JNMC, Belgavi Karnataka, India  
Chapter 58,59,60-Anatomy of Head, Infections of Head and Neck spaces, Neck, Thyroid. The book's cover looks impressive and the preface aptly reveals the objectives of the book. I agree **such a book is much needed** in present competitive times for our students

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Dr Anjana Avinash Mohite, Associate Prof, DY Patil medical college, Kolhapur, Maharashtra, India  
Chapter 8, CSOM (IT) (AA) Cholesteatoma, Complications of CSOM. This ENT **book is superb** in its presentation. It contains all the fundamentals required for undergraduates and will definitely make ENT diseases an **interesting reading**.

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Dr Arvind Sangavi.B. Associate Prof, Dept of ENT, Raichur Institute of Medical Sciences, Raichur., Karnataka.

Chapter 25,26 – Nasal polypi, Epistaxis. First of all, I would like to congratulate you for bringing out this excellent ENT textbook. we can see the efforts put in this book. Well written textbook written in a simplified way. **Excellent resource for** the undergraduate & PGs medical students. Topics have been covered in detail with large number of clinical photographs, radiographic images & diagrams making it easy to understand. **A must ENT textbook"**

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Dr Nagaraj Gowda, Prof ENT,MVJ Medical College & Research HospitalHoskote, Bangalore, Karnataka.  
Chapters 66,67-Surgeries of Larynx and Bronchus, Surgeries of oesophagus; Hearty congratulations and best Wishes for your upcoming Text Book for MBBS and Post Graduate Students. Cover page looks very elegant. It has been well written, **easy to understand** and very concise for the undergraduate students.

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Dr Remukananda, Prof of ENT, J J M medical college, Davanagere, Karnataka, India  
Chapter 23, 24-Allergic Rhinitis, Non-Allergic rhinitis; The book is very good for undergraduates. It is easy to read & remember. It is very concise. Even it is **good for Junior PG**. Sometimes during PG exam before entering exam hall students can have a glance.

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Dr B Jayaprakash Reddy,MS, DNB ,(ENT) Prof of ENT,Viswa Bharathi Medical college,Kurnool ,AP , India  
Chapter 52,Foreign bodies Airways. I have reviewed the text book authored by Dr Jagadish kumar. It is **simple superb** covering all the aspects. I can recommend this book to all the students appearing for exams.

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## TUMOURS OF HYPOPHARYNX and PHARYNGEAL DIVERTICULUM:

### A. BENIGN

### B. MALIGNANT

1. CARCINOMA OF PYRIFORM FOSSA.
2. CARCINOMA POSTERIOR PHARYNGEAL WALL ( PPW).
3. CARCINOMA POST CRICOID REGION.

## PHARYNGEAL DIVERTICULUM

### Core competency:

**EN 4.46** Describe the clinical features, investigations and principles of management of Malignancy of Hypopharynx.

**SU 20.1.5** Describe the etiopathogenesis, symptoms and signs of laryngopharyngeal cancer. Enumerate the appropriate investigations and discuss the principles of its treatment.

## MALIGNANT TUMOURS OF HYOPHARYNX

### Introduction:

Hypopharynx is the lowermost and longest of 3 segments of pharynx.

- **Benign tumours** are very rare here. Most common tumours are lipoma, leiomyoma, papilloma, adenoma, and fibroma.
- **Carcinoma is very common.**
- Hypopharynx is a roomy and silent area, allows tumours to grow for a period of time, before they become symptomatic. Hence patients present with advanced disease, and have worst prognosis.
- Their aggressive behaviour is due to strong tendency for submucosal spread.
- Nodal metastasis is early.
- There is high incidence of distant metastasis and direct invasion of adjacent structures.

### Incidence:

- It forms 3-5 % of all head and neck malignancies.
- More common in males in India, Brazil, central and western Europe.
- Peak incidence in 6<sup>th</sup> and 7<sup>th</sup> decade.
- Most common site is pyriform fossa- 60%, post cricoid area 30% and posterior pharyngeal wall 10%.
- 30% have local disease at the time of diagnosis.
- 70% have regional disease and
- 10% have distant metastasis.

### Sites:

Hypopharynx has 3 sub sites-

- Pyriform sinus,

- Post cricoid region and
- Posterior pharyngeal wall.

**Type: It is squamous cell carcinoma in 95 % cases** because most cancers arise from mucosa.

**Clinical features and Investigations** are described under individual subsites.

### STAGING OF GROWTH:

According to **TNM classification( AJCC cancer manual 8<sup>th</sup> edition)** stages are described as below. (simplified by author) common to all subsites.

**Stage 1:** T1,N0,M0- T1 is growth less than 2 cms in size

**Stage 2:** T2,N0,M0- T2 is growth 2-4 cms

**Stage 3:** T3,N0M0 ; T1-3,N1,M0- T3 is growth > 4cms, fixity of larynx, oesophagus involved

**Stage 4a:** T4a, N0-1,M0; T1-4a,N2,M0 – T4a is advanced local growth, thyroid/cricoid cartilage involved, extension to neck, oesophagus. N1 is single node<3 cms, same side ; N2 -one or more nodes, same side and opposite side, 3-6 cms size.

**Stage 4b:** T4b,N0-2, M0 ; T1-4b,N3,M0 – T4b is very advanced growth, spread to prevertebral fascia, carotid artery or mediastinum. N3 is node > 6cms size, same side or opposite side.

**Stage 4c:** T1-4b, N0-3,M1. M1 is confirmed distant metastasis.

### TREATMENT

It depends on stage of growth.

**Stage 1 and 2:** Radiotherapy alone; chemotherapy with partial pharyngectomy

**Stage 3 and 4:** Combination therapy with gastric pull up or colon transposition

## CARCINOMA OF PYRIFORM FOSSA

### Introduction:

These growths remain asymptomatic for long time as the cavity is roomy and hence symptoms appear relatively late.

### Incidence:

- It is seen commonly in men and in those above 40 years age.
- 60% of hypopharyngeal growths are seen in pyriform sinus.
- 60% pyriform tumours have positive neck nodes by the time patients come to OPD.
- 30-40% of patients with no neck nodes have occult tumour.

### ETIOLOGY:

#### 1. Smoking and chewing tobacco:

- Mutations in TP53 gene are found in large percentage of smokers and drinkers.
- TP53 gene is a tumour suppressor gene that codes for a protein that regulates cell cycle and hence functions as tumour suppressor. Any mutation of this gene results in abnormal cell growth leading to cancer.

2. Alcohol acts synergistically with smoking in inducing cancer growth.

#### 3. Genetic-

- Oncogenes are present in tumour cells. They are mutant genes which stimulate cell growth uninhibited. Proto oncogenes are normal genes present in cell and are needed for normal cell cycle. They get activated to oncogenes by viruses / tobacco, which are responsible for cell multiplication unhindered.
- Loss of heterozygosity at 9p, mutations in p21 gene and chromosome 11 affect tumour suppression and promote cancer.

4. Prior radiotherapy to neck for other growths induces cancer

### SPREAD:

#### 1. Local: spread

- Above to vallecula and base of the tongue,
- Below to post cricoid region,
- Medially to aryepiglottic folds /supraglottis,
- Laterally to thyroid cartilage, thyroid gland.

#### 2. Lymphatic: spread

- Pyriform fossa is very rich in lymphatic network and hence it spreads quickly to lymph nodes.
- 60 % patients have lymph node metastasis and 50% have bilateral nodes at initial presentation.

- upper and middle deep cervical nodes – level 2 and 3 -are affected.
- nodes can appear even after excision of the primary growth.

3. Distant: seen in lung, liver and bones late in the disease.

### SYMPTOMS:

**Asymptomatic for long time.** Symptoms can be grouped under:

#### Pharynx:

1. Sticking sensation in the throat / FB sensation / lump in the throat
2. Non-specific sore throat, typically unilateral and well localised, aggravated by eating hot and spicy food.
3. Odynophagia
4. Dysphagia- **common cause of dysphagia in the elderly**, progressive dysphagia more to solids.
5. Hot potato voice -due to involvement of base of tongue.
6. Halitosis

#### Larynx:

- Hoarse voice – indicates RLN involvement or direct invasion of glottis.
- **Stridor**
- Choking spells at night due to aspiration of pooled saliva
- Hemoptysis

#### Ear:

- Ear pain – due to internal laryngeal nerve involvement (branch of superior laryngeal nerve -branch of 10<sup>th</sup> CN)

#### Neck:

- Neck mass – indicate metastatic cervical nodes

#### General:

- Loss of weight

### SIGNS:

1. IDL exam-
  - Proliferative or ulcerative growth,
  - Pooling of secretions in pyriform fossa (**Chevalier Jackson sign**)
  - VC movements reduced or fixed
2. Neck – upper deep cervical nodes are palpable; 50% cases present with nodes.
3. Neck exam- laryngeal widening or splaying or larynx is pushed forwards
4. Laryngeal tenderness

### INVESTIGATIONS:

#### Endoscopy:( Fig 42-1)

- 1.IDL scopy and biopsy under GA- general anesthesia
  - To know type and stage of growth,
  - To know the extent of growth
2. Flexible /rigid hypopharyngoscopy- and biopsy

#### Radiology:

1. X-Ray Neck- lateral /AP view [soft tissue]
    - for airway patency
    - for cartilage erosion
  2. CXR-
    - for mediastinal widening,
    - for aspiration pneumonia,
    - for secondaries in the lungs
  3. Barium swallow with screening- sensitivity- 90%, findings are -
    - filling defects
    - mucosal irregularities
    - stasis
    - aspiration
  4. CT / MRI neck- to know the extent and nodal involvement
  5. PET scan for locally advanced lesions
- Cytology:**
- FNAC of neck nodes



**Fig 42-1:** Carcinoma right pyriform fossa.

[Courtesy: Dr TM Joseph

<https://drjosephm.blogspot.com/India>

#### TREATMENT:

1. Early growth without nodes- Radiotherapy- with organ preservation
2. Stage I and II- Radiation alone
3. Stage III & IV- Surgery + Radiotherapy
  - a) Surgery- Total laryngectomy and partial pharyngectomy with neck dissection
  - b) Radiotherapy- Tele radiotherapy- 6500 Rads over 5 weeks.
  - c) Chemotherapy -followed by surgery or radiotherapy.
  - d) Reconstruction with gastric pull up, colon transposition.

#### PROGNOSIS:

1. Good in early stages
2. Stage I & II- 80% - 5 years survival
3. Advanced cases – poor prognosis

#### CARCINOMA POST CRICOID REGION

- 30% of Hypo pharyngeal growths are seen in post cricoid region.
- **Common in young females- 20-30 years group.**
- **Ulcerative lesions are more common.**

#### Etiology:

1. As above that of hypopharynx
2. Plummer Vinson syndrome ( also called Siderophenic dysphagia)

#### Spread:

1. Local-
  - annular spread to other parts of hypopharynx
  - downwards to cervical oesophagus, arytenoids and RLN may be involved
2. Lymphatic: Para tracheal nodes on one or both sides

#### Symptoms:

1. Dysphagia- predominant and progressive
2. Hoarse voice / aphonia
3. Weight loss
4. Undernutrition

#### Signs:

1. IDL- oedema and redness in post cricoid region
2. Pooling of saliva in pyriform sinus (Chevalier Jackson sign)
3. Laryngeal crepitus- absent
4. Larynx is pushed forwards



**Fig 42-2:** Post cricoid carcinoma- in a case of Plummer Vinson syndrome

#### INVESTIGATIONS:

##### Blood:

- CBC- Vit B12 and folate; to know Hb% ,TLC
- Serum Iron, Calcium
- Liver function tests
- Thyroid function tests [ in advanced cases]

##### Radiology:

- X-Ray-Neck- lateral view soft tissue- increased prevertebral shadow.
- Modified Barium swallow- will show the lower extent of the disease.
- CECT scan neck and chest- to assess growth progression to oesophagus, tongue base

involvement, cricoid cartilage invasion, and lung metastasis.

- CT Scan abdomen – to rule out liver metastasis
- Bone scan – rules out bone metastasis.
- PET scan –for local disease, nodal involvement, metastatic lung disease

#### Endoscopy:

Triple endoscopy – Laryngoscopy, bronchoscopy and oesophagoscopy – to rule out second primary.

#### pathology:

Hypopharyngoscopy and biopsy under GA.

#### Treatment:

1. Stage 1 -Radiotherapy- preserves laryngeal function
2. Stage 2 -Radiotherapy with chemotherapy
3. Stage 3 and Stage 4 a and failed radiotherapy cases:

Surgery- Laryngo pharyngo oesophagectomy with stomach pull up plus post operative radiotherapy or chemotherapy

#### Prognosis:

Poor even with combined therapy

### CARCINOMA POSTERIOR PHARYNGEAL WALL (PPW).

This should be read along with tumours in oropharynx- posterior pharyngeal wall. Refer to chapter- 41.

#### Incidence:

- Forms 10% of the hypopharyngeal growths.
- Seen in males above 50 years age.
- It is usually exophytic type but may be ulcerative type.

#### Spread:

1. Local: prevertebral fascia, muscles and vertebrae

2. Lymphatic: bilateral UDC nodes because it is midline lesion and retropharyngeal nodes are involved.

#### Symptoms:

1. Dysphagia- insidious and progressive
2. Spitting of blood
3. Neck mass alone with no other symptoms.

#### Signs:

1. IDL mirror exam- exophytic or ulcerative growth is visible and extent of growth to be noted.
2. Hypopharyngoscopy by rigid endoscope – to assess the extent of growth.

#### Investigations:

- X-Ray neck soft tissue -lateral view – to know extent vertically, into lumen and to vertebra
- CT scan- Neck- to know the extent and lymph nodes involvement
- Panendoscopy- of larynx, bronchi and oesophagus - for second primary
- Biopsy: to know the type of growth

#### TREATMENT:

1. Early lesions: Radiotherapy or surgery –excision by lateral pharyngotomy approach.
2. Advanced lesions: Laryngo-pharyngectomy and block dissection of the neck

#### Treatment according to stage:

- Stage 1: Radiotherapy or partial pharyngectomy
- Stage 2: Radiotherapy or chemo radiotherapy or total laryngo-pharyngectomy
- Stage 3: Partial pharyngectomy/ Total laryngo-pharyngectomy with radiotherapy
- Stage 4a: Total laryngo-pharyngectomy with radiotherapy or Chemoradiotherapy.

#### Prognosis:

Very poor- only 19% survive for 5 years.

## ZENKER'S DIVERTICULUM;| Zenker- German pathologist-1877| ( also called PHARYNGEAL DIVERTICULUM)

#### Definition:

It is a blind sac of the pharyngeal mucosa that comes out through the Killian's dehiscence [ also called "Gateway of tears"]-a triangular area of the lower part of inferior constrictor muscle posterolaterally.

- It is a pseudo diverticulum.
- It is oriented to left side in 90% cases;
- It does not contain all the 4 layers of pharyngeal wall.
- It is lined by squamous epithelium with a thin lamina propria. There is no muscular coat.

#### Incidence:

Seen in elderly aged above 60 years

#### Etiology:

Many hypotheses are suggested as follows.

1. Incoordination between cricopharyngeal sphincter relaxation and inferior constrictor contraction in the pharyngeal phase of deglutition, to push the food down to oesophagus from the pharynx.
2. Elevated resting tone of CP sphincter.
3. Loss of CP muscle elasticity.
4. Cricopharynx muscle myopathy or denervation atrophy
5. CNS injury with a focal spastic cricopharyngeus muscle
6. Cricopharyngeal muscle spasm due to GERD

#### SYMPTOMS:

**Pharynx**

- Dysphagia – in 80% cases- starts after a few swallows, when the food starts filling the pouch and compresses the oesophagus.
- Regurgitation at night in recumbent position (58%)
- Gurgling sound on deglutition
- Sensation of food sticking in the throat.
- Halitosis

**Larynx:**

- Coughing due to aspiration into larynx from the pouch.
- Aspiration of food into lungs

**Neck**

- Borborygmi in the neck

**general:**

- Loss of weight

**SIGNS:**

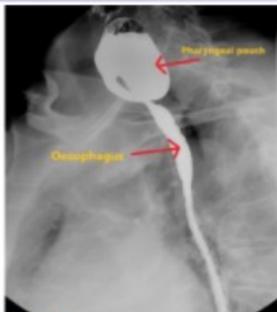
1. Swelling on the left side of neck
2. **Boycce's sign-** noise of splashing fluid present in the diverticulum.

**INVESTIGATIONS:****Endoscopy:**

- Flexible oesophagoscopy- pouch opening is wider than oesophageal opening and it is visible with a septum between the two
- FEES- Flexible Endoscopic Evaluation of Swallowing

**Radiology:**

- Barium swallow and Video fluoroscopy- Best investigation – shows site and size of pouch
- HRCT Neck and Thorax



**Fig 42-3:** Barium swallow- Pharyngeal diverticulum

**Treatment:**

1. **Simple excision:** is advised if it is less than one cm size sac and symptomatic.
2. Endoscopic diverticulotomy- is advised for bigger sacs – it is also called Dohlman's operation. It is done by using,

- CO<sub>2</sub> laser or KTP laser
- Stapling
- Ultrasonic scalpel.

**Complications of diverticulotomy:**

- RLN palsy
  - Bleeding
  - Mediastinitis
  - Perforation of the diverticulum
  - Perforation of the oesophagus
3. Excision of sac and cricopharyngeal myotomy by transvertical incision.
  4. **Recent advance- Mortensen et al**
    - Transoral cricopharyngeal myotomy with diverticulectomy.

In this procedure- **sac is inverted, excised and the area sealed with glue.**

**CASE STUDY 1**

Q1) A 24 years old adult female reported with foreign body throat sensation since many years, progressive dysphagia initially for solids, later on for liquids since 1 year, lost weight of about 8 kgs in 6 months, developed hoarseness of voice since 2 months. Recently complained of ear pain and swellings in lower lateral neck both sides. On examination, she was severely anaemic, had spoon shaped nails, tongue was smooth. Angular stomatitis was present. Ears and nose – were normal. IDL showed pooling of saliva in the pyriform fossa. Larynx was found pushed forwards and laryngeal crepitus was absent.

A) Diagnosis of this case is;

1. Carcinoma pyriform fossa
  2. Carcinoma oesophagus
  3. Postcricoid carcinoma\*\*
  4. Carcinoma supraglottis
- B) Ear pain and hoarseness are indicative of,
1. Internal laryngeal nerve and RLN involvement\*\*
  2. Vagus nerve involvement
  3. Glossopharyngeal nerve involvement
  4. Internal laryngeal nerve and vocal cord involvement
- C) Investigations to be done are;
1. CECT scan neck and chest for spread
  2. Modified barium swallow for lower extension
  3. Triple endoscopy – to rule out second primary

- |  |   |
|--|---|
| 4. All of the above**                  | 2. Bilateral lymph nodes metastasis     |
| D) Prognosis is bad due to all except; | 3. Young age of the patient**           |
| 1. Submucosal spread and skip lesions  | 4. Cartilage invasion & RLN involvement |
- 

**Answers:**

Q1) A-3, B-1, C-4, D-3

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**KEYPOINTS**

1. Amongst all head and neck tumours, hypopharyngeal carcinoma has worst prognosis.
2. Laryngeal crepitus is absent in patients with post cricoid tumours.
3. Mutations in TP53 gene, p21 gene, chromosome 11 are responsible for cancer growths. Smoking causes mutation in TP53 gene and viruses mutate p21 gene.
4. Post cricoid carcinoma is most common in young females and ulcerative lesions are more common. Plummer Vinson syndrome is an important premalignant condition.
5. Zenker's diverticulum occurs through Killian's dehiscence [ also called Gateway of Tears]
6. Boyce sign is the splashing noise heard in diverticulum case.
7. Recent advance in management of zenker's diverticulum is Mortensen's Transoral diverticulectomy.

**LEARN TO LOVE WITHOUT CONDITION, TALK WITHOUT BAD INTENTION, GIVE WITHOUT ANY REASON, AND MOST OF ALL, CARE FOR PEOPLE WITHOUT ANY EXPECTATION.**

# SECTION 5: LARYNX

## CHAPTER 43:

### ANATOMY AND PHYSIOLOGY OF LARYNX:

#### Core competencies

EN 1.1.6: Describe the anatomy and physiology of larynx

EN 1.1 Describe the anatomy & physiology of ear, nose, throat, head and neck.

EN 1.1.7: Physiology of larynx

#### Topic for integrated teaching under Anatomy

AN 38.1 Describe the morphology, identify structure of the wall, nerve supply, blood supply of larynx and actions of intrinsic and extrinsic muscles of the larynx.

#### INTRODUCTION:

Larynx is composed of a skeletal framework, connected by ligaments, membranes and joints, moved by muscles and lined by respiratory mucosa inside.

- It lies in the midline of neck opposite C3- C6 vertebrae.
- It lies in front of hypopharynx.
- In infant superior margin of larynx is at the level of C2.

**Larynx has 3 parts- supraglottis, glottis and subglottis.**

Epilarynx includes arytenoid, aryepiglottic folds and suprahoid epiglottis which forms inlet of larynx.

#### SKELETON OF LARYNX:

**Larynx has,**

- 3 paired and 3 unpaired cartilages, 2 joints,
- 3 extrinsic membranes, 4 intrinsic membranes,
- 2 groups of intrinsic and 2 groups of extrinsic muscles.

#### LARYNGEAL CARTILAGES:

There are 3 paired and 3 unpaired cartilages. Thyroid, cricoid and arytenoid are hyaline, can undergo calcification starting at 25 years age and the rest are fibroelastic cartilages.

- **Paired:** Arytenoids, corniculate, cuneiform. [Remember – ACC]

It is important to note that ossification does not occur in elastic cartilages like epiglottis, cuneiform, corniculate cartilages. Also vocal process of arytenoid cartilage does not ossify.

- **Unpaired:** Epiglottis, Thyroid, Cricoid [Remember – ETC]

**1. Epiglottis:** It is leaf like, attached to hyoid bone by hyoepiglottic ligament which divides it into suprahoid and infrahyoid parts.

- Stalk like process of this cartilage is attached to thyroid cartilage in the midline just above the attachment of vocal cords.
- Anterior surface of the epiglottis is separated from thyrohyoid membrane and upper part of the thyroid cartilage by **pre-epiglottic space** [also called **space of Boyer**] which is filled with fat. Posterior surface of epiglottis is concave above and convex below, has multiple pits which lodge mucous glands.
- It has perforations which provide direct communications between laryngeal surface of epiglottis and pre-epiglottic space. Cancer spreads through these perforations.

**2. Thyroid:** It is the largest cartilage of all, has 2 laminae, meeting in the midline forming 90° in females and 120° in males.

- Vocal cords are attached to middle of the thyroid cartilage angle.
- On its outer surface, there is oblique line to which **Stemothyroid, Inferior constrictor and Thyrohyoid muscles are attached.** [Remember **SIT**]
- It calcifies earliest amongst all laryngeal cartilages and it is in figure of 8 pattern, starting at 20 years age and complete by 70 years age.
- It is important to note that this pattern is destroyed when carcinoma invades thyroid cartilage.

**3. Cricoid:** It is of signet ring shape and it is the only cartilage forming a complete ring.

It is broader posteriorly called lamina and anteriorly arch shaped and narrow.

4. **Arytenoid cartilages:** it is paired and pyramidal in shape.

- It has a base which forms cricoarytenoid joint with cricoid cartilage.
- It has 2 processes- muscular process and vocal process.
- Vocal cord is attached to the vocal process and
- Two muscles – posterior cricoarytenoid and cricothyroid are attached to muscular process.

5. **Corniculate cartilage:** it is attached to the apex of the arytenoid, like a horn.

6. **Cuneiform cartilage:** it is rod shaped, and lies in the aryepiglottic fold.

#### LARYNGEAL JOINTS:

##### Cricoarytenoid joint:

- It is a **synovial joint** with a fibrous capsule between cricoid lamina upper border and the arytenoid base.
- It **rotates** side wards, abducting and adducting the vocal cords.
- It **glides** towards the other arytenoid which helps in opening or closing the posterior glottis.

##### Cricothyroid joint:

It is a synovial joint between the inferior cornua of thyroid lamina and cricoid cartilage.

It rotates on a transverse axis.

#### LARYNGEAL MEMBRANES & LIGAMENTS:

Classified into two types:

- Extrinsic membranes which are attached to hyoid or trachea.
- Intrinsic membranes which are attached to parts within the larynx.

##### 1. Extrinsic membranes and ligaments:

a) **Thyroid membrane:** connects thyroid cartilage and hyoid bone, is reinforced in the midline as- Median thyrohyoid ligament and laterally as Lateral thyrohyoid ligament. These lateral ligaments may contain – small cartilage called- **cartilage triticea**.

Nerve laryngeal vessels and internal laryngeal nerve pierce this membrane to enter the larynx.

b) **Cricotracheal membrane** and ligament connects cricoid cartilage and trachea.

c) **Hyoepiglottic ligament:** connects hyoid and epiglottis.

##### 2. Intrinsic membranes and ligaments:

a) **Quadrangular membrane:** it extends from aryepiglottic folds above to false vocal cords below, lies between the epiglottis and arytenoid cartilages, upper border merges with aryepiglottic fold and the lower border forms the

vestibular ligament which lies within the false vocal cord.

b) **Cricovocal membrane:** it is triangular fibro elastic membrane, its upper border forms the vocal cord stretching between the thyroid angle to the arytenoids, and its lower border is attached to the arch of the cricoid cartilage.

c) **Cricothyroid membrane** and ligament: membrane is between the thyroid and the cricoid, and ligament is in the middle part. It has 2 parts- median thick and strong ligament narrow above and broader below ( see fig 43-2) and lateral ligament on each side, thinner and deficient at places. It forms an elastic cone together with the opposite ligament which is named as **conus elasticus**. It extends between the lower border of the vocal ligaments and the upper border of the cricoid cartilage. Hence vocal ligament is considered as free upper border of conus elasticus. Tumours spread beyond the larynx through the gaps in the lateral ligament.

d) **Thyroepiglottic ligament:** is between thyroid cartilage and the epiglottis

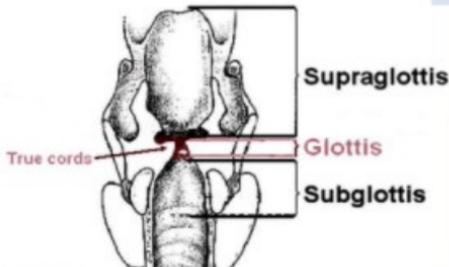


Fig 43.1: Interior of larynx – note 3 parts-Supra glottis, Glottis, Subglottis.

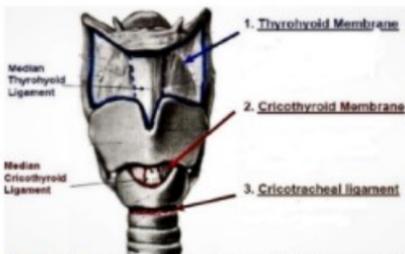


Fig 43-2: Extrinsic membranes and ligaments of Larynx

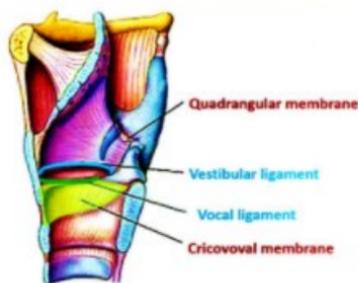


Fig 43-3: Intrinsic membranes and ligaments of larynx

### LARYNGEAL MUSCLES:

- They are classified into extrinsic and intrinsic;
- The former connects the larynx to surrounding structures and the latter connect the laryngeal cartilages with each other.

**Interarytenoid is the only unpaired muscle in the larynx. It is supplied by both RLN.**

### 1. INTRINSIC MUSCLES OF LARYNX:

They are grouped into two – based on their action on vocal cord or laryngeal inlet.

#### a) Acting on vocal cords:

- **Abductor- PCA-posterior cricoarytenoid. It is important for inspiration. Hence it is called "Safety muscle" of larynx. PCA muscle is the only abductor muscle of vocal cord.**
- **Adductors – LCA -lateral cricoarytenoid (main), CT [ Cricothyroid,]**
- **Tensors- are 2 and they are cricothyroid and vocalis [ internal thyroarytenoid].**
- **Cricothyroid is the only muscle supplied by SLN; hence VC adduct in RLN palsy.**

#### b) Acting on the laryngeal inlet

- **Opener: Thyroepiglotticus – a part of thyroarytenoid**
- **Closer: Interarytenoid**

**Cricothyroid muscle is the only intrinsic muscle which lies outside the laryngeal framework.**

### 2. EXTRINSIC MUSCLES:

They are grouped into - elevators and depressors of larynx:

#### a) Elevators-

- **Primary –stylopharyngeus, palatopharyngeus, salpingopharyngeus.**
- **Secondary – mylohyoid, stylohyoid, digastric, thyrohyoid and geniohyoid.**

- c) **Depressors:** sternohyoid, sternothyroid and omohyoid

### LARYNGEAL CAVITY

It starts from the laryngeal inlet and ends at the lower border of cricoid cartilage. It communicates with pharynx above and trachea below.

#### Mucosa of the larynx:

It is stratified squamous non-keratinising epithelium in vocal cords and AE folds, rest is lined by pseudostratified ciliated columnar epithelium. Mucous glands are present throughout except on vocal cords, and they are numerous in saccules, posterior surface of epiglottis and aryepiglottic folds.

#### Cavity of the Larynx:

It is divided into 3 parts by two pairs of folds vocal fold and vestibular fold - vestibule, ventricle, and subglottis.

**Vestibule:** extends from the laryngeal inlet to vestibular fold ( false vocal cord).

**Ventricle:** is between the true and false vocal cord. It is a deep elliptical space which extends laterally upwards between the thyroid cartilage and the false VC, called saccule of the larynx- it is also called as "oil can of the larynx". There are many mucous glands in the saccule which lubricate the vocal cords.

#### Vocal cords:

- These are 2 pearly white folds extending from the middle of the thyroid angle to the arytenoids.
- It consists of 3 layers – mucosa, (scanty submucosa) , lamina propria , vocalis muscle.
- Lamina propria has 3 layers-
  - a) Superficial – Reinke's space
  - b) Intermediate layer & Deep layer- together form vocal ligament
- It has scanty blood supply and poor lymphatic drainage .
- **Vocal cords appear pale on endoscopy because there is no submucosa and no blood vessels.**

#### Vestibular folds [false vocal cords]:

There are two folds one on each side; each fold contains vestibular ligament, thyroarytenoid muscle and mucus glands.

**Glottis:** It is the space between the two vocal cords anteriorly and vocal processes of arytenoids posteriorly. So, anterior two thirds is membranous called phonatory glottis and posterior one third is bony called respiratory glottis. Its length is 24 mm in men and 16 mm in women.

#### Subglottis:

It is between the true vocal cords and the lower border of the cricoid cartilage.

It is narrowest area in infants. Oedema in this site causes respiratory distress early.

## SPACES OF LARYNX:

### 1. Pre-epiglottic space of Boyer:

It is between the epiglottis posteriorly and thyrohyoid membrane with thyroid cartilage anteriorly. It is between two ligaments- Hyoepiglottic above and Thyroepiglottic below.

#### Boundaries:

- Anterior- Thyrohyoid membrane and upper part of thyroid cartilage
- Posterior-Infrahyoid epiglottis and quadrangular membrane.
- Superior - Hyoepiglottic ligament
- Inferior- Thyroepiglottic ligament

It has fat and lymphatics.

It is continuous with paraglottic space.

### 2. Paraglottic space of Tucker:

It is immediately adjacent to thyroid laminae. It contains fat, blood vessels and nerves.

#### Boundaries:

- Anterolateral- Thyroid cartilage and thyrohyoid membrane
- Posterior- Pyriform fossa mucosa
- Medial- ventricle with quadrangular membrane
- Inferomedial- Conus elasticus

Its importance in spread of malignancy is described under applied anatomy below.

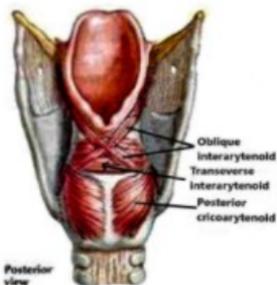


Fig 43-4: Intrinsic muscles of larynx

### 3. Reinke's space:

It is potential subepithelial space in the vocal cord. Vocal cords have outer epithelium and inner vocalis muscle. In between these two, there is lamina propria.

- Lamina propria has three layers- superficial, middle and deep.
- Superficial layer is an amorphous gel like substance which makes the vocal folds pliable

and allows them to vibrate during phonation. This is called Reinke's space.

- Middle and deep layers are called - elastin and collagen layers.
- These two layers fuse to form vocal ligament.
- Reinke's space is between the epithelium and vocal ligament.

Boundaries of the Reinke's space:

- It is limited by arcuate lines above and below,
- Anteriorly - anterior commissure
- Posteriorly - vocal process of the arytenoid
- Medially -epithelium of the vocal cord
- Laterally -vocal ligament.

Oedema of this space produces a fusiform swelling called Reinke's oedema.

Vocal nodules and polyp arise from this space.

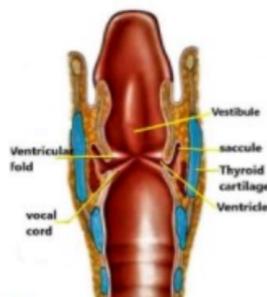


Fig 43-5: Cavity of larynx- vestibule, ventricle and saccule

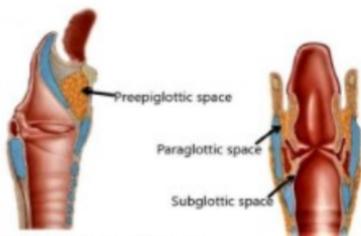


Fig 43-6: Spaces of larynx

**ARTERIAL SUPPLY:** ( Remember - S I T A - Branches of Superior and Inferior Thyroid Arteries).

- Superior laryngeal artery - branch of superior thyroid artery supplies supraglottis
- Cricothyroid artery - branch of superior thyroid artery
- Inferior laryngeal artery - branch of inferior thyroid artery supplies subglottis.

Inferior thyroid artery also supplies RLN

#### Venous drainage:

- Above the vocal cord - through superior thyroid vein to internal jugular vein
- Below the vocal cord- through inferior thyroid vein to left brachiocephalic vein.

#### Lymphatic drainage:

- **Supraglottis drains to upper and middle deep cervical nodes**
- Subglottis drains to lower deep cervical and mediastinal nodes directly or through paratracheal and prelaryngeal nodes.
- Glottis has poor lymphatic drainage except anterior commissure which drains to prelaryngeal node ( delphian node).
- Aryepiglottic folds have richest lymphatic supply in larynx.

#### Nerve supply:

- Sensory – SLN -internal laryngeal branch supplies supraglottis and upper surface of vocal cords, RLN supplies subglottis and lower surface of vocal cords.
- Internal branch again divides into two branches – sensory and secretomotor branches.
- Laryngeal inlet has maximum sensory innervation
- Vocal cords have least sensory innervation
- Three branches of internal laryngeal nerve supplies -vallecula, epiglottis and pyriform fossa.
- Motor supply: RLN supplies all the intrinsic muscles of larynx except the cricothyroid. External branch of the SLN supplies cricothyroid.
- Length of right RLN is 6 cms and left RLN is 12 cms.

#### Applied anatomy:

- Larynx can be moved from side to side, which produces grating sensation, called laryngeal crepitus. It is absent in post cricoid carcinoma and prevertebral lesions.
- It moves vertically and anteroposteriorly during deglutition and phonation.
- Epiglottis is not essential for swallowing and hence can be amputated in carcinoma with no complication of aspiration pneumonia.
- Cricoarytenoid is a synovial joint which can get involved in rheumatoid arthritis, causing joint fixation and vocal cord fixation similar to vocal cord palsy.
- Thyroid and cricoid cartilages start ossifying from 25 years age and end by 65 years age. This may be mistaken for foreign body.

- Supraglottis is the most common site for laryngeal foreign bodies.
- Malignant lesions of the epiglottis, supraglottic larynx and tongue base can extend through the pores in the epiglottis to the pre-epiglottic space.
- **Tucker space:(Paraglottic space)** This space surrounds laryngeal ventricle. Transglottic spread of malignancies occur through this space. Tumours from inside larynx spread to hypopharynx and to extralaryngeal tissues outside the larynx through this space.
- Sacculae in the supraglottis, can dilate to become laryngocele. Sacculae has mucous glands, which lubricate the vocal cords. Sacculae is called the "oil can of larynx" because its secretions lubricate the vocal cords.
- **Glottis is the narrowest part of the airways in adults**, and hence foreign bodies get stuck in glottis. Subglottis is narrowest part of larynx in children. There are no mucus glands in the vocal cords.
- There are no lymphatics in the vocal cords and hence there is no lymphatic metastasis from **vocal cord carcinoma.**
- Vocal cords remain adducted in RLN palsy, due to unopposed action of cricothyroid muscle supplied by SLN.
- **A neonate can respire without difficulty while suckling milk due to high position of the larynx against C1 -2, by which epiglottis meets the soft palate and creates nasopharyngeal channel for airway.**
- **Change in voice pitch is caused by cricothyroid muscle, which adjusts the length of the vocal cords.**

#### DEVELOPMENT OF LARYNX:

It is divided into prenatal and postnatal stages.

- **Prenatal stage** is divided into two phases-embryonic phase of organogenesis upto 8 weeks and foetal phase of organ maturation which is upto 36 weeks.
- **Postnatal stage-** is again divided into two phases- first phase from 2 to 6 years age, second phase -during adolescence

#### TIMELINE:

##### **PRENATAL STAGE:**

##### **Organogenesis:**

- Larynx starts growing by 4<sup>th</sup> week, begins as a slit like diverticulum, in the ventral column of pharynx. It is clearly identifiable by 8<sup>th</sup> week.

##### **Organ maturation:**

- 8<sup>th</sup> week -Laryngeal lumen is occluded and recanalization occurs by 10<sup>th</sup> week of gestation.
- 9<sup>th</sup> week- arytenoids have vocal processes. Laminae of thyroid cartilage fuse in midline.

- 18<sup>th</sup> to 25<sup>th</sup> week- epiglottic cartilage matures, corniculate and cuneiform are formed
  - By 7<sup>th</sup> month, epiglottic cartilage matures.
  - By 9<sup>th</sup> month, arytenoid is fully grown to adult size.
- ✓ At birth, larynx lies opposite cervical vertebrae C3-4 vertebral level.
  - ✓ During swallowing, it goes up to C1/C2 level so that, epiglottis lies close to soft palate making an air channel for breathing, while the baby feeds through the mouth uninterrupted.
  - ✓ This is unlike in adults, when breathing stops during deglutition.

#### POSTNATAL STAGE:

##### First phase:

- 2<sup>nd</sup> year onwards, larynx starts descending in the neck and reaches its adult position to lie between C4-C7 by 6<sup>th</sup> year of life.
- Larynx elongates with appearance of spaces between the cartilages.
- Cricoid keeps growing till 10 years age.

##### Second phase:

- In the adolescent age, thyroid angle becomes prominent in males and vocal cords become longer leading to physiological voice changes of an adult male.

#### Developmental origin of different parts of larynx are as follows.

- Mucosa** of the larynx develops from foregut endoderm.
- Muscles** and cartilages develop from mesenchyme.
- Cartilages:**
  - Epiglottis, and upper part of thyroid cartilage are from 4<sup>th</sup> arch,
  - Lower part of thyroid cartilage, cricoid cartilage, arytenoid are from 6<sup>th</sup> arch
- Muscles:**
  - Intrinsic muscles of larynx- are from 4<sup>th</sup> and 6<sup>th</sup> arch;
- Nerves:**
  - Superior laryngeal nerve is from 4<sup>th</sup> arch
  - Recurrent laryngeal nerve is from 6<sup>th</sup> arch.

#### DIFFERENCES BETWEEN PAEDIATRIC AND ADULT LARYNX.

	Paediatric	Adult
Position	Larynx is opposite C3-4, glottis is at C3 level and goes up to C1-2 level during swallowing. [Epiglottis reaches soft palate which helps nasal breathing during swallowing].	Larynx is opposite C3-6; glottis is at C5 level
Size	Equal in both sexes	Bigger in males than females.
Shape	Conical and funnel shape	Cylindrical shape
Narrowest part	Subglottis	Glottis
Epiglottis	Large and folded, omega shaped	Leaf like
Cartilages	Soft & collapse easily, injury does not lead to fracture	Ossified and rigid, so injury causes fracture.
Thyroid cartilage	Flat	Angled; In men, thyroid laminae meet at 120°, in females at 90°
Submucosal tissues	Loose, become oedematous easily, can cause stridor	Less tissue and dense, does not lead to stridor.
Vocal cords	6-8 mms	15-23 mms
cricothyroid and thyrohyoid spaces	Very narrow; hyoid overlaps thyroid and thyroid overlaps cricoid	wider

Table 43-1: Differences between paediatric and adult larynx.

## PHYSIOLOGY OF LARYNX.

**Main functions of larynx are:**

1. Protection of the airways
2. Phonation
3. Respiration
4. Chest fixation

**A. PROTECTION OF AIRWAYS:**

This is the primary function of the larynx. During deglutition, airways is protected by

- sphincteric action,
- laryngeal elevation,
- laryngeal tilting,
- cessation of respiration
- cough reflex.

There are 3 tiers of sphincters

- laryngeal inlet with epiglottis and aryepiglottic folds
- true vocal cords
- false vocal cords

**Cessation of respiration reflex-** Afferent sensory is 11<sup>th</sup> CN and Efferent motor supply is 10<sup>th</sup> CN.

**Cough is a protective reflex**, which prevents entry of any foreign bodies into larynx.

**Laryngeal reflexes in paediatric larynx**

Following vital protective reflexes are known to occur in an infant.

1. **Laryngeal adductor reflex-** during the act of swallowing, vocal cords adduct and larynx gets elevated.
2. **Oesophago-glottal closure reflex- EGCR** – when the stomach contents regurgitate to oesophagus, it causes reflex adduction of vocal cords, to prevent aspiration.
3. **Pharyngoglottal closure reflex-** presence of fluid in pharynx causes closure of vocal cords, higher the amount, faster the closure.

**B. PHONATION:**

Larynx not only produces sound but also modifies the pitch and volume of the sound. The strength of exhaled air from the lungs contributes to loudness. Larynx, similar to lungs, creates pressure differences required for sound production. A constricted larynx can be raised or lowered affecting the volume of the oral cavity as required in glottal consonants. False vocal cords are not responsible for sound production and are only used for resonance.

**THEORIES OF PHONATION-**

1. Vibrating string theory ( Ferrein 1741)
2. Neurochronaxic theory (Husson 1950)
3. Aerodynamic theory
4. Myoelastic theory
5. Two mass theory ( Broad 1973) ( Ishizaka and Flanagan 1972)

6. Muco viscose, cover body and flow separation theory. ( Broad 1979, Hirano 1974, Ishizaka and Matsudaira 1968):

The tone produced by vocal folds gets amplified by the resonating chambers of mouth, pharynx, nose and chest. This amplified tone gets modified to speech by modulatory actions of lips, tongue, palate, pharynx, nose and chest.

Mechanism of phonation is explained by the following theories.

**1. VIBRATING STRING THEORY:**

According to this theory, vocal cords are presumed to vibrate like strings of a violin and produce tone. Vocal tract acts as resonating chamber but it needs amplification for the tone to be heard. Only pressure of escaping air from lungs can produce such amplification. Hence this theory is not accepted.

**2. NEUROCHRONAXIC THEORY**

This theory presumes that vibration of the vocal folds is realised by rapid contraction and relaxation of the vocal cord muscles. Vocal folds vibrate upto 400 times per second during speech and 2000 times per second during crying of a baby. No muscle can vibrate at such rates and nerves can produce maximally 1000 impulses per second. Hence this theory got discarded.

**3. AERODYNAMIC THEORY:**

When air flows through a narrow passage, its pressure drops but velocity increases according to Bernoulli's principle. Due to this lower pressure, vocal folds get sucked in and close the glottic passage. This is called aerodynamic effect. When the subglottic pressure raises due to air pressure coming from lungs, the vocal folds are forced apart. Once the air passes fast, pressure drops, and vocal folds again get sucked in. This cycle gets repeated again and again. Subglottic air pressure remains constant, but the rate of vocal fold vibration keeps changing, which can not be explained by this theory. This is explained by these following theories.

**4. MYOELASTIC THEORY:**

**There are 4 factors-**

**Length :** Longer strings produce lower tones and shorter strings in violin produces higher tones. Males have longer vocal cords and hence produce low pitch sounds and women have shorter vocal cords and hence produce high pitch sounds.

**Elasticity:** of the vocal folds determines the rate of vocal fold vibration. Tense folds vibrate faster than slack folds, like a tense violin string produces faster vibrations than a slack string.

**Thickness and tension :** thick and slack vocal fold vibrates slowly than a thin vocal fold. This is similar to a thick guitar string produces lower tone than a

thin and tense string. Vocal folds change from forming thick fleshy lips to thin bands, thus changing the rate of vibration.

These 4 factors – namely length, elasticity, tension and thickness of vocal folds constitute myoelastic effects.

### 5. TWO MASS THEORY: (ISHIZAKA AND FLANAGAN 1972)

Lower parts and upper parts of vocal folds execute separate but related movements. When lower parts are forced open, the upper part still remain closed. When the upper parts start opening, lower parts begin to close again. Thus opening and closing of the two parts are not in the same phase. This lag between the two phases, ensures complete closure of the tracheal space and maintenance of the subglottic air pressure. This principle is called Two-mass theory.

### 6. MUCO-VISCOSE, COVER, BODY and FLOW SEPARATION THEORY

Outer edges of vocal folds has viscous (thick and sticky) surface. Deeper body of vocal cords is muscle body and is different than the outer edges. Hence they both react differently to air stream. This is called muco-viscose and cover body theory. At the top edge of the vocal cords, eddies of air currents develop due to sudden change of the air stream. These eddy

currents influence vibration of the vocal folds at the top edge.

In summary, Aerodynamic theory explains how the vocal folds open and close quickly. Myoelastic theory explains how the vocal folds vibrate, without Bernoulli effect. Two mass theory explains how vocal folds achieve complete closure all the time. Muco viscose, cover body and flow separation theories explain oscillation characters of the vocal folds. Phonation is hence explained by many theories and not one theory alone

### C. RESPIRATION:

Larynx regulates air entry; vocal cords abduct for inspiration and adduct during expiration.

### D. CHEST FIXATION:

Rima vestibuli – space between false vocal cords act as exit valves, which allow only entry of air. Closure of larynx helps in fixing the chest wall, facilitating functions like lifting heavy weights, parturition, micturition, defecation and vomiting.

**E. OTHER FUNCTIONS:** Larynx also participates in various other functions such as swallowing, coughing, laughing, hiccupping, and postural adjustments. False vocal cords resist airflow from the chest and serve expectorative function.

### CASE STUDY 1

Q1) A 45 years old female underwent total thyroidectomy following which she developed breathing difficulty. During surgery, there was bleeding and surgeon had tough time to manage. On examination, vocal cords were paramedian and the glottic chink was 3 mm.

A) Which structure got injured during surgery in this case?

1. Vocal cords
2. SLN
3. RLN\*\*

4. Both nerves
- B) RLN supplies all the muscles except;
1. Thyroarytenoid
  2. Cricoarytenoid
  3. Cricothyroid\*\*
  4. Interarytenoid
- C) Phonatory glottis is;
1. Anterior 1/3<sup>rd</sup> of vocal cords
  2. Middle 1/3<sup>rd</sup> of vocal cords
  3. Posterior 1/3<sup>rd</sup> of vocal cords
  4. Anterior 2/3<sup>rd</sup> of vocal cords\*\*

### Answers:

Q1) A- 3, B-3, C-4

### KEYPOINTS

1. Larynx has 3 paired and 3 unpaired cartilages. Epiglottis, cuneiform and corniculate cartilages do not ossify. Epiglottis is leaf like and cricoid is the only cartilage with a complete ring.
2. Interarytenoid muscle is the only unpaired muscle and is supplied by both RLN.
3. Posterior cricoarytenoid is the only abductor of the vocal cords, important for inspiration and hence called "safety muscle" of the larynx.
4. Cricothyroid is the only muscle supplied by SLN.
5. Vocal cords appear pale on endoscopy because there is no submucosa and no blood vessels. Also, very poor in lymphatics and hence no lymphatic metastasis with excellent prognosis and cure by radiotherapy.

6. Vocal ligament is as solid as knee joint ligament, which has the capacity to absorb very high tensile stress. It is formed by intermediate and deep layer of lamina propria.
7. Glottis is the narrowest part of airway in adult and subglottis is narrowest in a child.
8. Anterior  $2/3^{\text{rd}}$  of vocal cord is called phonatory glottis and posterior  $1/3^{\text{rd}}$  is called respiratory glottis.

**THE DROPS OF RAIN MAKE A HOLE IN THE STONE NOT BY VIOLENCE, BUT BY OFT FALLING.**

## CONGENITAL LESIONS OF LARYNX:

1. LARYNGOMALACIA:
2. CONGENITAL VOCAL CORD PALSY:
3. CONGENITAL SUBGLOTTIC STENOSIS.
4. LARYNGEAL WEB /ATRESIA:
5. LARYNGOCOELE:
6. CONGENITAL SUBGLOTTIC HEMANGIOMA LARYNX:
7. LARYNGOTRACHEAL CLEFT

### Topics for integrated teaching under paediatrics

**PE 28.7** Discuss the etiology, clinical features and management of stridor in children

**PE 28.9** Elicit, document and present age appropriate history of a child with upper respiratory problem including stridor.

Errors in embryogenesis or intrauterine events that affect embryonic and foetal growth produce congenital anomalies.

Symptoms range of congenital anomalies in larynx are,

- Respiratory distress, dyspnoea with cyanosis
- Stridor
- Weak or hoarse cry
- Dysphagia
- Aspiration into lungs
- Failure to thrive
- Sudden death

Congenital lesions in larynx are important causes of apyrexial stridor in children.

**80-85% children below 3 years with stridor have congenital cause.**

- 60% of these anomalies are in larynx.
- 20-25% of anomalies are in trachea and bronchi.
- 45% of patients have more than one anomaly.

### CLASSIFICATION OF LARYNGEAL ANOMALIES:

#### 1. Supraglottis –

- Laryngomalacia ,
- Laryngeal cyst ,
- Supraglottic web,
- Supraglottic cleft,
- Congenital laryngocoele

#### 2. Glottis-

- Glottic web,
- Vocal cord paralysis,
- Cri-du-chat syndrome

#### 3. Subglottis-

- Subglottic stenosis,
- Subglottic web,

- Subglottic hemangioma,
- Laryngotracheal cleft

#### Most common lesions are -

1. Laryngomalacia (60%),
2. VC palsy(20%),
3. Subglottic stenosis(15%),
4. Subglottic hemangioma(1.5%)
5. Laryngeal web and laryngocoele.

All these patients must get genetic screening and cardiovascular status evaluation especially of aortic arch.

**LARYNGOMALACIA:** | Also called Congenital laryngeal stridor | ( Jackson and Jackson- 1942)

**It is the most common anomaly causing chronic stridor in infancy.**

- It appears at birth or first month of life, steadily increases over next 6 months and then gradually disappears by 2- 5 years age.
  - There is no racial and sex predilection. Seen in all races and both sexes.
  - It is more common with Down's syndrome.
  - Infant is generally happy and thriving well.
- There are 3 types- Mild, Moderate and Severe.

• **99% cases are mild type.**

#### Pathology:

- In this condition mucosa is wrinkled and loose especially over arytenoid cartilages.
- Cartilages are soft, thin, hypocellular and immature
- Supraglottis is bulky and excessively flaccid and collapses / sucked in during inspiration causing stridor and cyanosis. It may affect epiglottis and arytenoids.

- Epiglottis is omega shaped, aryepiglottic fold is floppy,
- Arytenoids are prominent and laryngeal inlet takes a cruciate appearance.
- Subepithelial inflammation and oedema is seen secondary to GERD.

**Pathogenesis: Theories of causation:**

**There are 3 theories;**

1. Improper maturation and development of cartilages.
2. Gastro-oesophageal reflux disease- GERD exaggerates this condition and is present in 50-100% of cases.
3. Immature neuromuscular function

**Precipitating factor:**

4. Foetal warfarin syndrome ( also called warfarin embryopathy): pregnant mothers taking warfarin give birth to children with laryngomalacia amongst other anomalies.
5. Co-existent Down syndrome



**Fig44-1:** Omega shaped epiglottis – Laryngomalacia  
(Courtesy: Dr Simon Browning, Asso Prof, Swansea University Medical School, South Wales, UK)

**Symptoms:**

- 1) Stridor- high pitch, croaking sound, noticed within a few days of birth,
  - Increases on crying, in supine position, during sleep, agitation, during URTI, during and after feeding.
  - Decreases in prone position and neck extension.
  - Increases during first 8 months, maximum between 9 to 12 months age, then starts decreasing.
  - Often intermittent during feeds, crying, in supine posture only
- 2) **Voice is normal**
- 3) Cry is normal
- 4) Feeding difficulty
- 5) Choking or coughing during feeding

- 6) Slow weight gain

**Signs:**

1. Tachypnoea
2. Inspiratory stridor , heard just above the suprasternal notch
3. Chest and lower neck retractions during inspiration
4. Child is otherwise healthy

**D/D**

1. Tracheomalacia
2. Innominate artery compression
3. Vascular rings of trachea
4. Hypocalcaemia
5. Foreign body larynx
6. Laryngo-tracheo-bronchitis [ Croup]

**INVESTIGATIONS:**

**Endoscopy:**

- 1) **DL scopy** – reveals the omega shaped epiglottis,
  - whole supraglottis is deepened and narrowed,
  - arytenoid cartilages are prominent and elongated.
- 2) Flexible laryngoscopy – shows the typical features as described above Look for collapse of the supraglottis on inspiration.
- 3) Triple endoscopy- laryngoscopy, bronchoscopy and oesophagoscopy with the same scope and pass the scope in both nasal passages, to rule out unilateral choanal atresia. It is important to rule out second pathology, which may be present in many cases.
- 4) Rigid bronchoscopy- to rule out other anomalies causing stridor / respiratory distress.

**Radiology:**

- Airway Fluoroscopy – shows supraglottic collapse and hypopharyngeal dilatation

**TREATMENT:**

- 1) **Reassurance-** is the most common mode of treatment, as the disease is self-limiting
- 2) To **keep the child in prone position** as it reduces symptoms
- 3) Proton pump inhibitors for GERD
- 4) if symptoms are severe, following procedures are advised.
  - a. Epiglottoplasty / supraglottoplasty – is a procedure in which, there is excision of wedge of aryepiglottic folds on both sides, trimming of epiglottis, excision of corniculate, cuneiform cartilages and redundant arytenoid mucosa. This can be done by, CO2 laser or microlaryngeal scissors or microdebrider
  - b. Laser epiglottomy – in this procedure, epiglottis is permanently fixed to aryepiglottic folds. This is done in cases of laryngomalacia with aspiration pneumonia for permanent protection of the airways. Adequate space exists for breathing and phonation.
5. O<sub>2</sub> inhalations if SpO<sub>2</sub> is below 90%.

6. Tracheostomy-done in life threatening stridor cases and it is maintained till 2 years age, by which time, child will have recovered fully from laryngomalacia

**Prognosis:**

Excellent. Disappears by 2<sup>nd</sup> birthday.

**CONGENITAL VOCAL CORD PALSY:**

This is the second most common congenital laryngeal anomaly, 15-20% of all cases.

- Bilateral palsy is more common than unilateral type.
- Unilateral case is idiopathic or due to birth trauma to vagus or RLN.
- Most cases recover within 6 months age.

**Etiology:**

- 1) Idiopathic.
- 2) CNS lesions due to Arnold-Chiari malformation, meningomyelocele, hydrocephalus and cerebral palsy
- 3) Iatrogenic- prolonged intubation, birth trauma causes strain on cervical spine and the palsy lasts for 6- 9 months; surgery for cardiovascular anomalies or neck surgery or for trachea-oesophageal fistula
- 4) Congenital myasthenia gravis
- 5) Cardiomegaly or great vessels anomalies, mediastinal lesions
- 6) Benign congenital hypotonia

**Symptoms:**

1. Dysphonia
2. Hoarse voice or near normal voice
3. Hoarse and breathy cry in unilateral palsy, worsens by agitation
4. Normal voice and cry in bilateral palsy
5. Stridor at rest and worsens with agitation
6. Symptoms of pneumonia – due to aspiration in bilateral vocal cord palsy cases.
7. Unilateral vocal cord palsy – may remain asymptomatic
8. Feeding difficulties.

**Signs:**

1. Inspiratory stridor
2. Flexible endoscopy-VC in median or intermediate position depending on the cause and if RLN palsy or combined RLN and SLN palsy

**INVESTIGATIONS:**

**Blood:**

- Blood CBP

**Radiology:**

- CT Scan – Brain, neck, chest- for vagus nerve lesion and mediastinal lesions

**Endoscopy:**

- Flexible laryngoscopy
- Rigid bronchoscopy- to rule out co-existing airway anomalies

- DL Scopy

**Electrical**

- Laryngeal EMG to rule out vocal cord fixation and for prognosis.

**TREATMENT:**

**Unilateral vocal cord palsy:**

1. No treatment
2. Observation
3. Manage feeding by upright position to avoid aspiration.

**Bilateral vocal cord palsy:**

Spontaneous recovery can occur in upto 58% cases.

1. Cordopexy- Cord lateralization after 5 years age.
2. Endoscopic arytenoidectomy or
3. Transverse laser cordotomy- done at 11 yrs age or more.
4. Suture lateralisation
5. Tracheostomy – is maintained upto 2 years age when spontaneous recovery of palsy may occur. It may be necessary in 50% cases.
6. Endotracheal intubation

**CONGENITAL SUBGLOTTIC STENOSIS**

**Introduction:**

- Subglottis is the narrowest airway since it is complete, nonexpandable, non-pliable ring of cartilage.
- It is the third most common congenital airway problem in children.
- It forms 15% of all congenital laryngeal anomalies
- May be associated with Down syndrome
- It can present as life threatening airway emergency.
- It is the most common indication for tracheostomy in infants.
- It is seen in 1<sup>st</sup> week to 1<sup>st</sup> month of life.
- Incidence- Male: female= 2:1.

**Etiology:**

- It is due to abnormally thick cricoid cartilage or
- excessive submucosal fibrous tissue in the subglottis.
- defective canalisation of cricoid cartilage and /or conus elasticus

Precipitating factor:

- Respiratory tract infection

**Pathology:**

There are 4 types of abnormalities-

1. Abnormal submucosal thickening
2. Abnormally shaped cricoid cartilage
3. Cricoid of small dimensions
4. Displaced 1<sup>st</sup> tracheal ring

**There are 4 grades of obstruction- Myer-Cotton**

- Grade 1- 0-50% obstruction – needs no surgery
- Grade 2- 51-70% obstruction
- Grade 3- 71- 99% obstruction

- Grade 4 – 100% obstruction

#### Recent classification:

1. **Membranous** - most common and is mild form. There is circumferential submucosal hypertrophy.
2. **Cartilaginous** - due to abnormal cricoid cartilage shape, may be thickened anterior and posterior laminae

#### Symptoms:

1. Resembles croup -with barking cough but it is recurrent or persistent unlike laryngotracheobronchitis (LTB).
2. stridor or respiratory distress, dyspnoea
3. Cry is normal



Fig 44-2a : Subglottic stenosis- Mild stenosis

#### Signs:

1. Biphasic stridor
2. Dyspnoea
3. Chest retractions
4. Cyanosis
5. Difficult intubation, extubation or decannulation- suspect subglottic stenosis



Fig 44-2 b: Subglottic stenosis- Elliptical



Fig 44-2c: Subglottic stenosis- Incomplete

#### INVESTIGATIONS:

##### Radiology:

1. Plain X-Ray Neck – PA and Lat view- shows Steeple sign in PA view and narrow line in lat view.
2. Fluoroscopy
3. Barium enhanced oesophagogram – to rule out vascular malformations & GERD

##### Endoscopy:

1. Flexible Naso pharyngo laryngoscopy
2. Rigid laryngoscopy/ bronchoscopy- subglottic diameter less than 4 mm in normal neonate and 3 mm in premature infant is suggestive of SGS.
3. Rigid bronchoscopy to rule out coexisting other airway anomalies

##### TREATMENT:

Most cases may resolve spontaneously.

- 1) Treatment according to Myer-cotton grading system:

- Grade 1 – no surgical treatment
- Grade 2 – Laryngotracheal reconstruction LTR- with anterior cartilage grafting without stent
- Grade 3 mild-- anterior graft with post cricoid split with stent.
- Grade 3 severe- anterior and posterior grafts with stent. Alternately do PCTR- partial cricotracheal resection.

- a. Laryngotracheal reconstruction: LTR ( also called Laryngotracheoplasty) - reserved for severe cases. This procedure involves augmentation of laryngotracheal complex by anterior and/or posterior midline incision of cricoid with costal cartilage grafts to expand airway.
- b. PCTR: This procedure involves complete resection of stenotic segment with end to end anastomosis of tracheal stump to thyroid cartilage.

- 2) Other treatment options:
- 3) Antacids / proton pump inhibitors in case of GERD
- 4) Endoscopic dilatation with steroid injections
- 5) Laser incisions with steroid injections, topical mitomycin
- 6) Tracheostomy.
- 7) Endotracheal intubation

#### LARYNGEAL WEB /ATRESIA:

##### Introduction:

- It is a rare anomaly. Extreme type is called atresia.
- Associated with Shprintzen syndrome – chromosome 22 anomaly
- Mostly it is seen between the vocal cords, rarely in subglottis or supraglottis
- Majority involve anterior glottis, but also seen in posterior interarytenoid region

- It is acute in onset, immediately after birth.
- It may be thin or thick web; complete or incomplete.

#### Etiology:

- It is due to incomplete recanalization of larynx.

#### Symptoms:

- 1) Hoarse voice, dysphonia – high pitched squeaky voice
- 2) Stridor - if the web is in posterior glottis.
- 3) Hoarse cry or weak cry or no cry

#### Signs:

1. Inspiratory stridor
2. Severe chest retractions
3. Web may be thin or thick, complete or partial, anterior or posterior

#### Investigations:

1. Flexible laryngoscopy
2. Plain X-Ray neck lateral view- shows “**SAIL sign**” . it resembles ship sail.

#### Treatment:

1. Thin web may be divided endoscopically by knife or CO2 laser. This is followed by endoscopic suturing of cut edges to prevent restenosis.
2. Thick web - excision via laryngofissure and placement of a silicon keel and subsequent dilatations
3. Longer and thicker webs- First tracheostomy, then correction done at 3-4 yrs age via laryngofissure.



Fig 44-3: Congenital laryngeal web

### LARYNGOCOELE:

Details described in chapter 49.

### CONGENITAL SUBGLOTTIC HEMANGIOMA LARYNX:

It is a potentially life threatening condition due to possibility of airway obstruction.

- It is third most common congenital benign tumour
- It is not hereditary
- Sex: female : male = 2:1

- Cavernous type of haemangioma
- If the child also has haemangioma in the chin- in “ beard” pattern and a sternal pit, PHACES syndrome should be ruled out.

#### Etiology:

It arises from mesenchymal rests of vasoactive tissue in the subglottis. It is a vascular malformation.

#### Symptoms:

- Asymptomatic at birth: symptoms start after an attack of urti.
- Respiratory distress -insidious and progressive, starting from 2<sup>nd</sup> month or after 6 months age. It is intermittent initially and becomes continuous later
- Stridor increases by agitation, crying
- Barking cough
- Cry is normal
- Failure to thrive

#### Signs:

- Biphasic stridor
- Dyspnoea
- Cyanosis
- Chest retractions
- Associated with cutaneous haemangioma in 50% cases.
- Mediastinal haemangioma

**PHACES syndrome-** nearly 47% patients have haemangioma with this syndrome. [Posterior fossa brain malformation-Haemangioma-Aorta coarctation- Eye anomalies- Sternal cleft]

#### INVESTIGATIONS:

##### Radiology:

1. X-Ray-Neck –soft tissue- PA & lat views- shows asymmetric narrowing of subglottis.
2. MRI – Neck

##### Endoscopy:

1. Flexible laryngoscopy is done to rule out other anomalies.
2. Rigid bronchoscopy – is needed to confirm the diagnosis.
3. DL Scopy-
  - pear shaped ,purple or reddish blue mass seen in the subglottis.
  - asymmetric, compressible ,
  - SC Injection of a few drops of 1: 1000 adrenaline causes shrinkage of the mass, visible during DL scopy.

**Biopsy is contraindicated** as it causes severe bleeding.



**Fig 44-5:** Subglottic haemangioma larynx-  
See black arrow

#### DIFFERENTIAL DIAGNOSIS:

- Croup: it can be mistaken for "croup" but lack of fever and rhinorrhoea must rule out croup.
- Vascular malformations are similar to haemangiomas. They are present at birth, grow rapidly proportionate with the growth of the child. They do not involute spontaneously.
- Haemangiomas may not be present at birth, grow rapidly faster than the child's growth, but involute spontaneously.
- To distinguish haemangiomas from vascular malformations, there is a Immunohistochemical markers for haemangiomas- called GLUT 1- Glucose Transporter protein. GLUT immunoreactivity is seen in 97% cases of haemangiomas and in none of the cases of vascular malformation.

#### TREATMENT:

- 1) Tab propranolol- is used as first line treatment now- shrinks the capillaries in capillary haemangioma.  
Gives involution in 97% cases by its vasoconstriction action.
- 2) **Depending on the size of the lesion-**
  - a) Very small – No treatment
  - b) Small – CO<sub>2</sub> laser excision, cryosurgery
  - c) Medium – Steroid is indicated and given in the following doses and routes.
    - Systemic: Inj dexamethasone 1mg/kg/day for 1 week, then tab prednisolone 3mg/kg in divided doses for 1 year
    - Local: Intralesional steroid injection, interferon, sclerosants
  - d) Large - Primary submucous resection
  - e) Very large- Tracheostomy and wait for resolution

#### CASE STUDY 1

Q1) A 6 month old female Caucasian, well fed, thriving infant was brought by the mother with

3) Tracheostomy- for acute stridor

#### Prognosis:

- It regresses spontaneously at about 2 to 5 years age.
- It is life threatening and carries 50% mortality if untreated.
- Recurs if a part of the lesion is left undetected.

#### CONGENITAL LARYNGEAL/ LARYNGOTRACHEAL CLEFT

It is a rare congenital anomaly. It is caused by non fusion of posterior cricoid lamina and incomplete development of the tracheoesophageal septum which leads to communication between the larynx/trachea with oesophagus. submucous cleft may be present if only cartilage is defective but mucosa and inter arytenoid muscle are intact. Its incidence is 1 in 2000 to 50000 live births. Other anomalies like tracheoesophageal fistula, oesophageal atresia, cleft lip and palate are also seen in most patients.

#### Classification:

Most accepted classifications are;

- a. Benjamin's anatomical types 1 to 4
- b. Evan's functional types 1 to 3.

**Symptoms:** New born children with laryngeal clefts suffer from respiratory distress, feeding difficulties and recurrent aspiration.

#### Investigations:

1. Modified barium swallow
2. Microlaryngoscopy with palpation of the interarytenoid area under GA

#### TREATMENT:

**Medical :** Conservative management is advised in

#### Type 1 type

- a) Use of thick liquids, upright posture for feeding liquids and aggressive treatment for GERD and Eosinophilic oesophagitis
- b) Ryles' tube feeding

**Surgical:** if aspiration is severe;

- a) Injection laryngoplasty
- b) Endoscopic cleft repair

history of stridor, which started 2 months after birth and was gradually increasing in severity. Mother

was taking warfarin for venous thrombosis during her pregnancy. Stridor was of high pitch, inspiratory type, was more on crying, during sleep, in supine position, during and after feeds. It used to reduce on lying in prone position. Child was afebrile. Voice and cry were normal.

A) Diagnosis of this case is;

1. Tracheomalacia
2. Laryngotracheobronchitis
3. Laryngomalacia\*\*
4. Hypocalcaemia

B) Next steps in the management includes;

1. Triple endoscopy
2. Airway fluoroscopy
3. Observe supraglottis during inspiration
4. All of the above\*\*
5. Only 1 & 2.

C) Ideal treatment of this case is;

1. Reassurance, sleep in prone and wait for 2 years\*\*
2. Immediate epiglottoplasty
3. Elective tracheostomy next day
4. Laser epiglottoplexy

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#### Answers:

Q1) A -3, B-4, C-1

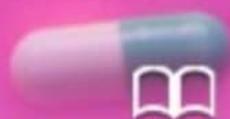
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#### KEYPOINTS:

- 1) Laryngomalacia is the most common congenital anomaly causing chronic stridor in infancy. 99% cases are mild and has excellent prognosis, disappears by 2<sup>nd</sup> birthday. Advice is to put the child in prone position and reassurance is the most common mode of treatment.
- 2) Congenital vocal cord palsy is the second and congenital subglottic stenosis is the third most common congenital anomaly in children.
- 3) Laryngeal web is seen in Shprintzen syndrome – occurs due to chromosome 22 anomaly. Glottic web is the commonest.
- 4) Laryngocoele occurs due to herniation of laryngeal mucosa through the thyrohyoid membrane. Bryce's sign is seen in this condition, which is gurgling and hissing sound in the throat on compressing the neck mass.
- 5) Congenital laryngeal haemangiomas can be distinguished from vascular malformations by positive presence of immunohistochemical markers – GLUT 1 protein.
- 6) Congenital subglottic stenosis is classified to 4 grades by Myer-Cotton.

**WHEN A MAN LOSES HIS HEALTH, HE BEGINS TO TAKE CARE OF IT.— JOHN BILLINGS**

Highlights on Medicine and Medical  
Science  
Vol. 16



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## Cases

M. Amellal, L. Mermad, S. Moughil

*Highlights on Medicine and Medical Science*

Vol. 16, 14 July 2021, Page 146-155

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## **An Approach of QRS Detection Using Fractional Order Digital Differentiators**

B. T. Krishna

*Highlights on Medicine and Medical Science*

Vol. 16, 14 July 2021, Page 156-162

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## **Study on Ambulatory Proctological Surgery as a Novel Method of Practice**

Manoj D. Togale, Manisha S. More, S. S.

Shimikore

*Highlights on Medicine and Medical Science*

Vol. 16, 14 July 2021, Page 163-168

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# Study on Ambulatory Proctological Surgery as a Novel Method of Practice

Manoj D. Togale<sup>1\*</sup>, Manisha S. More<sup>1</sup> and S. S. Shimikore<sup>1</sup>

DOI: 10.9734/bpi/hmms/v16/2973F

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## ABSTRACT

Ambulatory proctological surgery is becoming more popular due to time and financial constraints. Our research focuses on ambulatory proctological surgery as an innovative and cost-effective procedure. The first ambulatory anorectal surgery was performed in 1962 at the University of California, Los Angeles, and has since evolved through the years. The study comprised 30 patients who underwent elective anorectal operations with posterior perineal block at KLES hospital Belgaum between November 2004 and November 2005. All of the patients in the posterior perineal block group were ambulatory in less than half an hour after surgery, proving that ambulatory proctological surgery is a revolutionary procedure in today's practise. The majority of the patients experienced just minor discomfort following surgery. Urinary retention occurred in 16.7% of patients after surgery, however it was statistically insignificant. Within 24 hours of surgery, 86.67% of patients in the posterior perineal block group were discharged. According to our findings, ambulatory proctological surgery is recommended as a novel method of practise, particularly under posterior perineal block, because there is less post-operative pain and patients are discharged sooner, lowering costs and making healthcare more affordable.

*Keywords: Ambulatory proctological surgery; anorectal surgeries.*

## 1. INTRODUCTION

Ambulatory proctological surgery is becoming more popular in today's world of time and financial constraints. It is expected that 90 percent of all anorectal treatments will be conducted in an ambulatory setting at some point in the future [1]. The recent advances in anaesthesia, newer drugs have helped to improve outcomes and promise a better patient care. Since its beginning at University of California, Los Angeles, in 1962, ambulatory anorectal surgery under local anaesthesia has evolved over the course of years to include increasingly complex and invasive procedures [2,3]. Although Marc-Claude Marti (1941-2001) was the first to describe the posterior perineal block. Lateral internal sphincterotomy for anal fissures has been performed under local anaesthesia with advantage of lesser hospitalization, reduced postoperative discomfort and early healing of wounds [4]. Another study in 1986 adds that more than 90% of anorectal surgeries can be done in an outpatient setting. The use of local anaesthesia for anorectal surgery enhances patient safety as well as it reduces the costs [1]. Another study comparing local and epidural anesthesia for haemorrhoidectomy mentions majority of patients were satisfied with outpatient local anesthesia, helped in reducing their costs and few patients had minor symptoms on discharge in form of bleeding, pain, mucous discharge, urinary retention [5]. Ambulatory surgery encompasses those surgical interventions that are more complex than office-based procedures performed under local anesthesia but less complex than major procedures requiring at least an overnight stay. The potential benefits of ambulatory surgery include more rapid return to the comforts of a home environment, diminished opportunities for nosocomial complications and diminished cost [6-9]. Even stapled haemorrhoidectomies are being performed under local anesthesia with results equivalent to those with general / spinal anaesthesia [10]. Recently a manometric study of the anal sphincter during

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haemorrhoidectomy using posterior perineal block before and after procedure revealed significant reduction of resting and squeeze pressures of anal canal allowing surgeons to perform radical haemorrhoidectomy in the overnight stay setting with optimal intra and postoperative analgesia, safe sphincter relaxation, lower postoperative complications, and lower costs to the public health service [11] Our study is aimed at studying ambulatory proctological surgery as a novel and cost effective method.

### **1.1 Aims and Objectives**

To study ambulatory proctological surgery as a novel method in today's practice.

## **2. MATERIALS AND METHODS**

### **2.1 Study Design**

Prospective clinical trial.

### **2.2 Source of Data**

Patients who were undergoing elective anorectal surgeries as per the inclusion and exclusion criteria at KLES hospital Belgaum between November 2004 to November 2005 formed the subjects of the study.

Sample size included a total of 30 patients.

### **2.3 Inclusion Criteria**

1. All patients undergoing elective anorectal operations for hemorrhoids, anal fissures and anal tags.
2. Age: 18-65 years

### **2.4 Exclusion Criteria**

1. Ano-rectal and perianal abscess, fistula in ano
2. Known allergy to local anaesthesia
3. Uncooperative patients
4. Bleeding / coagulation disorders
5. Patient with ischaemic heart disease
6. Pregnant patients

### **2.5 Anaesthesia Used: Posterior Perineal Block**

After a thorough physical examination routine investigations were done in form of complete blood count, random blood sugar, serum creatinine, blood urea, urine routine, bleeding time, clotting time, ECG, xylocaine test dose given following which posterior perineal block was given. Patients were post-operatively assessed with respect to mainly for onset of postoperative ambulation.

### **2.6 Procedure of Posterior Perineal Block**

After giving a test dose under strict aseptic precautions the procedure involves injection of mixture of 15 ml of 1% lidocaine, 15 ml of 0.25% bupivacaine with epinephrine 1: 2,00,000 and sodium bicarbonate 8.4% 3ml. 1 to 2 ml of this mixture is injected intradermally, with needle pushed towards sacrum and 5 ml injected presacally. Afterwards another 10 ml is injected around ischioanal muscle, and then the needle is moved deeper in lateral and cranial directions, and peri-anal area is injected.

## 2.7 Statistical Analysis

Statistical analysis was done applying p value where  $P < 0.05$  was significant.

**Table 1. Onset of post operative ambulation**

Post-operative duration (hours)	PPB (No. of patients)
<0.5	30

**Table 2. Degree of pain post-operatively at 1hr**

Degree of pain/VAS	PPB
Mild	24
Moderate	6
Severe	-

**Table 3. No. of patients with urinary retention over a 12 hour post operative period\**

No. of patients with urinary retention over a 12 hour post operative period	
PPB	5

**Table 4. Hospital stay in days**

Hospital stay in days	PPB
3	26
4	4
5	-

**Table 4. Gender wise distribution of patients**

Type of block	Males	Females
PPB	15	15

**Table 5. Disease wise distribution of patients**

Type of block	Fissure in ano	Hemorrhoids	Hemorrhoids + Fissure in ano
PPB	18	9	3

## 3. RESULTS

1. Onset of post operative ambulation as depicted in Table (a), all the 30 patients in PPB group were ambulatory in less than 30minutes (0.5 hour) post-operatively.

Onset of duration of post. op ambulation	P value	Significance
<30mts(0.5hr) post op.	0.00	Significant

2. Most patients had mild pain postoperatively as per VAS score.
3. 5 patients developed urinary retention postoperatively.
4. Hospital stay as depicted in Table (d), 26 of 30 cases of PPB got discharged on 3<sup>rd</sup> day of admission p values at 3<sup>rd</sup> day are  $< 0.0001$  indicating significance.
5. Most of operated patients were fissure in ano compared to hemorrhoids showing statistical significance.

#### **4. DISCUSSION**

Anorectal diseases are one of the commonest diseases which present frequently to surgical department. When operative option is given to these patients, naturally the patients prefer the shortest course of hospital. The present study of ambulatory proctological surgery as a novel method in today's practice holds true as all the patients with posterior perineal block group were ambulatory in less than half an hour of surgery. Most of the patients had mild pain post-operatively. 16.7% patients had urinary retention post-operatively but it was statistically insignificant. 86.67% of patients in the posterior perineal block group were discharged within 24 hours of operation. Of the remaining 3 patients were discharged in the next 48 hours 2 were diabetic who were observed for an extra day for evidence of any local infection, while the other patient had moderate degree of localized pain. Our study also showed significant statistical differences when the underlying anorectal condition is either fissure in ano or haemorrhoids. A large number of fissure in ano patients have formed a large group with early ambulation, showing partly synonymous results with studies by Gordon PH, Vasilevsky CA who have done lateral internal sphincterotomy under local anaesthesia, and suggested reduced hospitalisation and post-operative discomfort which is minimal and wounds heal quickly [4]. Our study of early post-operative ambulation and hospital discharge is partly consistent with study by Gabrielli F, Cioffi U, Chiarelli M, Guttadauro A, De-Simone M, [11]. Our study is also consistent to the previous studies done by B. Roche and M.C Marti on outpatient proctological surgeries under posterior perineal block in 3725 cases with lesser complications over a 12-year period [12]. The limitations of this study or the scope for further work lie in conducting similar studies over a larger population.

#### **5. CONCLUSION**

From our study we conclude that ambulatory proctological surgery is suggested as a novel method of practice especially under posterior perineal block as there is less amount of post-operative pain, patients get discharged early, thereby reducing costs and making healthcare more affordable.

#### **CONSENT**

It is not applicable.

#### **ETHICAL APPROVAL**

It is not applicable.

#### **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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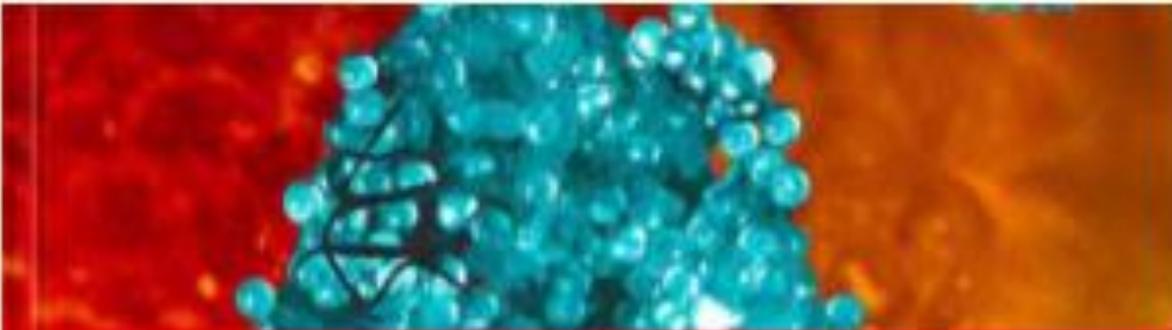
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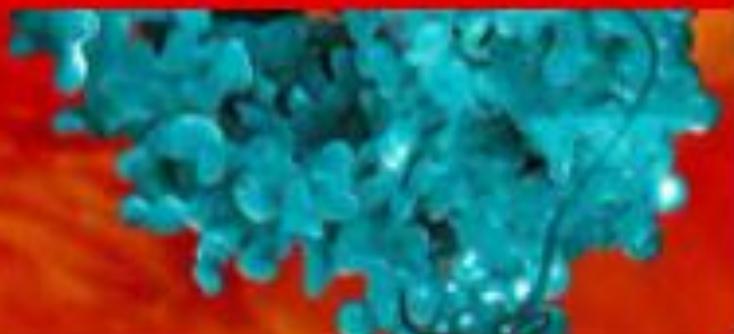
This chapter is an extended version of the article published by the same author(s) in the following journal. International Journal of Recent Trends in Science and Technology, 8(3): 216-218, 2013.



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## Chapter

# Therapeutic Applications of Monoclonal Antibodies in Urologic-Oncology Management - An Update

*Maya Kulshekar, Shridhar C. Ghagane, Sridevi I. Puranik, Rajendra B. Nerli and Murigendra B. Hiremath*

## Abstract

The idea of utilizing immunotherapy for the treatment of cancers has been appealing to scientists and clinicians for over a several decades. Immunotherapy for cancers encompasses knowledge gained from a wide range of disciplines and has the potential to procure the 'magic bullet' for the treatment of cancer. Monoclonal antibody-based treatment of cancer has been recognized as one of the most successful therapeutic strategies for both hematologic malignancies and solid tumours in the last 20 years. The discovery of hybridoma technology in late 1975 and the development of chimeric, humanized, and human antibodies have increased the availability and utility of immunotherapy for the treatment of cancer. Metastatic or recurrent cancer continues to be the bane of the urological oncologist. Despite recent improvements in therapeutic management and outcomes for clinically localized disease overall survival rate in patients with the majority of metastatic and recurrent genitourinary malignancies remains relatively unchanged. By targeting tumours through specific or associated antigens, it is possible to selectively eliminate tumour cells and maintain an acceptable toxicity profile. Therapeutic antibodies that target immune cells are also being developed with the goal of breaking local tolerance and stimulating the patient's anti-tumor immune response. As with other treatment modalities, immunotherapy is far from perfect and requires additional study to optimize clinical response and overcome therapeutic resistance. Modern advances in the field of immunotherapy hold the promise of providing the clinical urologist/oncologist with new tools to fight urological cancer. However, the literature on monoclonal antibody-based immunotherapy with a particular emphasis on target antigens, monoclonal antibody design and potential applications in the field of urology is limited. Hence, the present chapter focuses on the applications of Immunotherapy using monoclonal antibodies for urologic oncology settings such as prostate, bladder, renal, testicular and penile with a hope to highlight its clinical efficacy and also its mechanisms of action in each of these cancer types.

**Keywords:** Monoclonal antibodies, Immunotherapy, Applications, Urologic-oncology

## 1. Introduction

Modern advances and a quantum leap in the field of cancer therapy has been promising to oncologists with new tools to fight many cancers. The immune system has multifunctional units referred to as antibodies, mostly polyclonal which facilitate humoral and cellular reactions to antigens [1]. However, it is possible to produce large quantities of an antibody from a single B-cell clone which are called as *Monoclonal Antibodies* (MAbs). Using these antibodies for therapeutic purposes is termed as Immunotherapy. Immunotherapy in recent times has been propitious across a number of cancer types. Stimulating results with MAbs directed towards both established and emerging targets indicate its potential key role as a therapeutic agent [2]. These are being tested in early- and late-stage clinical trials. In the last 35 years over 100 Monoclonal Antibodies have been considered potential as drugs and many have been approved. The usage of the monoclonal antibodies in cancer therapy requires the understanding of the biological role of various antigens involved in tumor growth [3]. In cancer patients' immunity system is often altered. The purpose of immunotherapy with monoclonal antibodies is to interfere with synergic activity of immunosuppressive environment created by T cells, cytokines, interleukins and tumor growth factor [4]. In many cancer treatments, the monoclonal antibodies have been robust enough, however in some, combinatorial treatments including monoclonal antibodies, chemotherapy and vaccines have been successful thereby bringing together cancer immunologists and clinicians required for the management of cancer in the near future [5]. This chapter will focus on Immunotherapy using Monoclonal antibodies for many urologic oncology types such as prostate, renal, bladder, testicular and penile with a hope to highlight its clinical utility and also its mechanisms of action in each of these cancer types.

## 2. Types of monoclonal antibodies and their mode of action

**There are several ways by which the mAbs are made. They are as follows:**

- Human: These are derived from the human source. Called as 'umabs'
- Murine: These are derived from mouse. Called as 'omabs'
- Humanized: Here the mouse proteins are attached to the human protein. Called as 'zumabs'
- Chimeric: variable regions are from humans and constant regions are from mouse. Called as 'ximabs'

**Following are the types of Monoclonal antibodies:**

### 1. Naked monoclonal antibodies

- a. These are the most common types of antibodies which are not attached to the radioactive material or any chemotherapy drugs. They act independently and have been extensively used to treat cancer. They attach themselves to antigens on cancer cells, or even non cancerous cells and other free-floating proteins. They can also act as immune checkpoint inhibitors [6]
- b. E.g., alemtuzumab. This is used in the treatment of multiple sclerosis and leukemia (CLL).

c. E.g., trastuzumab is a monoclonal antibody that acts against the HER2 protein and used in the treatment of carcinoma of the breast in which this protein is expressed in larger amounts on the surface of the cancer cells. It thereby causes the inactivation of the protein by blocking it [7].

## 2. Conjugated monoclonal antibodies

As the name suggests these are in combination with the chemotherapy drugs or radioactive materials. These are referred to as tagged or labeled mAbs. They directly deliver the therapy to the target cells causing minimal damage to the normal cells surrounding them after precisely identifying them [8]. It then delivers the toxic substance where it is needed most. They can be of the following types;

a. **Radiolabeled antibodies:** These are conjugated with radiolabeled particles. An excellent example is Ibritumomab tiuxetan which works against the CD20 antigen found on B lymphocyte cells. It is made up of radioactive substance (Yttrium-90). The mAb works on the target cancer cells and then the radioactive materials target the destined cells and also the nearby cell. *Radioimmunotherapy* (RIT) is the name used for this type of treatment [9].

b. **Chemolabeled antibodies:** These mAbs have chemotherapy drugs attached to them. Eg: Ado-trastuzumab emtansine, an antibody that targets the HER2 protein (breast cancer). It is covalently linked to the cytotoxic agent DM1

## 3. Bispecific monoclonal antibodies

These can attach to 2 different types of antigens at the same time, these have also been explored in cancer therapy and drug delivery. Example is blinatumomab, used in the treatment of acute lymphoblastic leukemia. It works by directing the body's T-cells (part of the immune system) to target and bind with the CD19 protein on the surface of B-cell lymphoma cells [10].

## 3. Monoclonal antibodies and prostate cancer

Prostate cancer is one of the most common cancers with its incidence being high in Americans but lesser in the Asian population. It develops within the prostate gland that is responsible for the production of seminal fluid. Cancer therapy considered for prostate cancer includes radical prostatectomy, radiation therapy, chemotherapy, brachytherapy and hormone therapy [11]. The role of mAbs in Prostate cancer treatment has not been very successful. Several trials have been carried out to check for its efficacy, the details of which have been mentioned below.

Ipilimumab was the first immune checkpoint inhibitor which received FDA approval for the treatment of metastatic melanoma. It worked as the anti-cytotoxic T lymphocyte-associated protein 4 (CTLA-4). This stimulated its exploration for the treatment of prostate cancer. Use of this mAb in conjugation with radiation therapy did show antitumor activity in the form of decreasing PSA levels. This was a phase 1 trial. Hence, phase 3 clinical trials were conducted for further evaluation where subjects were randomized to ipilimumab after chemotherapy or radiation therapy. These trials did show progression free survival but missed its endpoint of overall survival [12].

Clinical trials on another mAb Nivolumab remains under investigation. In a first of its kind combination immunotherapy using monoclonal antibodies, Ipilimumab

plus nivolumab has been gaining responses as being reported in a phase 2 trial on metastatic castration resistant prostate cancer. Pembrolizumab is also an immune checkpoint inhibitor [13]. It has received approval from FDA for the treatment of prostate cancer. In these solid tumors, microsatellite instability (MSI) and mutations in mismatch repair genes (MMR) has been observed. Pembrolizumab is evaluated for in a patient after other effective treatments (such as sipuleucel-T, abiraterone, enzalutamide, docetaxel, cabazitaxel, radium-223, etc.) has been ruled out [14]. Combination therapies either with multiple immunotherapies or with immunotherapy and chemotherapy/RT, are currently being evaluated in prostate cancer. The optimal timing of immunotherapy in prostate cancer also remains unclear. Although much work remains to be done, the promise of prostate cancer immunotherapy remains unclear. There have been modern advances in the treatment of prostate cancer, however there is no curative treatment option once prostate becomes metastatic.

#### **4. Monoclonal antibodies and renal cell carcinoma**

Renal cell carcinoma is one of the urologic cancers that has lower incidence rates and poor prognosis. About 30% are diagnosed in their metastatic stage. It is a type of cancer that originates in the PCT. Therapy considered for this form of cancer include nephrectomy, radiation therapy, chemotherapy and embolization. The role of mAbs in Renal cell carcinoma is undertaken and studied in clinical trials treatment has not been very successful. Several trials have been carried out to check for its efficacy the details of which have been mentioned below as renal cell carcinoma (RCC) is a largely chemotherapy-resistant disease. It is immune responsive disease; therefore, checkpoint inhibitors can be considered as agents for the treatment of RCC [15].

The pivotal drug trial Checkmate 214 showed good objective responses in case of poor and intermediate risk patients in combination immunotherapy (Nivolumab/Ipilimumab) vs. the tyrosine kinase inhibitor sunitinib and can be considered as a first line treatment in these subjects for RCC. However, for favorable high-risk patients, the single agent sunitinib showed more response rate. Survival rates were similar in both arms. In another clinical trial Keynote 426, Pembrolizumab (anti-PD-1) plus axitinib, the responses were good and this led to its approval by leading to Food and Drug Administration (FDA) first line treatment. In another trial named, Javelin 101 Renal, avelumab (anti-PD-L1) plus axitinib vs. sunitinib the OS was not significantly different between the two arms [16].

In addition to this, there are many clinical trials that are underway for RCC (**Table 1**). Nivolumab was approved advanced clear-cell RCC by the FDA and is under investigation as pre- and postoperative therapy in mRCC. Combinatorial treatments with various drugs are also being studied in various clinical trials. Atezolizumab phase I trial involving 17 mRCC patients showed promising results as 7 had stable disease for more than 24 weeks. In another phase Ia study, of the 63 patients with clear-cell RCC whose OS was 28.9 months. Pembrolizumab is currently being investigated in two randomized phase II trials of mRCC patients. It has been found to be acceptable for safe use [17]. Several trials evaluating pembrolizumab in combination with various agents are also undergoing. Avelumab showed an acceptable usage when used in patients with advanced solid tumors and safety profile. Two ongoing trials are still being evaluated for avelumab in combination with axitinib Durvalumab. There are ongoing trials evaluating durvalumab in combination with other drugs, including tremelimumab for patients with advanced malignancies including RCC. Ipilimumab: Phase-II studies have been undergoing and the results are found to be partial response with adverse events being reported. In addition, Ipilimumab and nivolumab is being investigated and found to be favorable [18].

<b>mAbs</b>	<b>Targeted therapy</b>	<b>Phase</b>	<b>Population</b>
Nivolumab	Sunitinib Pazopanib	I	Advanced RCC, prior cytokine therapy allowed
Atezolizumab	Bevacizumab	Ib	Untreated, advanced clear cell RCC
Nivolumab	Bevacizumab	Neo- adjuvant pilot	Metastatic clear cell RCC, prior therapy allowed
Nivolumab	Temsirolimus	Ib/II	Metastatic RCC, prior therapy allowed
Pembrolizumab	Pazopanib	I/II	Untreated, advanced clear cell RCC
Pembrolizumab	Axitinib	Ib	Untreated, advanced clear cell RCC
Pembrolizumab	Bevacizumab	Ib/II	Metastatic clear cell RCC treated with failure of at least one prior therapy
Pembrolizumab	Aflibercept	I	Metastatic RCC treated with at least one prior VEGF TKI
Avelumab	Axitinib	Ib	Untreated, advanced clear cell RCC
Atezolizumab	Bevacizumab	III	Untreated, advanced clear cell RCC
Avelumab	Axitinib	III	Untreated, advanced clear cell RCC
Pembrolizumab	Axitinib	III	Untreated, advanced clear cell RCC

*RCC: Renal cell carcinoma; VEGF: Vascular Endothelial Growth Factor; TKI: Tyrosine kinase inhibitors.*

**Table 1.**  
*List of the Clinical trials that are underway for RCC.*

## 5. Monoclonal antibodies and bladder cancer

Bladder cancer is one of the common cancers which develop in the tissues of the bladder. It is a type of Urothelial cancer. There are several methods which have been developed as a cancer therapy for bladder cancer and the most common being the, Bacillus Calmette-Guerin which has a very high success rate. The role of immunotherapy in Bladder cancer has been detailed in a number of case report and clinical trial studies [19]. The incidence of Bladder cancer is comparatively found to be higher in America when compared to other forms of malignancy.

Here are the various monoclonal antibodies that have been considered as a cancer therapy for the bladder cancer. 2016-Atezolizumab, was the first mAb to be approved by the FDA and also accepted by the European Association of Urology (EUA) as second-line therapy for patients with advanced Bladder Cancer. It is a PD-1/PD-L1 checkpoint inhibitor It has been used for subjects even with metastatic or advanced bladder cancer. 2017-Avelumab was also approved by FDA for urothelial cancers. It acts against PD-L1. A phase Ib clinical trial had been carried out with metastatic urothelial cancer which showed inconvincing results. However in the phase II trial, avelumab exhibited a good antitumor response in patients with advanced urothelial cancer whose tumors progressed during or after platinum-based chemotherapy 2017-Durvalumab has also received approval by FDA for the treatment of Bladder cancer. Studies in phases I and II patients have confirmed the effectiveness of durvalumab: It has shown responses in a number of clinical trial studies. It is a drug that acts against the PD-L1. 2017-Nivolumab is a FDA and EUA approved human mAb that acts against the PD-1. It was accepted on the basis of a single-arm phase trial for 270 platinum pretreated patients. The result has been 20% response rate [20].

Nivolumab was also tested on advanced or metastatic Bladder cancer subjects. In this study many adverse events were reported. Unlike the above mentioned

mAbs, PD-L1 overexpression among patients was not significant. In another phase II clinical trial with subjects also receiving platinum-based chemotherapy showed a two-month progression-free period. In patients with PD-L1 overexpression compared to patients with low-expression, a difference in drug effects was observed. Many subjects did show adverse events [21].

Pembrolizumab has been showing positive responses in cases of advanced bladder cancer. It is a humanized monoclonal antibody used in the treatment of bladder cancer and is approved by the FDA and EAU. In a study conducted by on pembrolizumab by Bellmunt et al., it was observed that this mAb showed lower adverse events and longer survival by about 3 months which was significant when compared to chemotherapy drugs such as docetaxel and paclitaxel [22]. In a case report mentioning the treatment with pembrolizumab as reported by McDermott et al., it was observed that adverse events were not observed after 8 months and hence suggested that pembrolizumab can be considered as a PD -I inhibitor [23]. In patients with DNA repair defects, pembrolizumab can also be considered for treatment. This drug not only reduced the risk of developing newer cancers but also prevented premalignant hyperplastic lesion. This shall be a rational therapy. Pembrolizumab is also shown better survival rates when compared to chemotherapy as mentioned farina and his colleagues.

A novel murine monoclonal antibody KMP1 has been studied by cheng and his colleagues [24]. The study was conducted both in vitro and in vivo settings It identified the CD44 epitope on bladder cancer cells and bound to it due to O-linked glycosylation and thereby exhibit antitumor potential in both settings. Future studies may be recommended to understand the exact glycosylation mechanism also produce humanized forms and also conjugate types for better therapeutics. Enfortumab vedotin delivers toxic drugs to tumors. It is an antibody-drug conjugate that targets the Nectin-4 pathway, it has been approved for further study in case of bladder cancer. Immunotherapy has significantly reduced the risk of recurrence for bladder cancer while also increasing the percentage of patients who see a complete response post-surgery. Investigational bladder cancer immunotherapies also have the capacity change the outcomes positively for patients with this disease.

## 6. Monoclonal antibodies and testicular cancer

Testicular cancer is a disease of the male organ, testicles that produces the male hormones and sperms. Approximately 90% of testicular cancer start in the germ cells which make the sperm and are referred to as the Germ cell tumor (GCT). They are of two types: seminomas and non-seminomas. The testicular cancer are the solid tumors that can be treated by chemotherapy even in the metastatic condition. However, the role of immunotherapy is still under investigation. The incidence of Testicular cancer has observed an increasing trend in both America and Europe [25].

### 6.1 Testicular cancer

There are several trials that have been directed towards the Testicular cancer. Several of these trials are against the Immune check point inhibitors. Many case studies have reported immune checkpoint inhibition efficacy in refractory GCTs. However, the mechanism by which this occurs is not clear. Trials have been conducted with mAbs, nivolumab or pembrolizumab (both anti-PD-1 agents) on subjects with refractory GCT. The results are very inconvincing on a phase II trial of Adra et al. [26] who administered pembrolizumab to 10 refractory

GCT patients. Despite of the PD-L1 status there were no responses and hence this led to the termination of the trial. Although three of seven patients with refractory germ cell tumors treated with nivolumab or pembrolizumab did show response, there was partial remission. Some case reports did mention about the rapid progression of the disease with pembrolizumab on single dose and some 40% response with single dose of nivolumab. In a case study reported by Chi and Schweizer, treatment response to nivolumab was observed hence, use of single checkpoint inhibitors have been unstable in nature [27]. No responses were observed by nadal et al. for a case report on a study conducted using Nibolumab with cabozantini and bipilimumab [28]. Due to inefficacy of single agent durvalumab, the monotherapy arm was closed for a study conducted by Raggi et al. [29] Hence the results of immune checkpoint inhibitor monotherapy studies are disappointing and hence need more evaluation in many more clinical trials that shall be planned for future.

## **7. Monoclonal antibodies and penile cancer**

Penile Cancer is a disease in which a tumor growth occurs in the tissues of the Penis. Although the localized penile cancer can be treated by penectomy, the meta-static forms need better strategies to deal with such as the standard Chemotherapy or the novel Immunotherapy. About 95% of the penile cancers are squamous cell carcinomas and other forms include the sarcoma, melanomas and the basal cell carcinoma. Most of the penile cancer is caused by HPV (human papilloma virus) infection. Although the incidence of Penile cancer is only about 1 in every 1,00,000 individuals I America and Europe, several Immunotherapy drug trials are underway to strategize its importance.

Epidermal growth factor receptor is usually overly expressed in Penile squamous cell carcinoma. EGFR amplification has been observed and thereby reported in a number of studies on primary penile squamous cell carcinoma. This amplification has been observed with poor prognosis in patients with penile squamous cell carcinoma and increased risk of recurrence. Considering this aspect, it has been chosen for treatment of systemic penile cancer. Immunotherapy towards EGFR target, includes monoclonal antibodies cetuximab and panitumumab [28]. In a study considering cetuximab either alone or with cisplatin, there was partial response. In another study considering cetuximab, panitumumab, and nimotuzumab about 50% of the patients showed response to treatment. However, this was a second line of treatment.

In addition to anti-EGFR therapy, immune checkpoint inhibitor drug trials of avelumab and pembrolizumab are under progress. These drugs are evaluating the role of PD- L1 and PD-1 inhibition with the above mentioned mAbs respectively, exclusively in penile carcinoma. The combination of PD-1 and cytotoxic T lymphocyte protein 4 (CTLA4) blockade might improve antitumour activity across multiple malignancies, including PSCC. However, the majority of the trials with patients suffering from penile carcinoma are basket trials that include because incidence of penile squamous cell carcinoma is very low [30]. In addition, Cetuximab, a chimeric monoclonal antibody is an epidermal growth factor receptor (EGFR) inhibitor and has still not received FDA approval for the treatment of penile cancer. Phase I trials of Nivolumab are also underway which is a conjunction of chemotherapy and lymphokine working against the HPV. As the frequency of this disease is very low, it has been difficult to conduct many trials. However, continual progress in the area of Immunotherapy with fewer trials has still been gaining approvals and success.

## 8. Conclusion

Immune status modification as strategy of cancer therapy does hold a significant place. Although, the conventional cancer treatments such as surgery, chemotherapy, and radiotherapy are still being referred to as the prominent ones, for some cancer types, immunotherapies are considered as first-line of treatment. One of the most important discoveries in the last several years in immunotherapy has been the development of immune checkpoint inhibitor, monoclonal antibodies that promote antitumor activity. T cells are a form of lymphocyte which are produced within the thymus and performs a crucial function in stimulating body's immune reaction to combat most cancers. They apprehend the overseas particles (antigens) with the aid of using particularly variable T cell receptor. Unlike antibody, the TCR cannot bind antigen and as a substitute it wishes to have peptides of the antigen proven to it with the aid of using an antigen presenting cell (APC). The molecules at the APC that gift the antigen are called as major histocompatibility complexes (MHC). Many stimulatory alerts also are wanted at this time. B7 is a form of peripheral membrane protein observed on activated antigen-providing cells (APC). This B7 on an APC can bind to cytotoxic T-lymphocyte-related antigen 4 (CTLA-4) developing an inhibitory sign and TCR activation. Once the activated T-cell receptor is within the tumor surroundings it is able to apprehend the antigen supplied with the aid of APC within the tumor. At this time, the programmed cell death protein 1 (PD-1) receptor also sends an inhibitory signal to the T-cell when the receptor binds to programmed cell death 1 ligand 1 (PD-L1), that's regularly expressed on tumor cells. Monoclonal antibodies act by inhibiting the binding PD-1 to PD-L1 and thereby boost body's immune response against the tumor cells.

Checkpoint inhibitors specifically goal PD-1/PD-L1) and CTLA4 Immune checkpoint efficacy is stricken by diverse factors, among which are tumor genomics, host germline genetics, PD-L1 levels, and intestine microbiome. Generally, in tumors, mutated or incorrectly expressed proteins are processed through the immunoproteasome into peptides which can be commonly loaded onto MHC molecules, which similarly now no longer usually are capable of eliciting CD8+ T cell reaction. This may also cause producing MHC-supplied immunogenic neoepitopes. It turned into proven, that after the intratumor heterogeneity rises, neoantigen-expressing clones emerge as greater homogenous with the differential expression of PD-L1.

There are number of FDA approved monoclonal antibodies, that are considered for the treatment of Urology oncology. These have been detailed in the **Table 1** and include FDA-approved PD-1 inhibitors such as nivolumab, pembrolizumab, cemiplimab, and FDA-approved PD-L1 such as atezolizumab, avelumab, and durvalumab. But all the open literatures do believe that combinatorial strategies with immune checkpoint therapies may provide a better survival benefit which have been demonstrated in various clinical trials. These can be in combination with radiation therapy, tyrosine kinase inhibitors and also many chemotherapeutic drugs. However, the response to immunotherapy with monoclonal antibodies varies subjectively and hence research into PD-L1 expression, gene signature expression, messenger RNA subtype, mutational and neoantigen load is essential to determine the varying response to monoclonal antibody immunotherapy. Although older modalities of treatment for cancer, has been extensively exploited, array of new drugs that offer hope of not only prolonging life but also curing significantly more patients in the future bring a ray of hope to the scientific world.

### Conflict of interest

The authors declare conflict of interest as None.

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02 **Overview of Primary Cell Culture**  
03 **Models in Preclinical Research of**  
04 **Prostate and Bladder Cancer**05 *Kalyani Killekar, Sridevi I. Puranik, A. Aimen Akbar,*  
06 *Shridhar C. Ghagane, Rajendra B. Nerli*  
07 *and Murigendra B. Hiremath*08 **Abstract**

09 The number of patients diagnosed with prostate and bladder cancer is increasing  
10 worldwide and one of the most important challenges remains the development of  
11 effective, safe and economically viable antitumor drugs. Clinical approval for drugs  
12 tested in preclinical studies enabling them to enter phase I clinical trials is essential.  
13 Cell lines are *in vitro* model systems that are widely used in different fields of medi-  
14 cal research, especially basic cancer research and drug discovery. Their usefulness is  
15 primarily linked to their ability to provide an indefinite source of biological materi-  
16 al for experimental purposes. Under the right conditions and with appropriate  
17 controls, authenticated cancer cell lines retain most of the genetic properties of the  
18 cancer of origin. Studies conducted during the initial development of drugs such  
19 as toxicity, corrosion and drug activity were carried out on animals; however, in  
20 the past two decades, alternatives have been sought due to the fact that animals do  
21 not effectively model to human *in vivo* conditions and unexpected responses are  
22 observed in the studies. Also, more than 100 million animals were used and bil-  
23 lion dollars were spent for animal toxicity experiments. Cell culture studies made  
24 positive contributions to the initial development of drugs and is highly desirable,  
25 as it provides systems for ready, direct access and evaluation of tissues. Contrary to  
26 animal studies, less cost and the need for low drug and a short response time are the  
27 characteristics for *in vitro* cell culture methods. *In vitro* tumor models are a neces-  
28 sary tool, in not only the search for new substances showing antitumor activity but  
29 additionally for assessing their effectiveness. This chapter reviews the main features  
30 of primary cancer cell cultures, provides an overview of the different methods for  
31 their selection and management, and summarizes the wide range of studies that  
32 can be performed with them to improve the understanding of prostate and bladder  
33 cancer preclinical treatment processes.

34 **Keywords:** Primary cell culture, preclinical studies, prostate and bladder cancer,  
35 *in vitro* model

## 01 1. Introduction

02 Cancer is the one of the major death cause worldwide and accounted nearly 10  
03 million deaths in 2020 [1]. The rate of incidence in prostate cancer and bladder can-  
04 cer are increasing worldwide too. According to GLOBOCON 2018, prostate cancer  
05 is the second most frequent cancer and in men, it is fifth leading cause of death.  
06 Bladder cancer is also common in men ranking on sixth position and ninth leading  
07 cause of cancer death [2]. There are so many treatments available like radiotherapy,  
08 chemotherapy, hormonal therapy but these treatments are associated with adverse  
09 side effects and poor quality of post treatment life. Hence there is need in develop-  
10 ment of effective, safe and economically viable antitumor drugs.

11 Prostate cancer and bladder cancer are heterogeneous diseases where many  
12 molecular, environmental and genetic factors are involved in its progression and  
13 understanding the mechanism of this progression is difficult [3]. In recent years the  
14 cancer research has made significant progress, but many challenges remain as it is  
15 [4]. Currently, only 7% of potential anticancer drugs are gaining approval which  
16 is much lower than drugs for other diseases [5]. Hence, to improve this percentage,  
17 it is essential to clinically approve drugs which are tested in preclinical studies and  
18 enabling them to enter phase I clinical trials [6].

19 Experimental models are important tools in the cancer research. The model should  
20 be reproducible, able to successfully reflect disease stage that is being studied and  
21 mimic the disease; how it behaves in humans [4]. Cell lines are *in vitro* model systems,  
22 a necessary tool, in not only the search for new substances showing antitumor activity  
23 but additionally for assessing their effectiveness. They are widely used in different  
24 fields of medical research and pharmaceutical companies. Presently pharmaceutical  
25 industries mostly rely on *in vitro* models like two dimensional (2D), three dimen-  
26 sional (3D), boyden's chamber (to study chemotaxis and assessment of cell motility)  
27 [7], micro fluidic systems (It is small devices that can provide a specific fluid flow,  
28 constant temperature, fresh medium, flow pressure and chemical gradients which is  
29 same as *in vivo* systems to study migration and invasion [8], 3D bioprinting (mim-  
30 ics the processes that occurs in tumor micro environment) [9, 10]. Main reason for  
31 accepting *in vitro* model is it's because of physiological relevance, it helps in improv-  
32 ing the understanding of prognosis and treatment, it provides accuracy and it is also  
33 a low cost screening tool for researchers [11]. The usefulness of *in vitro* models is  
34 primarily linked to their ability to provide an indefinite source of biological material  
35 for experimental purposes. The *in vivo* model involves animals which provide valu-  
36 able information to understand many aspects in development of disease and initial  
37 development of drugs such as toxicity, corrosion and drug activity [12]. But from  
38 past two decades, alternatives have been sought due to the fact that animals do not  
39 effectively model humans in *in vivo* conditions, as it shows unexpected responses like  
40 anatomical variation and also difficulty in extracting quantitative mechanistic data  
41 in the studies. Mathematical models are also used in the cancer research to analyze  
42 tumor growth and progression, and helps in predicting the effects of some therapies  
43 [13]. Different clinical setting, cancer resistance and switching to another treatment,  
44 existence of unknown biological details these issues can affect the mathematical  
45 models [14–16]. Computer simulation is another model in the cancer research, helps  
46 to test complex multi scale cancer progresses, it also accounts for drug pharmaco-  
47 kinetics and pharmacodynamics, but has drawback in less common cancers because of  
48 less data, therefore it lacks perspective validation and accuracy [17].

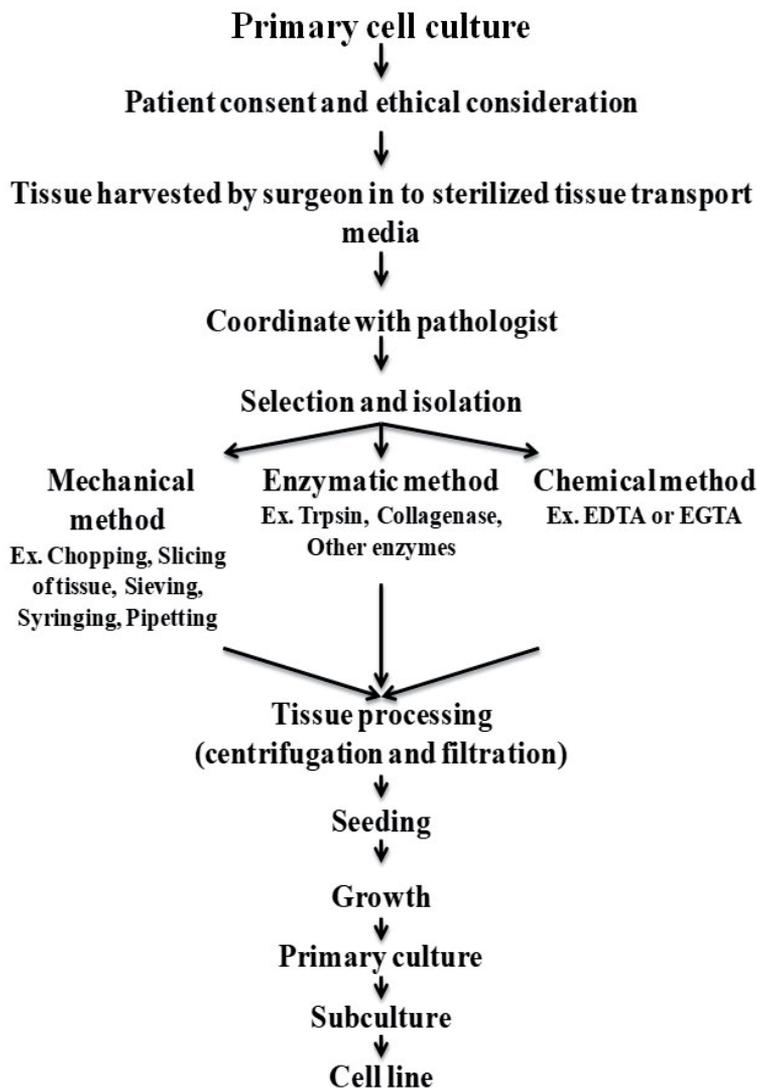
49 All models involved in the cancer research have pros and cons hence the cost  
50 duration, experimental design and data analysis in developing the anticancer drug  
51 should be considered for the selection of the model. It is necessary to choose more  
52 effective preclinical platforms to screen the antitumor compounds [18]. Practically

01 *in-vitro* models of tumors will not only give primary screening of potential anti-  
02 tumor drugs but it also prevents drugs with insufficient antitumor activity from  
03 entering into preclinical animal testing [19]. This chapter reviews the main features  
04 of primary cancer cell cultures, provides an overview of the different methods for  
05 their selection and management, and summarizes the wide range of studies that  
06 can be performed with them to improve the understanding of prostate and bladder  
07 cancer preclinical treatment processes.

## 08 2. Primary cell culture

09 Primary cell culture is a gold standard testing platform for *in-vitro* research in  
10 oncology as they reflect the tumor state more accurately compare to most commonly  
11 employed cell lines [20]. It is a powerful tool commonly used by scientists to study  
12 cellular properties and mechanisms of isolated cells in a controlled environment [21].

AQ1



13 **Figure 1.**  
Flowchart showing the process of primary cell culture technique.

01 Cell culture studies have made positive contributions to the initial development of  
02 drugs. Contrary to animal studies *in vitro* method requires low drug dose and short  
03 response time, which is characteristic feature of *in vitro* cell culture methods [22].  
04 Primary cell culture is also called as *ex-vivo*. Because primary cells are directly taken  
05 from tissue origin and cultured under favorable conditions hence it is more similar to  
06 the *in-vivo* state and exhibit normal physiology. It maintains the cross talk between  
07 malignant and healthy components [23]. This is the main reason why primary cell  
08 culture is called as excellent model system to carry studies in metabolic, aging, signal-  
09 ing studies and effects of drugs, toxic compounds in the cell.

10 Primary cells are non-immortalized and non-transformable as they imitate the  
11 appearance of living model and hence these can help to model 3D tissues. In this  
12 culture, cells will grow in 3D aggregates and presents interesting application [24].  
13 It helps for detection, isolation, growth and developmental stages of viruses and  
14 helps to analyze the mode of infection. Drug candidate and its toxicity screening  
15 rely on results of early-stage *in vitro* cell based assays. Particularly in pharmaceuti-  
16 cal industry primary cell culture is used to synthesize variety of biomolecules in high  
17 scale, various research project on cell-based product are developed. It is alternative  
18 for animal model to test effect of drugs and cosmetics [25]. There are few techni-  
19 cal hurdles associate with primary cell culture. For instance, culturing might be  
20 difficult if the quality of the surgical material is poor. Also, due to early onset of  
21 cell senescence, difficulty arises to maintain sufficient number of cell passages but  
22 researchers have made many attempts to resolve this problem [26, 27].

23 Primary cell culture has been subdivided in to adherent cell culture and suspen-  
24 sion cell culture. In the adherent cell culture, cells are arranged in monolayer and  
25 attach to the surface of the culture flask. Adherent cells are usually derived from  
26 tissues of organs. Growth is limited to surface area and it needs to be detached  
27 from the surface before cells get sub-cultured. Viral vaccine, gene therapy and cell  
28 therapies depend only on adherent cell culture. Suspension cells are derived from  
29 the peripheral blood and do not require any attachment for growth. They do not get  
30 attached the surface area of the cultural flask. The cells are free floating and growth  
31 is limited to the concentration of cells. The steps involved in the primary cell culture  
32 are represented in (Figure 1).

### 33 3. Isolation of cells

34 Before going to any further tissue processes, it is important to keep in mind  
35 that all tissue processing has to be carried out in a biosafety cabinet and all the  
36 sterilization protocols has to be maintained properly [28]. Now moving towards cell  
37 isolation, it is a process where one or more specific cells are isolated from hetero-  
38 genous cell mixture. Isolation of primary cells from cancer cells is an important  
39 phenomenon of cell culture biology as they are more reliable sources to understand  
40 the human cell. There are many standard protocols available for culturing the  
41 normal and neoplastic cells [28]. Human prostate and bladder are composed of  
42 many cell types which can be isolated and cultured. Hierarchy of the epithelium has  
43 been reviewed most [29, 30]. There are 3 main epithelial lineages namely neuro-  
44 endocrine, basal and luminal. Prostatic homeostasis is mainly depends upon the  
45 epithelial cells and stromal cells; stromal cells guides to the epithelium cell for their  
46 dedifferentiation, proliferation and also progression of carcinogenesis [31].

47 Now, how to understand which cell is cancerous and which cell is non- cancerous  
48 because cell does not contain tags on it. There are specific cell markers (Antigen)  
49 which will identify the difference between cancerous and non-cancerous for ex.  
50 ARA70 (Androgen receptor-associated protein 70) is a cell marker which was noted

Cell marker	Cell type
Cytokeratin 5 [33]	Basal cell
CD59 [34]	Basal cell
c-Met [35]	Basal cell
CD95 [34]	Basal cell
Cytokeratin 8 [36]	luminal cell
CD9 [37]	luminal cell
15-LOX-2 [36]	luminal cell
CD24 [34]	luminal cell

01

**Table 1.**  
*Biomarkers for prostate culture.*

Cell marker	Cell type
CD9 [38]	Urothelial
CD104+ [38]	Basal
CD13+ [38]	Stromal cells of the lamina propria
CK5 [37]	Basal
p63 [37]	Basal
CK8 [37]	Luminal

02

**Table 2.**  
*Biomarkers for bladder cell culture.*

Antigen	Antibodies	Cell type
Cytokeratin 8/18 (Prostate)	Mouse IgG1	Luminal cells and intermediate cells
High molecular weight cytokeratin (Prostate)	Mouse IgG1	Intermediate cells
Trop2-APC (Prostate)	Mouse IgG2a	Epithelial cells
CD49f-PE(Prostate)	Rat IgG2a	Epithelial cells
CD + 9 (Bladder)	antibody clone M-L13	Urothelial
CD104 (Bladder)	clone 439-9B	Basal

03

**Table 3.**  
*Primary antibodies for prostate and bladder epithelial cultures [38, 40].*

04 to be expressed at high levels in normal primary cultures compared with prostate  
 05 cancer cell lines [32]. Many cell markers are available depending upon cell type  
 06 which is listed in **Table 1**. Also in bladder cancer depending upon cell type there are  
 07 different CD (Cluster of Differentiation) cell markers which are depicted in **Table 2**  
 08 [38]. Identification of stem cell marker has uncovered a cellular hierarchy of epithe-  
 09 lium during development and in response to injury [39]. Cell markers (Antigens)  
 10 have specific antibodies and these have to be evaluated histochemically. These  
 11 reactions are evaluated by specific kits which are available in market (**Table 3**). For  
 12 isolation, first tissues will be collected from prostate cancer patients and bladder

Method	Mechanism	Advantages	Disadvantages
Chemical Method	By using EDTA or EGTA it binds with cations and disrupt the intracellular bonds [42]	Easy and cost saving	It does not adequately dissociate all types of tissue
Mechanical Method	Cutting, scratching, the tissues in to small pieces the in order to separate the cells wash it with gentle agitation [42]	It is a rapid technique works best for loosely associated tissue.	Decreases in the surviving capacity of the cell, incision of scissor, scalpel for cutting, scratching can damage the cell. Correct temperature should be maintained for enzyme.
Enzymatic Method	Enzymes to cut or digest tissue pieces in free cells. Combination of enzyme also can be used Ex.- Collagenase, Trypsin, Hyluronidase [43].	It has great specificity with specific enzymes	Enzyme dissociation can modify proteins on cell surface

01

**Table 4.**  
*Mechanisms for isolation of cells.*

Sl. No.	Components	Function
1	Buffering systems 1. Natural buffer system 2. Chemical buffers system	<ul style="list-style-type: none"> <li>• CO<sub>2</sub> balances the pH, 5 to 10% CO<sub>2</sub> incubation, non-toxic and cost effective [44]</li> <li>• HEPES, buffering capacity 7.2–7.4, in high concentration it is toxic, costly [45, 46]</li> </ul>
2	Inorganic salt	Maintains osmotic balance and membrane potential by providing sodium, potassium, and calcium ions [47]
3	Amino acids	Require for proliferation of cells and provides nitrogen Ex. L-glutamine provides NAD, NADPH and serve as secondary source of energy in metabolism [48].
4	Carbohydrates	Carbohydrates are major source of energy, most of the media use glucose and Galactose.
5	Proteins and peptides	Major proteins and peptides in media are albumin, fibronectin and transferrin. Albumin helps to remove toxic substances from cell culture media
6	Fatty acids and lipids	Particularly added when serum free media is used [44].
7	Vitamins	Important for cell growth and proliferation as cells cannot produce sufficient amount, need to provide through culture media [44].
8	Trace elements	Copper, Zinc, Selenium required in trace amount for proper growth and many biological process
9	Antibiotics	Control's growth of bacteria and fungi ex. Penicillin, Streptomycin, fluconazole [49].
10	Serum in media	Serum is a complex mixture provides all above elements. Ex. Fetal and Calf bovine serum [44].

02

**Table 5.**  
*Basic components of media and their functions.*

03 cancer patients who are undergoing biopsy. This collection of tissues needs to be  
04 well coordinated between urology, pathology and the investigator and it has to  
05 proceed for primary culture within 2 hours after collection of tissues [33–37, 39–41].

01 After collection, tissue should be placed in sterile container which has HBSS (Hanks'  
02 balanced salt solution) with HEPES (Hydroxyethyl piperazineethanesulfonic acid)  
03 and store at 4°C for 2 hours to increase cell viability. To assess tumor cells in the  
04 dissected material Hematoxylin and Eosin (H&E) stain is used in the histopathology  
05 lab. To get a single cell suspension from tissue dissociation obtained after surgery,  
06 there are three mechanisms available for isolation: Chemical, Mechanical and  
07 Enzymatic method (**Table 4**).

08 Although this is first step in primary culture, there is still no standardized pro-  
09 tocol for this. There is a variety of options available. Tissue has to be mechanically  
10 minced from autoclaved scalpel or scissor; if tissue is measuring from 1 to 20 grams  
11 semi-automated dissociator can be used. Manual method has to be done in ice cold  
12 PBS (Phosphate-buffered saline). Commercially available formulation showed 10%  
13 increased viability compare to collagenase I, II, IV. (**Table 5**) [33]. In another study  
14 mechanical and enzymatic method has been used. In mechanical method, they used  
15 lacerate and scalpels and in enzymatic method collagenase type I and hyaluronidase  
16 type I enzymes with medium agitation at 37°C for 18 hours was used [34]. EDTA  
17 (Ethylenediaminetetraacetic acid)/Trypsin mixture used with 5 minutes of incuba-  
18 tion in 37°C degree for prostate tissue [35]. Both the mechanisms, mechanical disag-  
19 gregation with disposable disaggregator and enzymatic by collagenase and trypsin  
20 used for prostate tissue [36, 37]. In some cases, trypsin/EDTA 1:5 solution and  
21 incubation for 15 minutes for bladder tissue was used. In some studies for dissocia-  
22 tion of bladder tissue 1:1 collagenase II and dispase enzymes are used at 37°C for  
23 12 hours [40–43]. Also there is a need to monitor tissue digestion process for every  
24 2 hours by gently shaking the digestion mixture by checking the viability of cells  
25 under the microscope [50–53].

#### 26 **4. Tissue processing**

27 After digestion, cells are strained by strainer to separate the debris from it. Then,  
28 cells micro clumps are washed with PBS or HBSS twice or trice followed by centrifuga-  
29 tion [54]. Cell pellet collected from centrifugation is suspended in 2 ml of culture  
30 media. Count the viable cell by hemocytometer or by tryptophan dye exclusion  
31 method [55]. Cell viability also can be measured by the intracellular adenosine tri-  
32 phosphate levels which are commercially available kit [56]. Immunohistochemistry  
33 and immunofluorescence techniques used to localize, identify and quantitate the  
34 cells based on cell surface marker [57].

#### 35 **5. Culture media**

36 Cell pellets collected from centrifugation has to be placed in micro well plate or  
37 flask that contains culture media. It provides artificial environment for cell to grow.  
38 Basic requirement of culture media are controlled temperature, substrate to attach  
39 cell, growth medium and incubator to maintain pH [45]. Main step in culture is to  
40 choose culture media. It generally composed of amino acid, vitamins, inorganic  
41 salts, glucose, hormones, growth factor, and attachment factor which provides  
42 energy and helps to complete the cell cycle. Commercially available cell media for  
43 primary epithelial cancer cells are less effective compare to tissue specific primary  
44 cell media prepared in lab (**Table 6**) [46–49].

45 Choice of culture media is very important to get significant result in experiment.  
46 Selection of media completely depends upon type of cell, purpose and recourse  
47 [62]. As primary culture provides valuable research data, preparation of quality

01

SL.No.	Cell type	Components of media
1.	Fibroblast cell culture [28]	DMEM media with 7.2 pH + Fetal calf serum(FCS) + 100 U/ml penicillin,100 µg/ml streptomycin +1% amphotericin B added in culture media.culture plate incubated at 37°C a humidified chamber of 95% air and 5% CO <sub>2</sub>
2.	Prostate cancer (Bone metastatic variant) [29]	DMEM Glutamax +4.5 g/L D-Glucose with pyruvate +10%FCII +1% penicillin-streptomycin+37°C with 5% CO <sub>2</sub> .
3.	Bladder cancer (Epithelial cells) [58]	EMEM (ATCC) +10% FCS +1% penicillin + streptomycin + humidified incubator at 37°C with 5% CO <sub>2</sub> .
4.	Prostate cancer (Epithelial cells) [59]	KSFM medium+ + 25 mM HEPES +1% penicillin + streptomycin +0.5 mg/mL fungizone +100 mg/mL gentamicin +37°C, 5% CO <sub>2</sub> humidified incubation.
5.	Epithelial cells [40]	serum-free RPMI 1640 without phenol red+ penicillin 100 IU/mL+ streptomycin 100 µg/mL+ metronidazole 1 µg/mL+ amphotericin B 2.5 µg/mL + gentamicin 20 µg/mL + 37°C and 5% CO <sub>2</sub> for 6 days.
6.	Bladder cancer (Urothelial cells) [50]	Glutamine + insulin + Phosphoethanolamine+ ethanolamine + hydrocortisone+ transferrin + EGF + BPHE+5% FBS +5% CO <sub>2</sub> at 37°C
7.	Prostate cancer (Epithelial cells) [60]	DMEM + Glucose +100 U/ml penicillin +100 mg/ml streptomycin sulfate+0.29 mg/ml glutamine + Euroclone
8.	Prostate cancer (Epithelial cells) [61]	DEME /Ham's (1:1) + BSA (0.01%) + FAS (2%) + Epidermal growth factor (10 ng/mL) + (insulin-transferring-selenium-1%) + hydrocortison (0.5 µg/mL) + Tryiodotyronone(1 nM) + phosphpethenolamine(0.1 mM) + cholera toxin (50 ng/mL) + fibronectin(100 ng/mL) + futine(20 µg/mL) + penicillin/ streptomycin (100 U/mL,100 µg/mL) + R1881(0.1 nM).

02

**Table 6.**  
*Components of media from different studies.*

Sl.No.	Name of media	Supplier
1.	Human Endothelial-SFM	Life Technologies
2.	Endothelial Basal Media	Sigma Aldrich
3.	EndoGRO-LS Complete Media Kit	MilliporeSigma
4.	HUVEC Basal Medium CB HUVEC	AllCells
5.	Endothelial Cell Medium	ScienCell
6.	Epithelial cell medium	ScienCell
7.	EpiGRO primary epithelial cells	MilliporeSigma
8.	RPMI 1640	Sigma Aldrich
9.	αMEM	ThermoFischer
10.	k- SFM	ThermoFischer

03

**Table 7.**  
*Commercially available media for epithelial cells [44, 63].*

01 culture media is required, or to avoid limitation (cell number) of primary cell  
02 culture, commercially produced medias are available (**Table 7**) [58–61].

03 It is very important to maintain cell viability after isolation process which is  
04 totally depends on skillful handling and culture conditions. The culture condition  
05 will differ depending on the cell type. Cell growth has to be observed till 11 or  
06 12 days. Additional extra media, Fetal Bovine Serum (FBS) and antibiotics need  
07 to be provided to avoid contamination. Culture media has to be changed between  
08 2 and 3 days [60]. Initially apoptosis is 5% from 0 to 1 day but as days will pass  
09 apoptosis rate will increases from 7 to 14 days. But functional validity of benign and  
10 prostate cancer cells was 5 days after confirming it with histochemically, biochemi-  
11 cal and by immunohistochemical assay [63]. Use of serum free culture media  
12 with low calcium condition increases the longevity of the cell. Cryopreservation  
13 (Preservation of structurally intact cells) can be achieved by adding 10% FBS (Fetal  
14 bovine serum) and 10% DMSO (Dimethyl sulfoxide) in 80% confluence primary  
15 cell culture [64].

16 Each day morphological changes have to benoted. Normal cells get counted  
17 every day and cancer cells get counted every 2 days [65]. Cell viability is determined  
18 by trypsin blue dye, equal volume of PBS and trypsin blue dye allowed tosit on  
19 cells for few minutes then to count the cells samples are loaded on hemocytometer,  
20 cells scored as leaving or dead based on uptake of tryptophan blue dye [66]. Once  
21 confluence reaches to 80 to 90% it has to get counted by Neubauer camera at 1:2  
22 dilution with tryptophan dye exclusion, MTT assay (3-(4,5-dimethylthiazol-2-yl)-  
23 2,5-diphenyl tetrazolium bromide) can be used to determine cell viability [67]. Cell  
24 growth curve can be plotted from the graph to check the time when the cell viability  
25 increases in the culture. Once cell get cultured properly depending upon need of  
26 investigator, cells can be passaged and characterization of the cells can be done.

## 27 **6. Cancer cell lines**

28 Most established prostate cancer cell lines namely PC-3, DU145 (Duke  
29 University 145) and LNCaP (Lymph Node Carcinoma of the Prostate) developed  
30 in the 1970s and 1980s are in the majority of the published studies [68–70]. T24  
31 cells (cell line from transitional cell carcinoma of the bladder) are exemplified for  
32 bladder cancer research [71]. These immortalized cancer cell lines are not always  
33 predictive of the real cancer behavior for the preclinical studies as these cells are  
34 adapted to 2D monolayer culture conditions [72, 73].

## 35 **7. Cell culture models**

36 Traditionally animal models were commonly employed for carrying out study of  
37 different types of cancer for the past three decades [74]. These animal studies have  
38 many drawbacks including lack of high-throughput drug screening, longer time  
39 consumption to conduct tests and ethical controversies concerning animal testing.  
40 Cell culture is the most widely used alternative to animal studies and cell culture  
41 techniques can broadly be classified into 2D and 3D methods [75]. The potentialities  
42 of primary cancer cell models' cultures in preclinical studies for cancer research  
43 and drug discovery has amplified over the past few years. Primary cell cultures  
44 provide a good model system to understand normal and malignant biological activi-  
45 ties. Carcinogenesis-related behavior such as apoptosis, proliferation, adhesion,

01 differentiation, migration, senescence, invasion, angiogenesis, and other metabolic  
02 pathways have been studied in recent years. One of the major advantages is that the  
03 heterogeneity of cell populations composing a primary culture mimics the tumor  
04 microenvironment, crosstalk, and interactions between malignant and healthy  
05 cells, neither of which is possible with cell lines [76].

06 Most studies have shown that the cellular responses to drug treatments in 3D  
07 cell culture are significant and more similar to that of *in vivo* architecture when  
08 compared to 2D cell culture. One of the most improved successful assays using 3D  
09 culture for cell-based screening in the early phase of drug discovery is cancer cell  
10 viability assessment. This assay is particularly useful to test the cytotoxic effects  
11 of compounds that may lead to cell death. It plays an essential role in checking  
12 how many cells are viable at the end of each experiment. Cell viability assay is  
13 closely followed by cell proliferation, cell migration and then cell signaling assays  
14 [77–79].

15 Currently a number of anticancer drugs belonging to different classes  
16 chemically are available. To be used as a potential anticancer agent, the testing  
17 compounds need to inhibit the growth and proliferation of cancer cell lines.  
18 This will further inhibit the signaling pathways by knocking in or knocking out  
19 a candidate gene thereby stopping the progression of tumor to fatal stages. For  
20 instance, antiproliferative investigations were performed on prostate cancer cell  
21 line DU-145 *in vitro* and *in vivo* using salvia miltiorrhizabunge [80]. Another  
22 example to justify this concept will be a study performed on PC-3 cell line.  
23 Generally, cancer cells express higher amount of Transferrin Receptors (TfR)  
24 for an increased uptake of iron in relative to normal cells. This higher amount of  
25 intracellular free iron is required for the growth and proliferation of cancer cells.  
26 Anhydrodihydroartemisinin (ADHA) was used to inhibit PC-3 cell lines through  
27 caspase-dependent pathway [81].

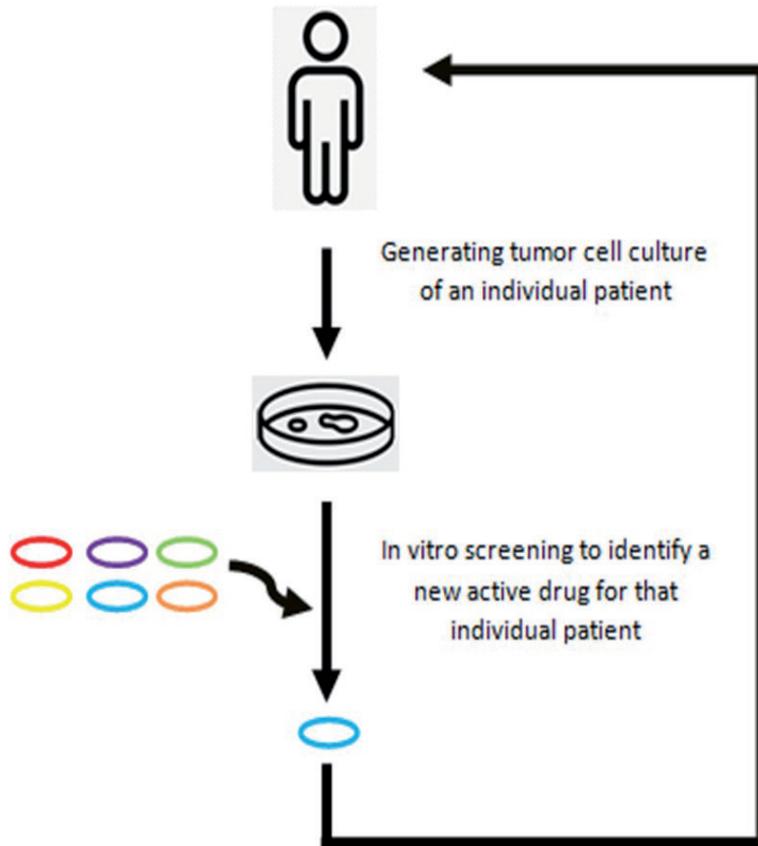
## 28 **8. Applications: cell culture in drug discovery and screening**

### 29 **8.1 Drug candidate identification**

30 Often the rate-limiting step in preclinical drug discovery is the target iden-  
31 tification and validation step. 3D cell cultures have the potential to discover  
32 the molecular perturbations governing carcinogenesis and to accelerate target  
33 identification and validation, given that the gene expression patterns found in  
34 3D models are relative to *in vivo*, when compared to 2D monolayer models [81].  
35 For instance, a study reported that CXCR7 (C-X-C chemokine receptor type 7)  
36 and CXCR4 (C-X-C chemokine receptor type 4) were co-expressed in LNCaP,  
37 DU145 and PC3 cell lines in 2D culture. A marked up-regulation of both receptors  
38 was observed in PC3 cells when cultured in 3D using Matrigel suggesting that  
39 inhibition of CXCR7/CXCR4 may assist in controlling prostate tumor growth and  
40 subsequent progression [82].

### 41 **8.2 Toxicity profiling**

42 Cultured cancer cells are powerful in assessing drug-induced toxicity and to  
43 determine suitable drugs and methods for selectively destroying different types of  
44 cancer. It is useful to investigate effects of drug responses on metabolic signaling  
45 pathways or candidate genes conceding drug screening practices with impressive  
46 progress in the last decade. A study investigated features such as vascularization



01 **Figure 2.**  
02 *Assay-guided treatment choosing the best active drug for an individual patient.*

03 and perfusion of antineoplastic drugs on human T24 bladder cancer [83]. It allowed  
04 in the understanding of basic paracrine signaling mechanisms that regulates tissue  
05 homeostasis, development of new methods for urinary bladder reconstruction and  
06 tissue engineering, and generation of models of malignant and benign diseases.  
07 This study suggested that the use of 3D urinary bladder cultures could be a pos-  
08 sible approach in clinical practice to select for the best antineoplastic drug for each  
09 patient and to investigate the effect of drug combinations or new antineoplastic  
10 drugs [84, 85]. The below (**Figure 2**) suggests how assay-guided treatment can be  
11 useful in choosing the best active drug for an individual patient.

### 11 **8.3 Testing anticancer activities**

12 By far the most useful *in vitro* model which is used to analyze the anticancer  
13 activity is Cell culture. Treatments including radiotherapy, chemotherapy, hormone  
14 therapy, novel and experimental therapies can be evaluated. Extracts of plants can  
15 also be utilized to check for anti-cancer behaviors such anti-inflammatory, destabi-  
16 lized membranes through which invasion and migration can occur. For instance, leaf  
17 extracts of *Leea indica* were used to study *in-vitro* antioxidant and anticancer activ-  
18 ity on DU-145 and PC-3 human prostate cancer cell lines [86]. An example of drug  
19 combination is the synergistic effect of cisplatin and sunitinib malate – based chemo-  
20 therapy on T24, 5637, and HT1376 human urinary bladder cancer cell lines [87].

## 01 9. Conclusion

02 Primary cell cultures have its application in various fields like toxicology,  
 03 virology, drug screening, genetic engineering, gene therapy, genetic counseling,  
 04 cancer research but main important application is model system. It provides best  
 05 model system for studying basic cell biology and biochemistry, effects of disease-  
 06 causing agent and cell, effect of drugs on cell, process which triggers aging and  
 07 apoptosis. Primary cell culture represents excellent model for transitional preclini-  
 08 cal experiments to understand cancer in in-vitro system. Primary cell culture acts  
 09 as gold standard for cell line experiments because it provides broader spectrum of  
 10 cell types from greater number of patients to be studied without any induction of  
 11 artificial genetic mutation and it also maintains same phenotype throughout the  
 12 culture. It involves both, clinician and researcher in the culture, it helps in under-  
 13 standing the drawback of treatments and lack in laboratory methodology and hence  
 14 it is possible to overcome from it.

15 There are many models in cancer research; each model has different potentialities  
 16 and inadequacy. In primary cell culture, complexity arises due to poor tissue  
 17 quality, collection and inappropriate culturing may decrease the cell viability. Hence  
 18 management of primary cell culture is difficult. But to overcome from these difficul-  
 19 ties proper collection with the help of pathologist and selection of proper isolation  
 20 method and culture media based on tissue type can help to increase the cell viability.  
 21 Considering the current clinical system towards precision medicine, patient derived  
 22 cancer models are powerful epitome in cancer research. Nowadays 3D model system  
 23 is emerging system. Primary cell culture can help to model 3D culture, in future  
 24 technological perspectives like 3D culture can replace the *in vivo* model system. In  
 25 conclusion, this chapter reviews several aspects of primary cell culture, provides  
 26 overview on selection of tissues, different methods of isolation, culturing media and  
 27 management of cells after culture. It summarizes the wide range of studies to improve  
 28 the understanding of prostate and bladder cancer preclinical treatment processes.

## 29 Author's contributions

30 KK & SIP: Worked on collection of data and drafted the chapter, AAA: Worked  
 31 on the draft of cell lines images and edited, SCG: Developed the study designed and  
 32 edited the chapter, RBN & MBH: Collected the literature and guided throughout  
 33 the study. All the authors reviewed and approved the chapter.

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## 36 Conflict of interest

37 The authors declare conflict of interest as none.

## 38 Abbreviations

39 ADHA Anhydrodihydroartemisinin  
 40 BPHE Brazed Plate Heat Exchangers

01	BSA	Bovine Serum Albumin
02	CD cell markers	Cluster of Differentiation cell markers
03	DMEM	Dulbecco's Modified Eagle Medium
04	DMSO	Dimethyl sulfoxide
05	DU145	Duke University 145
06	EDTA	Ethylenediaminetetraacetic acid
07	EGTA	Ethylene glycol tetraacetic acid
08	EMEM	Eagle's Minimum Essential Medium
09	FBS	Fetal Bovine Serum
10	FCS	Fetal Calf Serum
11	FGF	Fibroblast Growth Factors
12	HBBS	Hanks' balanced salt solution
13	HEPES	Hydroxyethylpiperazineethanesulfonic acid
14	IgMI	Imunoglobuline M Immunostain
15	KSFM	Keratinocyte Serum Free Medium
16	LNCaP	Lymph Node Carcinoma of the Prostate
17	PBS	Phosphate buffer saline
18	RPMI 1640	Roswell Park Memorial Institute ( <i>RPMI</i> ) media
19	TfR	Transferrin Receptors

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# Role of Dietary Supplements in Prevention of Renal Stones: An Update

*Akshata Sangolli, Shridhar C. Ghagane and Rajendra B. Nerli*

## Abstract

Kidney stone disease is an oldest known and widespread medical condition characterised by its high prevalence in all over the world. Literature suggests that around 9–12% of population in industrialised countries have kidney stone disease in their lives with the 30–50% of reoccurrence rate. Because of high prevalence, recurrent and unpredictable nature of stone formation and its predominance mainly in adults contributes to the substantial impact on society, individual and health care system. In light of these trends, it's imperative to use optimum preventive strategies to reduce the burden of kidney stone disease on individual and society. The aetiology of kidney stone disease is a multifactorial and it's related to diet, environmental factors, genetics, metabolic syndromes and various life style factors. Its noteworthy that dietary and life style modification are the major contributors in the prevention of kidney stone reoccurrence. Dietary interventions aim to reduce the urinary abnormalities known to promote lithogenesis. Therefore, modification in the dietary factors is appealing way to patients and physicians in the treatment and prevention of stone recurrence as it is relatively inexpensive and safe. So, the present chapter is focusing on the role of dietary supplements in prevention of renal stones.

**Keywords:** kidney stones, dietary factors, prevention, health

## 1. Introduction

Kidney stone disease or renal calculi is a serious medical condition though not life-threatening disorder. In medical terms it referred as urolithiasis or nephrolithiasis where “Lith” meaning stone [1]. Renal stone formation is an oldest and widespread disease in the world affecting human beings. Its prevalence in the Europe is around 7–9%, Asia 1–5% and in North America 6–12%. The lifetime prevalence of renal stones in India is 5–11% [2]. This prevalence represents threefold increment and 5–6% absolute increment in last 20–30 years. Increased in the number of cases is reported in all groups irrespective of gender, racial and ethnic variation [3]. An alteration in normal mineral content of urine is the main cause for lithiasis [4]. Urinary components play a vital role in stone formation as they will be in their metastable state with several pre-existing substance which can crystalize to form calculi. These substances if exists in super saturation level makes urine unstable and will lead to crystallisation of excess of solutes [5].

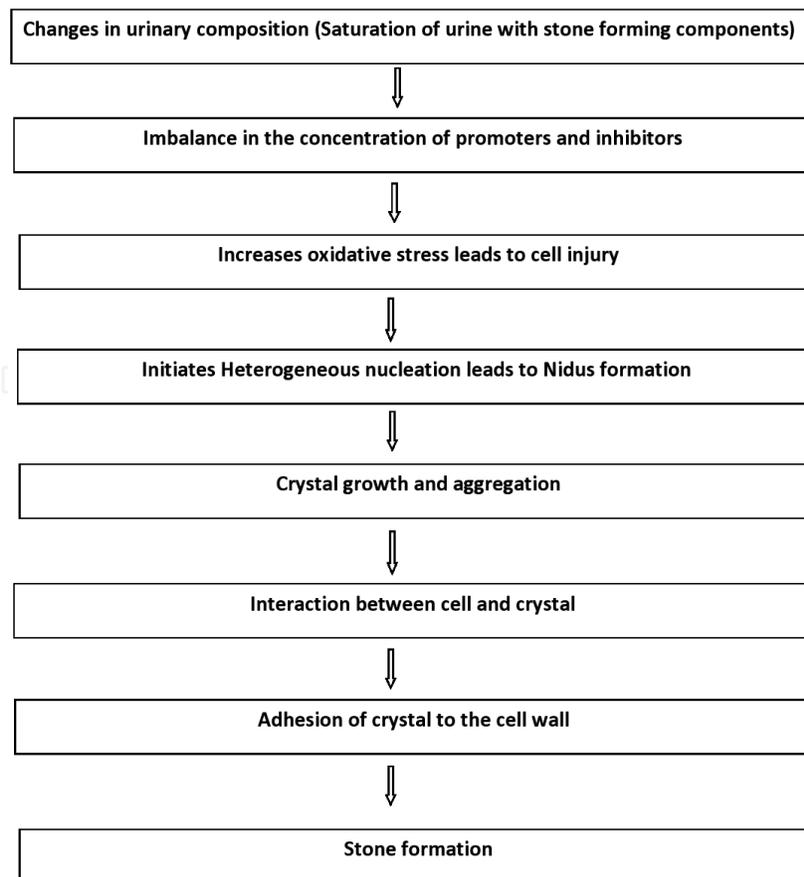
Kidney stone may be found with different shapes, sizes and colours depending on their composition. Smaller stones may pass in the urine without any symptoms, but often stones grow in their size and develop a level of discomfort while passing through urine. In some case it may cause a severe pain if the surface of the stone is rough or it may require medical intervention as bigger stone cannot pass through the urinary system [6]. Other complications such as urinary tract infections, sever pain, or decline in the renal function may be associated with urolithiasis [7]. If neglected it may lead to the substantial damage to the kidney [6]. Since significant number of patients may have to undergo surgical interventions for the treatment, the management of the kidney stone has become considerably expensive [8]. Because of high prevalence, recurrent and unpredictable nature of stone formation and its predominance mainly in adults contributes to the substantial impact on society, individual and health care system [9]. In light of these trends, it's imperative to use optimum preventive strategies to reduce the burden of kidney stone disease on individual and society. Thus, awareness regarding importance of preventive measures particularly on consumption of healthy diet certainly help to reduce the cost of hospitalisation and will increase the compliance in general.

According to literature survey various preventive measures are available to reduce the risk of kidney stone formation such as life style modification, high water intake, less consumption of salt and modification in dietary habits. As diet has shown its strong association with stone formation, changes in dietary habits may help to reduce the burden of stone formation. Less awareness on effect of food on stone formation is one of the main reasons for increase prevalence. So, more studies have to be focused effect of various diets at molecular level to understand the actual mechanism behind stone formation. Thus, present chapter is focusing on role of various diets in prevention of kidney stone disease.

## 2. Types of kidney stones

Chemical constitutes of urine is the main factor for variation in chemical composition of the stones. These variations may be associated with other risk factors such as environmental factors, diet, climate and life style habits. Based on this, urinary stones can be classified in to five major classes.

- **Calcium stones:** Calcium stone can exist as calcium oxalate or calcium phosphate or calcium carbonate. Among all the types these are the prominent ones constituting around 70–80% of the total stone forms. Calcium oxalate can exist as calcium oxalate monohydrate (COM) or dihydrate (COD). COM is the more stable form and common compared to the COD. Various factors may contribute to calcium stone such as hypercalciuria, hyperoxaluria, hyperuricosuria etc. [10]
- **Uric acid or urate stones:** Uric acid stone accounts approximately for 5–10% of all the types of stones. High purine content of diet such as animal protein is main risk factor for the formation of uric acid stone. Other risk factors are low urine volume, hyperuricosuria, and low urinary pH [11].
- **Magnesium ammonium phosphate stones or struvite stone:** Also called as infection stones or triple phosphate stones. These stone occur at the extent of 12–15%. The main cause for the struvite stone is urinary tract infections where



**Figure 1.**  
*Steps for mechanism of stone formation.*

urease produced by microbes split urea into ammonia and carbon dioxide. This makes the urine alkaline and makes phosphate insoluble at its high pH. Thus, phosphate gets precipitated on the ammonia leading to the stone formation. Its more common in female compared to male [12].

- **Cystine stones:** The occurrence of cysteine stone is less than 3% among all the types of the stones. It occurs as a genetic disorder with defect in cystine amino acid transportation, which results in excess excretion of cystine in urine referred as cystinuria. It is an autosomal recessive disorder resulting in impaired renal tubular absorption of cystine and excretion of cystine in urine. As cystine is insoluble in urine results in the formation of stones in kidney [13].
- **Drug-induced stones:** These stone accounts for only 1% of total stones. Drugs such as triamterene, atazanavir, and sulfa drugs induce stone formation. Lithogenic drugs and their metabolites may get deposited to form nidus or on already existing stone. Some drugs may also interfere in purine and calcium oxalate metabolism and may lead to the stone formation (**Figure 1**) [14].

### 3. The aetiology of kidney stones

The aetiology of kidney stone formation is multifactorial. There are various risk factors associated with formation of kidney stones such as age, gender, ethnic and family background, life style habits, environmental variations, occupation

and dietary habits. Variations in these risk factors initiates super saturation of urine which may cause changes in the morphology of kidney, change in urine flow, urinary tract infections and metabolic abnormalities (**Figure 1**) [1].

- **Age:** The most vulnerable group for the urolithiasis is 20–60. The incidence of kidney stones is increased with age, thus middle-aged people are very prone to get kidney stone disease [15]. One of the most common reason which could be related to this age group is less fluid intake, dehydration, stress at the work place and unhealthy life styles. In some population the age distribution is different in males and females; male is affected after the age of 60 whereas females are affected at the age of 45–50 [16].
- **Gender:** According to most of the literature survey kidney stone disease is more common in males compared to female with the ratio ranging from 1.5 to 5. It may be associated with the changes in the dietary habits and testosterone promote the stone formation in males [17]. However, in recent decades this ratio is narrowed in many countries, which says that even females are more affected and prevalence is increase in both genders. The main reason for this could be standard living habits, high calorie food consumption and variations in occupations [18].
- **Climate:** Geographic and climatic changes are one of the major risk factors for urolithiasis, specifically temperature, seasonal variations, atmospheric pressure, humidity. High prevalence is seen in tropical and subtropical countries than in frigid zones. Considering seasons incidence will be high in summer compared to spring and winter. This may be associated with the concept of higher temperature leading to loss of water through the body fluids and dehydration which may lead to excretion of concentrated urine may become cause for formation of stone [19].
- **Dietary habits:** Diet also plays an important role in formation of stones in kidney. Diet rich with high amount of oxalate is the main precursor for stone formation. In addition, diet containing high amount sodium, protein, calcium also acts as risk factors for stone formation. This is the main reason for the raising trends of kidney stone disease in many of the Asian countries [20]. Oxalates present in the food gets metabolised in liver and Calcium in intestine combine with excess of oxalate and lead to formation of insoluble calcium oxalate stone [21]. Excessive consumption of animal meat will lead to increased uric acid concentration and results in hyperuricosuria, is the main risk factor for the uric acid stone formation. In addition, pH of the urine plays an important role in lithiasis as appropriate pH favours crystal precipitation, initial step of stone formation [22, 23]. Along with diet less fluid intake is also a main cause for stone formation. Water with high fluoride content may also become risk factor for stone formation. The fluoride in the intestine favours the absorption of oxalate and promotes excess of oxalate excretion and formation of calcium fluoride in urine [24]. Excretion of high concentration of magnesium in urine is also one of the causes for stone formation in kidney [25]. On other hand one of the studies conducted by Chandrajith et al., have not found any association between hardness of water and urolithiasis [26].
- **Occupation:** According to studies conducted on stone formation and occupation, sedentary life style is one of the risk factors for urolithiasis. Some studies reports that there is a positive association between more physical work and

kidney stone disease. The risk of kidney stone formation is more in case of people expose to the sunlight or high temperature for longer period like farmers, miners' drivers etc. than people working at room temperature [27]. People working in these conditions may consume less fluid and they will be more prone to have dehydration, which may lead to excretion of concentrated urine and lead to urolithiasis. However, there are some studies which have shown negative relation between stone formation and occupation [28].

- **Genetics:** Genetic factor also contribute to the renal stone formation, especially cysteine stones are formed by mutation in the gene SLC3A1 and ALC7A9. In addition, even in case of uric acid stones some mutations seen in SLC2A9 and SLC22A12. In some cases, calcium oxalate stones are formed because of the deficiency of enzymes such as glyoxylate reductase/hydroxy pyruvate reductase (GRPHR), alanine glyoxylate aminotransferase. As a result, synthesis and excretion of oxalate is increased leading to calcium oxalate stone formation [29].
- **Racial distribution:** The association of kidney stone disease with different racial background is still controversial. In Asian population the association is been reported by certain studies. Whereas studies conducted in Iran have not shown a significant association between racial difference and prevalence of urolithiasis. In general terms, dietary habits, life style changes and gene of various races are the main key factors for the variations [30, 31].

#### 4. Importance of diet

Intake of healthy and fresh diet plays an important role in maintaining the health status of human kind. Balanced diet has been immensely accepted all over the world owing to the increased awareness regarding the maintenance of health status among people. Balanced diet is comprised of all essential nutrients, which are required for good health of human beings [32]. Nutrients present in food provides energy to perform vital functions of life and also helps for growth and differentiation of cells. These nutrients can be classified into micro nutrients and macro nutrients based on the requirements. Micro nutrients are the one which are required in a smaller quality which includes vitamins and minerals whereas macro nutrients are the one which are required in a larger quantity which includes carbohydrates, lipids and proteins [33]. All these nutrients are present in the food materials like cereals, pulses, vegetables, fruits, meat and dairy products. Among these products high amount of protein is found in meat. The concentration of protein may vary in different kind of animal meat like beef, mutton, chicken fish etc. whereas carbohydrate will be present in cereals, potatoes, milk and lipids will be rich in nuts, peanuts, ghee, oil, butter etc. [34].

#### 5. Variations in the dietary habits

Variation in food habits arises from the people's origin and it is modified by resource of the respective place or origin. The major resources having impact on the food culture are climate, Land, soil, water, cultural and religion of the habitat [35]. The era of globalisation has changed the eating and life style habits which has shown a very strong impact on the health of human beings. Urban areas of most of the countries, have embraced more processed and packed food, which have led

to increased obesity and body mass in people. Diversified food habits have been seen in various parts of the world and also within the countries itself with different geographical areas. These food variations are the main factor for variations in prevalence for urolithiasis at different geographical places [35].

## 6. Role of dietary habits in stone formation

Among various risk factors of urolithiasis, food is considered as one of the important modifiable risk factors in the kidney stone disease. According to the study conducted by Maalouf et al. [36] states that a load of protein diet in food will lead to increased calcium excretion. This may lead to increased risk for kidney stone formation. High amount of protein diet induces acid load in the body because of production of protons during the metabolism by sulphur containing amino acids and also there will be increased calcium excretion followed by high protein diet [36]. In addition to this high intake of animal protein leads to increased concentration of calcium, oxalate, uric acid and phosphorus in the urinary tract. There are various mechanisms involved which may lead to increased concentration of these substances in the urine and may lead to the formation calculi [37]. High intake of carbohydrates and lipids also have shown similar effects on the urinary composition. Furthermore, less intake of fruits and vegetables may also act as risk factor for urolithiasis even though some of them will be rich in oxalates [38]. High intake of sodium in the form of excess of common salt is noticed in case of many industrialised countries lead to more calcium deposition in kidney. The role of magnesium and vitamin C in the kidney stone formation is still not clear. Few studies have reported with no significant association with stone formation, whereas the effect of these nutrients on urinary composition shows its role in urolithiasis [39]. Thus, most of the studies support the fact that there is a relation between dietary habits and kidney stone formation, although contradictory results are also available.

Different food items	Content of food	Role in urolithiasis	Reference
Milk, cheese, dark green vegetables, yogurt, calcium fortified beverages etc.	Dietary calcium	Decreases the risk of calcium oxalate stone formation	[40]
White meat poultry, lean beef, eggs, beans, etc.	Protein	High load of acid in the kidney increases risk of kidney stone formation Increase urinary excretion of calcium	[41]
Canned food, corn meal, Black eyed beans, beets etc.	Sodium	High level of urinary calcium	[42]
Green leafy vegetables, beets, berries, chocolates, cranberries	Oxalate	Increased oxalate absorption from the intestine lead to high amount of excretion	[40]
Citrus fruits, peppers, strawberries, blackcurrants, broccoli etc.	Vitamin C	High oxalate excretion in urine	[43]
Energy drinks, soft drinks, carbonated drinks, coffee etc.	Carbonated beverages	High level of oxalate excretion in urine	[44]

**Table 1.**  
*Role of various food stuffs on kidney stone formation.*

In the present chapter we are discussing in detail about the role of diet in KSD, so that we could summarise important preventive dietary habits for the urolithiasis (Table 1).

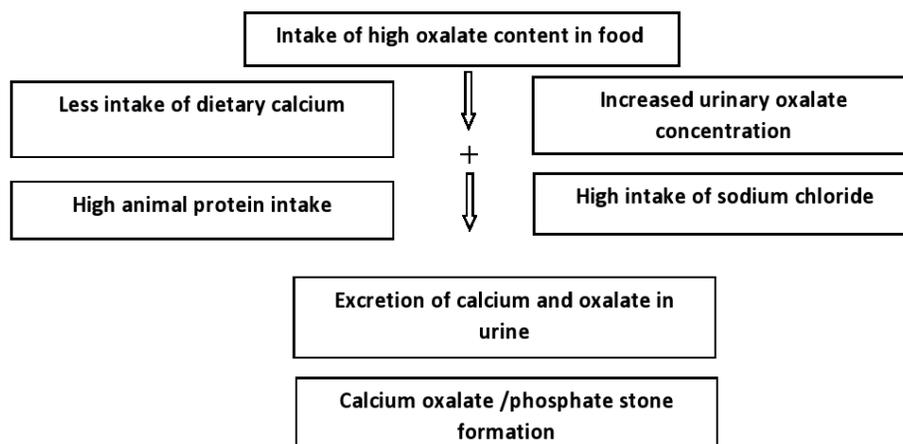
## 7. Impact of fluid on urolithiasis

Less fluid intake is one of the major risk factors in the stone formation, whereas adequate amount of urine excretion will eventually reduce the saturation of urine. To achieve 2 L/day of urine excretion fluid intake should be higher at the range of 2–3 L/day as water will be lost for extra renal functions like sweating, breathing and perspiration [45]. Along with volume of fluid intake, the quality and composition of fluid or water is also equally responsible for stone formation and it can be considered as a modifiable risk factor. Many studies have reported that high amount of fluid intake will eventually reduce the risk of urolithiasis [46].

Apart from water, other beverages like soda, tea, coffee and aerated or carbonated drinks consumption will also be having their impact on stone formation. High intake of sugar sweetened soda rich with fructose increases the risk of urolithiasis, as fructose promotes synthesis of uric acid and increases the excretion of uric acid, calcium and oxalate in urine [47]. Fructose rich food, makes the cells to utilise excess ATP for its uptake and such monosaccharides reduces phosphate concentrations within the cells and induces production of uric acid which leads to hyperuricosuria. So, in hyperuricosuria patients, it's advisable to reduce the intake of fruits, beverages and fruit juices rich with fructose content [48]. Another study conducted by Shuster et al. reported that intake of carbonated/aerated beverages is also one of the risk factors for formation of calculi as these beverages contains high amount of phosphoric acid [49]. On the contrary some studies also evidenced that citric soda content of the aerated drinks has a capacity to reduce the risk of stone formation by increasing the excretion of citrate. However low energy aerated drinks have not shown significant association in large cohort studies, suggesting that more than carbonated content fructose content of the drinks is the main culprit for urolithiasis [50]. A study conducted by Ferraro et al. [51] reports that beverages such as tea, coffee reduces the risk of calculi formation as studies have noticed that caffeine intake is associated with increased urinary output. Still excess consumption of tea, coffee is not advisable as it may interfere with other metabolic reactions which influence changes in the blood pressure. Hot beverages such as beer, alcohol have shown controversial results for their association with stone formation. In the study conducted by Ferraro et al., these drinks have shown to reduce the risk of stone formation as they reduce the activity of antidiuretic hormone and helps to excrete excess amount of diluted urine [51]. In contrast to this, a study conducted by Borghi et al. reports that alcohol intake should be avoided in case of urolithiasis patients as it will be rich in purine and it may cause hyperuricosuria [46]. Another study conducted by Rodgers et al., found that magnesium and calcium content of mineral water acts as protective in case of calcium oxalate stones [52]. Studies conducted on effect of various fruits juices have shown its impact on stone formation. Fresh lemon juice involved in the excretion of citrate and reduces excretion of calcium in urine. In concern with non-citrus fruits the results of the studies are still controversial as some fruits have shown beneficiary effect whereas some have not shown any significant association with urolithiasis [53]. Thus, these studies suggests that all fluids are not having same effect on urolithiasis. So, it's advisable to reduce the intake of sweetened beverages and high citrate content drinks as they have shown unfavourable outcomes in KSD patients.

## 8. Effect of carbohydrate diet on urolithiasis

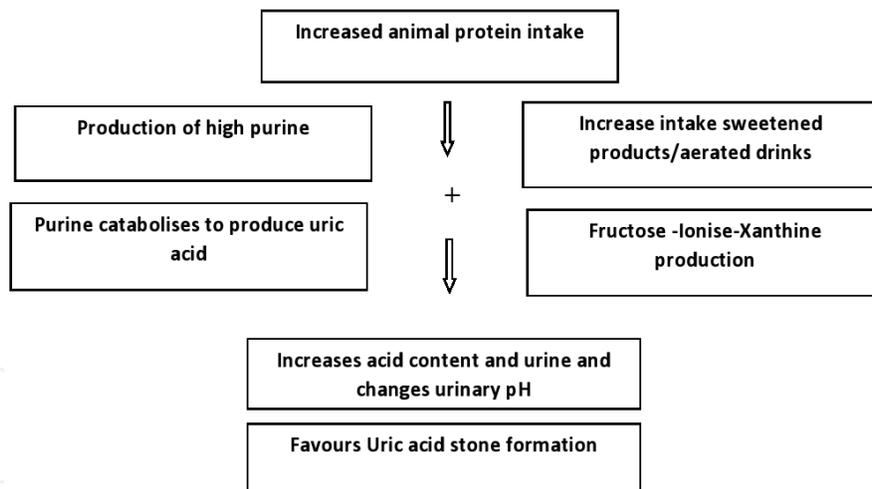
A study conducted by Nouvenne et al. reports that high carbohydrate food intake has shown increased excretion of calcium in urine compared to healthy individuals because carbohydrates decrease the calcium reabsorption in the renal tubules [54]. In contradictory to this some studies have reported that increased glucose concentration in diet has enhanced the calcium absorption in intestine. Various epidemiological studies have been conducted to find out the relation between insulin action and calculi formation specifically with uric acid stones. The insulin renal receptors show imbalance in acid handling which results in impaired excretion of ammonia in urine leading to excretion of acidic urine which favours precipitation of uric acid crystals leading to uric acid stones. This could one of the main reasons for high prevalence of urolithiasis in metabolic syndrome cases [55]. In addition to this high fructose intake has shown a strong association with formation of kidney stones as it enhances excretion of citrate and calcium in urine which favours the formation of stones in kidney. Increased fructose intake may cause insulin resistance and it may become trailing step for the formation of uric acid stone as it decreases the urinary pH and lead to uric acid stone formation [56]. Another study conducted by Curhan et al. reports that intake of sucrose has also shown its association with stone formation as high sucrose may increase the urinary excretion of calcium which is not dependent on the calcium intake (Figure 2) [57].



**Figure 2.**  
Effect of various food items in calcium oxalate/phosphate stone formation.

## 9. Effect of protein diet on urolithiasis

Various studies have shown a strong association of protein intake specifically animal protein with kidney stone formation. Animal protein will be rich in purines and after its degradation it produces uric acid [58]. These contains amino acids such as tyrosine, tryptophan and glycine and degradation of these amino acids produces oxalate which is the main component of calcium stones [59]. Increased oxalate content causes calcium and citrate resorption, renal acid excretion and increased urinary excretion of calcium which ultimately cause kidney stones [60]. Animal protein such as meat, poultry, fish shows unfavourable effect as their intake leads to uricosuria, calcinuria and phosphaturia and also reduces urinary pH. All these conditions increase the risk of precipitation of substances like calcium and uric acid and lead to calculi. Formation [61]. According a study conducted by Kerstetter et al. reports that in a normal healthy individual for every 20–25 g of increase in dietary animal protein, will rise the urinary calcium by



**Figure 3.**  
*Effect of various food items in uric acid stone formation.*

30–35 mg/day [62]. The final outcome of high animal protein intake by keeping volume of the urine constant is super saturation of urine with calcium oxalate and uric acid which are the main risk factors for stone formation. The underlying mechanism for uricosuria and phosphaturia is related to high content of these substances in animal protein. In addition to this increased calcinuria and change in urinary pH is mainly attributed by sulphureted amino acids such as methionine and cysteine which produces hydrogen ions leading to subclinical acidosis [63]. The reason for oxaluria is still not clear yet according to studies conducted, presence of oxalate in animal proteins produced by amino acids such as tryptophan, tyrosine increases endogenous production of oxalate which may create favourable environment for formation of stones [64]. Its notable that effect of vegetable proteins on urinary composition is different from those of animal proteins. A study conducted by Breslau et al. [65] observed that intake of exclusively vegetarian diet with vegetable proteins leads to less excretion of calcium, phosphate and more oxalate, citrate in urine with less acids as vegetable proteins contains different quantity of sulphates, purines, oxalates and fibres. On a whole, this suggests that vegetable proteins are less harmful for urolithiasis specifically in context with uric acid stones (**Figure 3**) [65].

## 10. Effect of lipid diet on urolithiasis

According to some observational studies there is an association between lipid intake and stone formation in kidney. A study conducted by Khan et al. [66] observed significant changes in the concentration of lipids in urine among stone formers and healthy individuals. The altered lipid content in the membrane enhances nucleation and retention of calcium oxalate crystals which are the initial steps of calculi formation [66]. Another study conducted by Naya et al. [67] reported that there is a relation between urinary lipids and crystal formation as it correlates with urinary oxalate excretion. This association is more evident in case of arachidonic acid content of diet as it increases absorption of oxalate from intestine and increases its clearance from kidney [67]. Another study conducted by Baggio et al. also supports these results as they evidence a high concentration of arachidonic acid in red blood cell membranes and plasma of urolithiasis patients [68]. Still some contradictory studies are also available which says that there is no correlation between lipid diet and urolithiasis [69].

## **11. Effect of milk and milk products on urolithiasis**

The requirement of calcium to body is satisfied by calcium rich food stuffs such as milk (100–120 mg/dl), cheese (approx. 500–600 mg/100 g) and yogurt (approx. 100 mg/100 g). The amount of calcium intake affects the level of calciuria in kidney stone patients and also in healthy individuals. Specifically, the absorption of calcium will be on higher side in kidney stone formers. This is suggesting that increasing in dietary calcium intake than its normal range have its impact on calcium stone formation. This was considered to be a risk factor for many years and physicians used to suggest to avoid calcium rich food in urolithiasis patients [70]. But according to most of the recent research work, the dietary calcium is no longer involved in formation stone as reduction in the dietary calcium did not show its impact on reduction of calciuria [71] and avoiding dietary calcium may lead imbalance in calcium concentrations and cause certain complications like osteoporosis or osteopenia over a long period. In addition to this when there is a restriction on dairy products, patients may compensate its protein by consuming high quantity of animal protein which may show its own complications in long terms [72]. According to the results of most of pathophysiological studies reported so far, the risk of stone formation is less in subjects who consume high quantity of calcium than in those people who consume less amount of calcium irrespective of gender. A randomised study carried out over 5-year period reports that intake of less calcium diet by reducing milk related products is less significant in preventing calculi recurrence than a normal calcium intake with low animal protein diet. Hence, in view of these results it's necessary to understand that no idiopathic stone formers should be advised for less intake of milk and milk product which may lead to complications because of hypocalcaemia [73].

## **12. Effect of sodium chloride and potassium on urolithiasis**

A significant relation between calcium stone formation and salt intake was first showed in a cohort study conducted by Curhan et al. [74]. Some studies conducted in further years did not succeed in confirming these results. A study conducted by Sabto et al. reports that daily intake of around 20–25 mmol of sodium will increase the calcium excretion in urine by 0.5–0.7 mmol/day, thus suggesting greatest impact of sodium on urinary calcium [75]. Salt present in the food stuff inhibits the tubular reabsorption of calcium thus leading to increased excretion of calcium in urine. In addition to this sodium chloride also inhibit the excretion of citric acid in urine, which is one of the significant risk factors for urolithiasis. The mechanism by which sodium decreases citric acid levels in urine is still unclear [76, 77]. Although there are no studies available to prove the fact that less sodium chloride intake will decrease the risk of calculi formation, but there are some studies which reports that beneficiary effect of low animal protein can be enhance by taking less sodium chloride. A well-balanced diet is with only required amount of sodium chloride will eventually help in preventing renal calculi [73]. Along with sodium even potassium is also involved in regulation of urinary calcium in human body. According to a study conducted by Muldowney et al., potassium deprivation was associated with increased calcium excretion in case of healthy individuals with normal diet with normal content of sodium chloride [78]. Another study conducted by Knight et al. also noticed in their study that sodium and potassium are involved in increasing urinary pH and its volume which are initial stages of cysteine stone formation [79].

### **13. Effect of fruits and vegetable on urolithiasis**

The role of fruits and vegetables in kidney stone formation is always been a controversial as these have shown both beneficial effects as well as harmful effects in case of Kidney stone disease. As fruits and vegetables are one of the important dietary sources of oxalate and this absorbed oxalate will be excreted in urine. If urine gets saturated with oxalate content it may become a risk factor for urolithiasis but however this oxalate is not withstanding [80]. Whereas there are some studies which have shown beneficiary effects of fruits and vegetables on urolithiasis as they contain high amount of magnesium and potassium and less amount of animal protein and sodium chloride. In addition, some fruits and vegetables also give alkaline therapy to the urine composition with their high content of bicarbonate and citric acid [81]. So it's important to note that not all the vegetables and fruits are harmful for urolithiasis as very few will be rich in oxalate such as spinach, beets, nuts wheat bran etc. which significantly results in oxaluria [82]. Along with effect of dietary oxalate content, the absorption rate of oxalate may vary person to person, as a study conducted by 80 showed that around 9–12% of idiopathic urolithiasis patients have shown increased oxaluria because of their increased intestinal absorption rate by 15–30% [83]. Another study conducted by Lemann et al. [84] reported that intake of fruits and vegetables can enhance magnesium excretion which is one of the important inhibitors for calcium crystallisation. And also favours the dissolution of uric acid by changing pH of urine [84]. By considering all above-mentioned factors, we suggest physicians to recommend intake of fruits and vegetable in their day today life to all the type of stone formers with a note of restricting foods having increase oxaluric activity to avoid calcium oxalate stone formation. Elimination of fruit and vegetables from diet of normal subjects causes unfavourable changes in urinary composition and may become risk factor for stone formation as their deficiency may significantly increase in super saturation of urine for calcium oxalate and calcium phosphate [85]. Considering above mentioned facts, we encourage physicians to advise their patients to consume fruits and vegetables regularly with restriction of vegetables showing hyperoxaluric effect to avoid increment in urinary oxalate content.

### **14. Effect of vitamins on urolithiasis**

The role of vitamins in the formation of stone is still uncertain. But according to literature review, vitamins with higher risk of causing urolithiasis are ascorbic acid (vitamin C), pyridoxine (vitamin B6) and calcitriol (vitamin D). A study conducted by Broadus et al., reported that the subjects with increased calcium excretion had high levels of vitamin D in their blood sample which lead to increased absorption of calcium in the intestine. Excluding some special cases, it's not suggestible to give supplementations of vitamin D particularly with combination of calcium to kidney stone patients [86]. High intake of vitamin C (ascorbic acid) has become a widespread practice all over the world as ascorbic acid helps in wound healing and preventing degenerative diseases. Vitamin C is a precursor of oxalate and it may increase excretion of oxalate in urine which a risk factor for calculi formation [87]. Intake of vitamin C around 1300–1500 mg/day is acceptable, if intake increases more than 1500 mg/day it will lead to initiation of crystal formation in urine [88]. Among vitamin B complex Vitamin B6 paly a vital role in reduction of risk of stone formation. Vitamin B6 (Pyridoxine) involves in the metabolism of oxalate, so deficiency of pyridoxine may lead to increased production of

endogenous oxalic acid. Intake of Vitamin B6 around 40–50 mg/day in diet will eventually help to reduce excretion of oxalic acid in urine and reduce the risk of urolithiasis [89, 90]. In a summary, with regards to vitamins adequate amount of all the vitamins should be consumed through the diet as they play important role in metabolism of vital biomolecules and also helps to maintain good health status of an individual. Kidney stone patients should avoid excess in take of ascorbic acid, and vitamin D supplementations as these have been reported as risk factors for urolithiasis. The patients can be advised to take good amount of pyridoxine as it is considered to reduce the risk of stone formation.

## **15. Conclusion**

The prevalence of kidney stone disease has increased in recent years as a result of modification in eating and life style habits. Changes in urinary composition and urinary saturation is the initial step for stone formation. So, focusing on reducing urinary saturation may help to reduce the initiation of urolithiasis. Various preventive measures are available which could reduce the burden of stone disease. Among all, dietary interventions show promising results in reducing the risk of stone formation as diet shows its direct impact on urinary composition. Among various types of stones, the most prominent stones such as calcium oxalate/phosphate and uric acid stones shows direct association with diet. According to our review of literature diet containing animal protein will increase urinary uric acid concentration which favours the uric acid stone formation. Diet with high oxalate content will increase urinary oxalate and combine with calcium to form calcium oxalate stones. Less fluid intake is one of the major risk factors for urolithiasis as fluid will help to dilute urine and reduce the saturation of urine. Considering these facts avoiding the foods with increased risk of stone formation and consuming balanced diet in kidney stone formers will help to reduce the reoccurrence and eventually help to reduce the prevalence of disease.

## **16. Summary**

Urolithiasis is a highly prevalent disease with its increased rate in recent years across the world. A change in food habits and intake of high calorie food is one of the main reasons for increased prevalence of kidney stone disease. The main aim of focusing on dietary interventions is to reduce urinary lithogenic risk factors such as increased calciuria, uricosuria, phosphaturia and low urinary pH. According to literature survey it's advisable to cut down high intake of animal protein and excess salt intake as animal protein increases uric acid concentration in urine and salt will increase mineral content of urine. Intake of high calorie food should also be reduced as it's involved in increasing saturation of urine and it may also lead to other health complications such as metabolic syndromes. High intake of aerated or carbonated drinks should be avoided in kidney stone formers as they contain high amount of sugar (Fructose). Along with reduction in consumption of above-mentioned food items it's equally important to consume food items which helps to alkaline the urine and reduce the risk of stone formation. According the literature survey it's advisable to consume good amount of green leafy vegetables with less oxalate content. Adequate amount of vitamins have to be taken in diet as their absence may lead to some deficiency manifestations in an individual. Excess consumption of vitamins such as vitamin D and C should be avoided as they may increase the risk of stone formation. In addition to diet, intake of high quantity of water will help to dilute

the urine sample and reduce urinary saturation. As some food items still shows contradictory results on stone formation, so more studies have to be conducted in this regard considering higher population in order to establish the relation of these food items in stone formation which will eventually help to reduce the burden of stone formation.

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The authors declare conflict of interest as none.

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**Section 1****COVID-19***Section Editor: Yash Pal Munjal*

1. **Epidemic Preparedness** ..... 3  
Srikant Kumar Dhar
2. **COVID-19 in Pregnancy** ..... 6  
Hari Kishan Boorugu

**Section 2****Cardiology***Section Editor: Gurpreet S Wander*

3. **Role of Ranolazine in Management of Chronic Stable Angina beyond Chest Pain** ..... 13  
Sajid Ansari
4. **CABG or Multivessel Angioplasty—Making the Right Choice** ..... 16  
Ruchit Shah, BR Bansode, Nihar Mehta
5. **An Art of Better Cardiac Prescription for Physicians** ..... 22  
D Prabhakar
6. **Cardiopulmonary Resuscitation: Current Guidelines** ..... 25  
Kothiwale VA, Shirol Vivek V
7. **Aortic Dissection—Are you Missing the Diagnosis in VIPs?** ..... 33  
P Paranthaman
8. **Lifestyle Therapy for ASCVD** ..... 38  
K Sathish Kumar
9. **Smoking and CVD** ..... 41  
Vipul Gupta, Girish Khurana, Hardik Khurana
10. **Late Gestational and Puerperal Cardiomyopathy** ..... 48  
NVBK Sai, Sudharani Busani

**Section 3****Diabetes Mellitus***Section Editor: Viswanathan Mohan*

11. **Current Concepts of Glucose Assessment in Diabetes Mellitus** ..... 59  
Prakash Govindasamy
12. **Intermittent Fasting in Diabetes: How Safely It may be Done?** ..... 65  
Adlyne Reena Asirvatham, Shriaram Mahadevan
13. **Artificial Sweeteners—Sweet or Bitter?** ..... 71  
M Venkatesh
14. **Diabetes and Diabetic Foot** ..... 78  
SS Dariya, Puneet Saxena, Deepak Chadha, Lalita Verma
15. **Syndromes of Ketosis-Prone Diabetes Mellitus** ..... 81  
Ravi Kant, Nisha Batra
16. **Resisting, Remitting, and Reversing Diabetes Mellitus** ..... 91  
Kailash C Jain

## CHAPTER

# 6

# Cardiopulmonary Resuscitation: Current Guidelines

Kothiwale VA, Shirol Vivek V

## Abstract

Cardiopulmonary resuscitation (CPR) is a group of life-saving interventions performed to manually preserve adequate oxygenation and circulation in the event of a cardiac arrest. It is an effective method of keeping a victim of cardiac arrest alive until a definitive treatment is delivered. The sequence followed for adult CPR is C-A-B, chest compressions followed by securing the airway, and lastly providing the essential breaths.

CPR is immediately performed on any unconscious and a pulseless patient. The indications of an immediate CPR are ventricular tachycardia, ventricular fibrillation, asystole, and pulseless electrical activity (PEA). Do not resuscitate (DNR) order is the only contraindication of CPR.

CPR consists of basic life support (BLS) and Advanced Cardiac Life Support (ACLS). The correct method of performance of the chest compressions are, the compression rate should be 120/min, and the compression depth should be 2 inches. According to the AHA 2010 Guidelines, the compression to ventilation ratio should be 30:2 till the placement of an advanced airway. Ventricular fibrillation is an indication for immediate defibrillation.

The biphasic defibrillator provides at 200 J and a monophasic defibrillator provides energy at 360 J. The important steps in ACLS are, immediately start CPR, provide supplemental oxygen, continuous BP and SpO<sub>2</sub> monitoring. Next the rhythm is checked. They are categorized as shockable and non-shockable rhythms. The shockable rhythms are ventricular fibrillation and ventricular tachycardia. The non-shockable rhythms are asystole and PEA. They must be treated by following the appropriate guidelines and protocols.

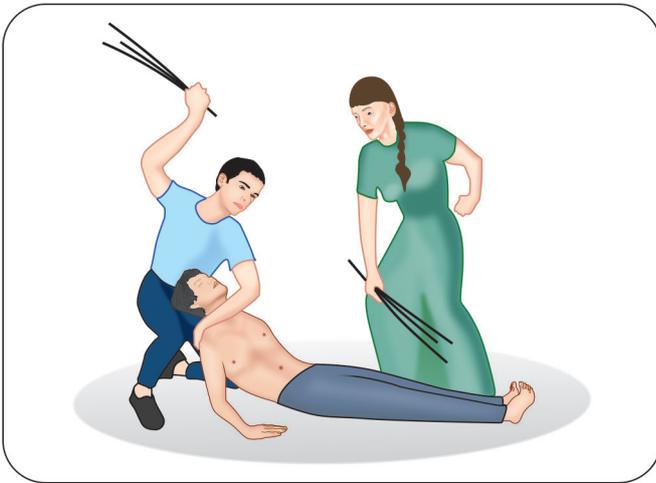
Survival rates of 1–6% have been reported in a few studies done in out of the hospital settings. The term extracorporeal cardiopulmonary resuscitation (ECPR) is used to describe a new technique of establishing a cardiopulmonary bypass, which is done during an ongoing effort of CPR. More data is needed from further studies including randomized trials to make solid recommendation pertaining to Extracorporeal CPR.

CPR is thus a life saving procedure, which when performed in a methodic way can save numerous lives. This life-saving art is ever evolving with newer and more efficient ways of CPR being developed, which needs further research and validation. This article is a humble attempt to emphasize the importance of the current guidelines of CPR.

## Introduction

Cardiopulmonary resuscitation (CPR) is a group of life saving interventions performed to manually preserve adequate oxygenation and circulation in the event of a cardiac arrest.<sup>1</sup> CPR is a fundamental component of the first aid. It is an effective method of keeping a victim of cardiac arrest alive until a definitive treatment is delivered.

The evolution of resuscitation has progressed enormously. The method like whipping a dead body with nettles was a primitive method of CPR. Here is a brief overview of the evolution of CPR down the years.<sup>2</sup> In 1500s when a person died, the body would be whipped in order to stimulate life. This was known as the whipping method of resuscitation. Around 1530, the bellows method



**Fig. 1:** Whipping method of CPR

of resuscitation came into practice. In this method, a fireplace bellow would be used to blow hot air into the mouth of the victim. The rationale behind this was to replace warm air in the lungs with the warm air of fireplace using a bellow (**Fig. 1**).<sup>2</sup>

CPR is an emergency procedure, which involves providing high quality chest compressions along with rescue ventilations. The sequence followed for adult CPR is C-A-B, chest compressions followed by securing the airway and lastly providing the essential breaths. The late 1950s was the time of the development of the modern day practice of CPR.<sup>3</sup> The benefits of external chest compressions were shown by Dr. Kouwenhoven, Dr. Knickerbocker, and Dr. Jude.<sup>4</sup> Dr. Kouwenhoven was the first person to describe external defibrillation in 1957. It forms an important part of the present day guidelines of CPR.<sup>5</sup> In 1960 the first basic life support (BLS) guidelines were formed and later in the year 1975, advanced cardiac life support (ACLS) was included as a part of CPR.

### Indications and Contraindications<sup>6</sup>

CPR is immediately performed on any unconscious and a pulseless patient. Some of the common conditions which are the indications for an immediate CPR are, ventricular tachycardia (VT), ventricular fibrillation (VF) asystole and pulseless electrical activity (PEA).

### Contraindications

Do not resuscitate (DNR) order is the only contraindication of CPR.

CPR consists of basic life support (BLS) and Advanced Cardiac Life Support (ACLS). The CPR provided in the field is the BLS. This helps in increasing the chances of survival of the patients, until emergency medical care staff reaches the patient to provide the ACLS.

The BLS stresses on the importance of following the American Heart Association (AHA) chain of survival:

- Quick recognition of the emergency.
- Immediate CPR initiation, which consists of efficient chest compressions and bag and mask ventilation.
- Early usage of automated external defibrillation.

The ACLS consists of the following in addition to the BLS components:

- Advanced airway management
- Rhythm monitoring with ECG
- Defibrillating when needed
- Drug therapy
- Post-resuscitation care

### Basic Life Support

Automated external defibrillation (AED) and CPR together consist of the BLS. The International Liaison Committee on Resuscitation (ILCOR) and American Heart Association (AHA) together framed the guidelines of BLS. The important elements are summarized here.

### Chest Compressions

The most important aspect of CPR is the correct performance of the chest compressions. The coronary and cerebral perfusion pressure falls very quickly if the compressions are delayed or not performed properly during CPR.

The important points to be followed when performing effective chest compressions are:

- The rate should be 120 compressions every minute.
- Compression depth should be 2 inches.
- Complete chest recoil should be allowed between each chest compression.

### Compression-only CPR

Reluctance of the rescuers to perform mouth to mouth ventilation is a common occurrence. In such conditions the AHA 2010 Guidelines recommend the performance of CPR with only the chest compressions. The rescuers should not struggle to palpate the pulses and CPR should not be discontinued till the emergency medical service

personnel arrives at the scene, or the patient himself wakes up.

## Ventilations

The importance of ventilation arises when the patient remains pulseless for a prolonged period of time. Ventilations must be given such that enough tidal volume is delivered, which is confirmed with an effective chest rise. Excessive ventilation must be avoided as it compromises the cardiac output.

## Compression-Ventilation Ratio

According to the AHA 2010 Guidelines, the compression to ventilation ratio should be 30:2 till the placement of an advanced airway. After an advanced airway is placed, continuous and effective chest compressions are to be provided. Ventilations are provided asynchronously at the rate of 6–8 times per minute.

## Defibrillation

Ventricular fibrillation is an indication for immediate defibrillation to ensure the survival of patients. The AHA 2010 Guidelines recommend in adults, defibrillation using the highest available energy. The biphasic defibrillator provides at 200 J and a monophasic defibrillator provides energy at 360 J.

## Phases of Resuscitation

There are three phases in the event of a cardiac arrest. The electrical phase consists of the first 5 minutes. Defibrillation is the treatment for this electrical phase. The hemodynamic phase extends up to the next 10 minutes. Effective chest compressions are crucial for the survival of the patients in the hemodynamic phase of cardiac arrest. This helps in generating adequate cerebral and coronary perfusion. The metabolic phase starts after 10 minutes of cardiac arrest. Survival of the patients who are in this phase is poor.

## Advanced Cardiac Life Support

The advanced cardiac life support (ACLS) Guidelines are usually followed in the in-hospital setting for the management of the cardiac arrest. It includes the following:

- Treatment with drugs
- Monitoring of the ECG

- Defibrillating when needed
- Advanced airway protocol

The following treatment measures are not to be used:

- Injection atropine for PEA and asystole.

Steps in ACLS (adult arrest protocol):

- Immediately start CPR
- Provide supplemental oxygen
- Continuous BP and SpO<sub>2</sub> monitoring
- Next the rhythm is checked
- The following are the shockable rhythms: ventricular fibrillation and ventricular tachycardia
- The nonshockable rhythms are asystole and PEA

*If it's a shockable rhythm, the following steps are undertaken:*

The treatment of VT and VF:

- Immediate defibrillation.
- CPR to be continued for 2 minutes.
- IV access is obtained immediately.
- Place an advanced airway.
- IV epinephrine is administered every 3–5 minutes.
- Pulse and rhythm are monitored every 2 minutes.
- If the rhythm is a nonshockable rhythm, then CPR is continued.
- A second defibrillation attempt is done if it's a shockable rhythm.
- Next administer IV amiodarone if the rhythm is a shockable.
- Meanwhile attempt is made to identify and treat the reversible causes.

*If it's a non-shockable rhythm, then the following steps are undertaken:*

The treatment of asystole and PEA:

- CPR to be continued for 2 minutes.
- IV access is obtained immediately.
- Place an advanced airway.
- IV epinephrine is administered every 3–5 minutes.
- Pulse and rhythm are monitored every 2 minutes.
- An attempt is made to identify and treat the reversible causes.

*Shock energy:*

- Biphasic: 120–200 J initial
- Monophasic: 360 J

*Drug therapy:*

- IV Adrenaline 1 mg every 3–5 minutes.
- IV Amiodarone 300 mg stat. Followed by IV Amiodarone 150 mg as the next dose.

## Advanced Airway

The placement of supraglottic airway or an endotracheal tube is known as advanced airway. Confirmation of the correct endotracheal tube placement is done by the waveform capnography. Ventilations are provided every 6 seconds and asynchronous with chest compressions. The advanced airway is to be placed within a period of no more than 10 seconds.

Oxygen administration, securing the IV lines, monitoring the ECG and patient's SpO<sub>2</sub> form the other important interventions as mentioned in the ACLS guidelines.<sup>7</sup> Many studies suggest that the chest compressions, which form the basis of the CPR are often performed with too many errors and with too many interruptions.<sup>8-12</sup> The new motto is: circulation, airway, breathing (C-A-B). Once the patient becomes unresponsive, resuscitation is initiated at once by aiding the circulation with the chest compressions. This is followed by opening of the airway, and then finally comes the delivery of the breath. Reduced blood flow is the main reason for the deficiency of oxygen to the brain.<sup>13,14</sup>

**Flowcharts 1 and 2** show the algorithm for the management of tachycardia and bradycardia.

## CPR and Survival

Assessments of survival from an event of sudden cardiac arrest vary widely. Survival rates of 1–6% have been reported in a few studies done in out of the hospital settings.<sup>15-17</sup> According to three systematic reviews, the survival of the patients who were treated by emergency medical services personnel was reported to be 5–10%. When the culprit rhythm was ventricular fibrillation, the survival rate rose to 15% when CPR was immediately provided.<sup>17-19</sup> Poor outcomes have been seen when the technique of CPR was faulty or when CPR was not provided immediately after the cardiac arrest.<sup>20</sup>

## The Changes in CPR Guidelines Since 2010<sup>21</sup>

*The 2015 European Resuscitation Council Guidelines are as follows:*

- Favorable outcomes are greatly dependent on effective CPR. The method and rate of the chest compressions remain unchanged. The rate should be 120 compressions every minute and the compression

depth should be 5 cm. Complete chest recoil should be allowed between each chest compression. Chest compression to ventilation ratio remains the same 30:2.

- Defibrillation within 3–5 minutes of cardiac arrest has shown to produce survival rates as high as 50–70%. Early defibrillation is the key to success.
- Waveform capnography should be used to confirm and monitor endotracheal tube placement, quality of CPR and indicate the return of spontaneous circulation (ROSC).
- The drug treatment during CPR remains unchanged.

*Cardiac arrest in special circumstances:*

- In the event of asphyxia induced cardiac arrest, the survival of the patients is poor. Severe neurological damage has been noticed. Early supplemental oxygen therapy during the CPR leads to better survival rates with low morbidity.
- Immediate rewarming is very essential for the survival of the patients who have suffered cardiac arrest associated with hypothermia. Extracorporeal life support plays an important role in the management of such subset of patients.
- For events associated with anaphylaxis, early treatment with IM adrenaline is the treatment of choice.

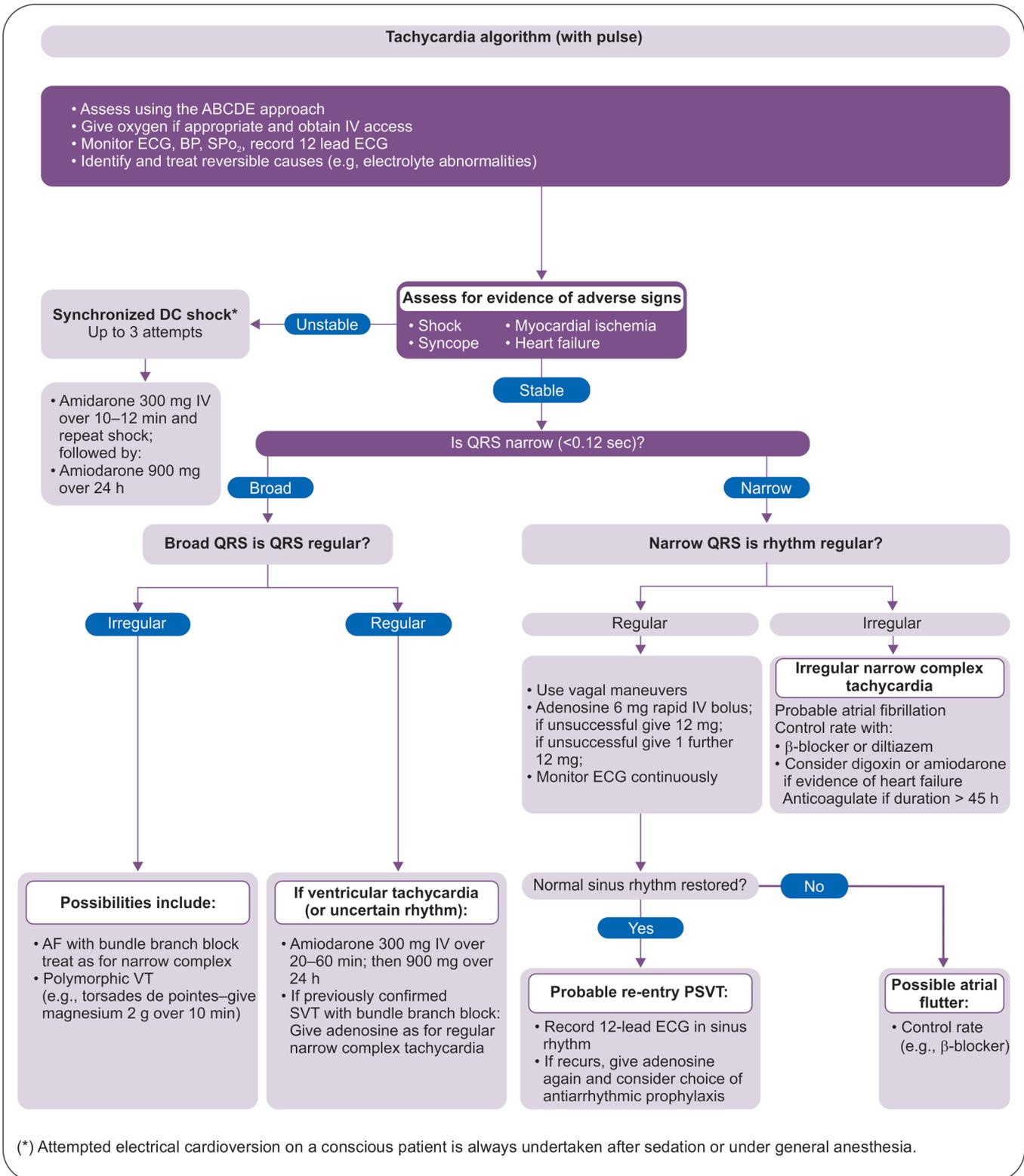
*Post resuscitation management:*

- For out-of-hospital sudden cardiac arrest (SCA) due to a cardiac event, early percutaneous coronary interventions have a great value in improving the survival rates.
- Temperature management of the patient is an important aspect in the post-resuscitation care. The temperature of 36°C remains the target optimum temperature for the care of patients who are recovering from an event of cardiac arrest.

*AHA Recommendations—Updated 2019<sup>22</sup>*

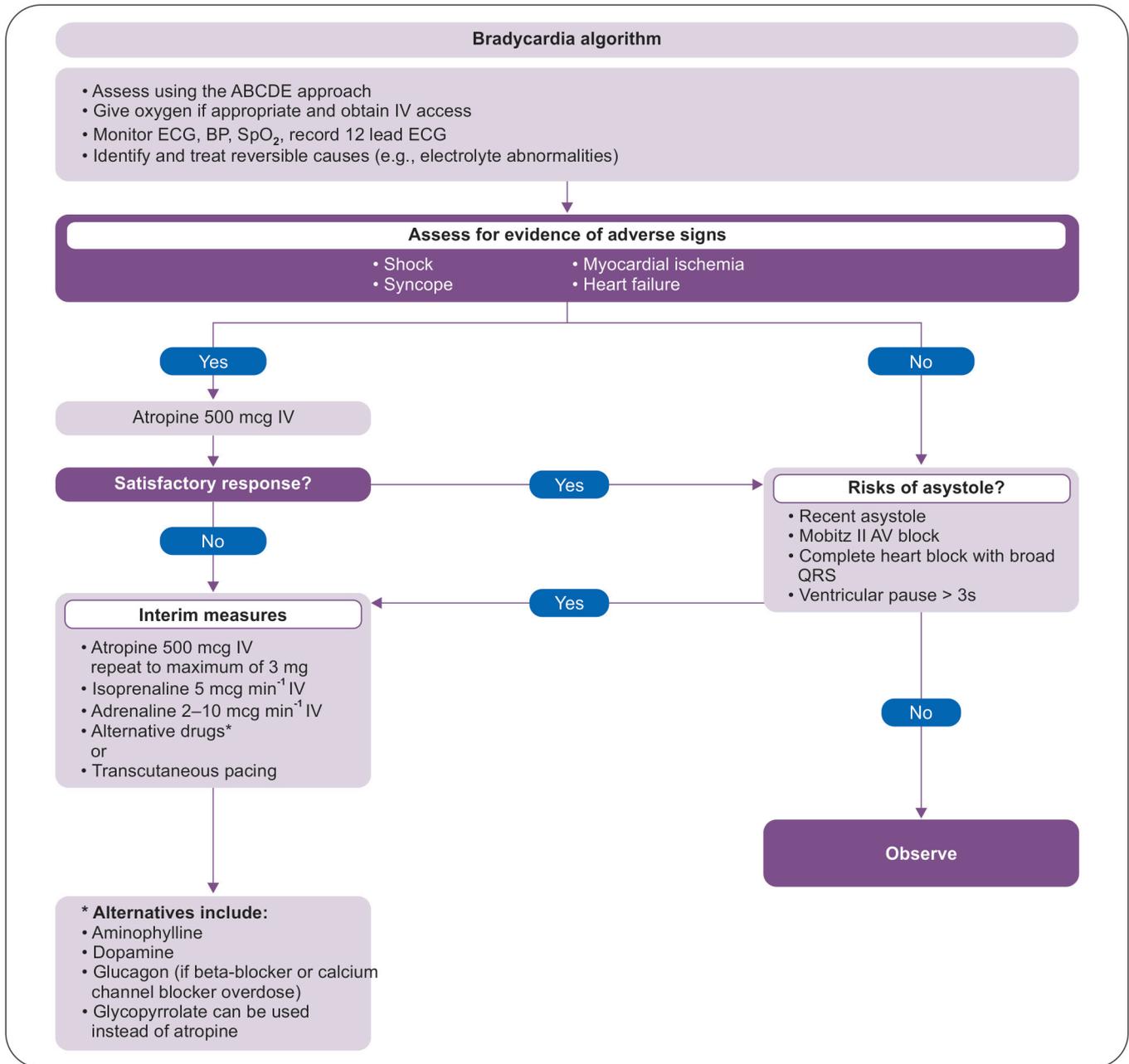
- Either bag and mask ventilation or an endotracheal tube is considered optimum for the performance of CPR.
- The supraglottic airway can be used as an alternative for adults in out-of-hospital cardiac arrest when endotracheal intubation success rate is minimal.
- IV adrenaline 1 mg every 3–5 minutes is recommended to patients in cardiac arrest.

**Flowchart 1:** Tachycardia algorithm (with pulse)

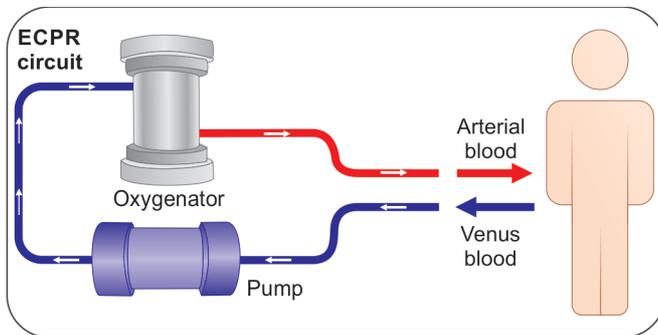


(\* ) Attempted electrical cardioversion on a conscious patient is always undertaken after sedation or under general anesthesia.

Flowchart 2: Bradycardia algorithm



- Vasopressin alone can also be used instead of adrenaline in cardiac arrest. But it offers no added advantage over adrenaline.
- Vasopressin can also be used in combination with epinephrine during cardiac arrest.
- It is advocated to administer adrenaline as soon as possible in the event of a cardiac arrest with a non-shockable rhythm.
- When the initial defibrillation attempts have failed in a case of cardiac arrest with a shockable rhythm, the next step is the administration of IV adrenaline.
- In a select few patients, extracorporeal CPR can be utilized as a rescue therapy when conventional CPR efforts have failed.



**Fig. 2:** Extracorporeal CPR

## Extracorporeal CPR

The term extracorporeal cardiopulmonary resuscitation (ECPR) is used to describe a new technique of establishing a cardiopulmonary bypass, which is done during an ongoing effort of CPR. IV access of a large vein and artery is established and a venoarterial extracorporeal circulation is begun with an effort to obtain adequate oxygenation during CPR.<sup>22</sup> When potentially reversible conditions are addressed, the goal of ECPR is to support end-organ perfusion.<sup>22</sup> Improved favorable neurological outcome was observed for both short-term and long-term follow-up in three studies dealing with ECPR.<sup>23-25</sup> Many systematic reviews, which evaluated the concept of ECPR, included young patients with less comorbidities.<sup>26</sup> For example, a young subject without comorbidities with a sudden arrest secondary to presumed cardiac arrhythmia may be considered a better candidate than an elderly patient with malignancy and cardiac arrest. More data is needed from further studies including randomized trials to make solid recommendation pertaining to ECPR (**Fig. 2**).<sup>22</sup>

## Termination of Resuscitative Efforts

Following are the scenarios, which can be considered for the termination of the resuscitative efforts:<sup>27-31</sup>

- Prolonged CPR effort of more than 30 minutes, but no establishment of spontaneous recovery of circulation.
- A prolonged period of time between the occurrence of the cardiac arrest and the beginning of CPR.
- Elderly patients with multiple comorbid conditions.
- Failure to elicit the brainstem reflexes.
- End tidal CO<sub>2</sub> of less than 10 mm Hg after 30 minutes of continuous CPR. This is a sign of circulatory collapse and irreversible damage.<sup>32-34</sup>

## Conclusion

CPR is thus a life saving procedure, which when performed in a methodic way can save numerous lives. This life saving art is ever evolving with newer and more efficient ways of CPR being developed, which needs further research and validation. It is the physicians' responsibility to keep oneself updated with the recent guidelines of such an important emergency procedure. This article is a humble attempt to emphasize the importance of the current guidelines of CPR.

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Chapter 4 .....	60
Fetal Echocardiography – Part I	
<i>Gurur Biliciler-Denktaş and Nazire Özcelik</i>	
Chapter 5 .....	96
Fetal Echocardiography – Part II – Congenital Heart Defects and Their Management	
<i>Nazire Özcelik, Arpit K. Agarwal, and Monesha Gupta</i>	
Chapter 6 .....	154
Prenatal Screening of Congenital Heart Disease	
<i>Arpit K. Agarwal, Chetan Sharma, Durga P. Naidu, Jennie Zarasvand, and Monesha Gupta</i>	
Chapter 7 .....	172
Fetal Arrhythmias	
<i>Nazire Özcelik and Gurur Biliciler-Denktaş</i>	
<b>Section III - Ethics</b>	
Chapter 8 .....	206
Ethical Issues in Managing Fetal and Neonatal Cardiac Lesions	
<i>Steven R. Leuthner</i>	
<b>Section IV - Changes in Oxygen Saturations at Birth and Pulse Oximetry Screening</b>	
Chapter 9 .....	232
Changes in Oxygen Saturations during the First Few Minutes of Life in the Delivery Room	
<i>Manisha Bhandankar and Dharmapuri Vidyasagar</i>	
Chapter 10 .....	256
Pulse Oximetry Screening for Detecting Congenital Heart Defects in the Newborn	
<i>Dharmapuri Vidyasagar and Nagamani Beligere</i>	

## **SECTION IV –**

# **CHANGES IN OXYGEN SATURATIONS AT BIRTH AND PULSE OXIMETRY SCREENING**

## CHAPTER 9

# CHANGES IN OXYGEN SATURATIONS DURING THE FIRST FEW MINUTES OF LIFE IN THE

MANISHA BHANDANKAR, MD  
AND DHARMAPURI VIDYASAGAR, MD

### Introduction

Physiologic events that occur during the transition from fetal to extra-uterine life at birth have attracted the attention of investigators for several decades. Because of the critical life-threatening possibilities during this transition, the period from birth to first breath was labeled as the “Period of Grace” by Clement Smith of Boston<sup>1</sup> more than a half a century ago. This reflected the fact that many children never manage to adapt to extra-uterine life and succumb immediately after birth without additional help. Sadly this remains the case even today in many developing countries around the world. However, the advances in perinatal and neonatal medicine gained during the last century are making their impact on better neonatal outcomes worldwide.

The physiology of the fetal circulation and the changes during transition have been discussed in detail in the first chapter of this book.<sup>2</sup> Nevertheless it is pertinent to review these critical changes to better understand the principles of neonatal resuscitation in the delivery room.<sup>3</sup> Resuscitation of the newborn is dependent on the initiation of respiration and effective oxygenation soon after birth. Until recently, assessment of the improvement in oxygenation of the newborn during resuscitation was mainly based on clinical observation.<sup>4</sup> However, clinical observation alone may be inaccurate for judging the degree of oxygenation. O’Donnell et al. have shown that clinical assessment of oxygenation based on color can be inaccurate.<sup>5</sup> The innovation of a non-invasive method of assessing oxygenation using pulse oximetry, and its simplicity of application in the newborn, has made it possible to measure oxygenation continuously

during transition soon after birth. Pulse oximetry may also be used to assess oxygenation during neonatal resuscitation.<sup>3,6</sup> In this chapter we will review the physiologic aspects of cardiopulmonary changes and the value of pulse oximetry during the first minutes of life in assessing the normal and abnormal transition that occurs soon after birth.

## **Fetal Circulation**

Fetal circulation is distinguished by its unique physiology.<sup>7,8</sup> Fetal blood is oxygenated at the placental level while the fetal lung remains dormant in its function as an organ of oxygenation. The main features of fetal circulation are: Oxygenated blood is carried by the umbilical vein from the placenta to the right atrium and deoxygenated blood is carried by the umbilical arteries to the placenta. Three shunts are functional during fetal circulation, namely the ductus arteriosus, ductus venosus and foramen ovale. High pulmonary vascular resistance and low placental resistance aid the exchange of gases at the placenta. The mechanisms for the presence of the high degree of fetal pulmonary vascular resistance have been explained on the basis of both active and passive resistances.<sup>8-10</sup>

The passive resistance is due to the compression of pulmonary capillaries by fetal lung fluid. The active vasomotor tone secondary to a hypoxic level of pulmonary venous blood is mainly responsible for the pulmonary vasoconstriction in the fetus.<sup>11,12</sup> Because of the high pulmonary vascular resistance, the majority of the blood pumped from the right ventricle enters the descending aorta through the ductus arteriosus for distribution to the lower part of the body and the placenta via the umbilical arteries, for oxygenation.

## **Transitional Neonatal Circulation**

Dramatic changes occur during the fetal to neonatal transition at birth, to adapt the baby to extra-uterine life. These events follow the initiation of the first breath of the newborn. The first breath of the newborn is triggered both by the physiologic interaction of low oxygen levels and high CO<sub>2</sub>, and environmental changes which stimulate the respiratory center. With subsequent breaths, the lungs continue to expand until normal functional residual capacity (FRC) is established. Concomitantly there is a marked decrease in the pulmonary vascular resistance, resulting in increased blood flow from the right ventricle to the lungs. The decrease in pulmonary vascular resistance increases the blood flow returning to the left atrium.

The pressure in the left atrium increases, which closes the foramen ovale by pressing the valve of the foramen ovale against the septum secundum. The foramen ovale closes functionally at birth.<sup>13,14</sup>

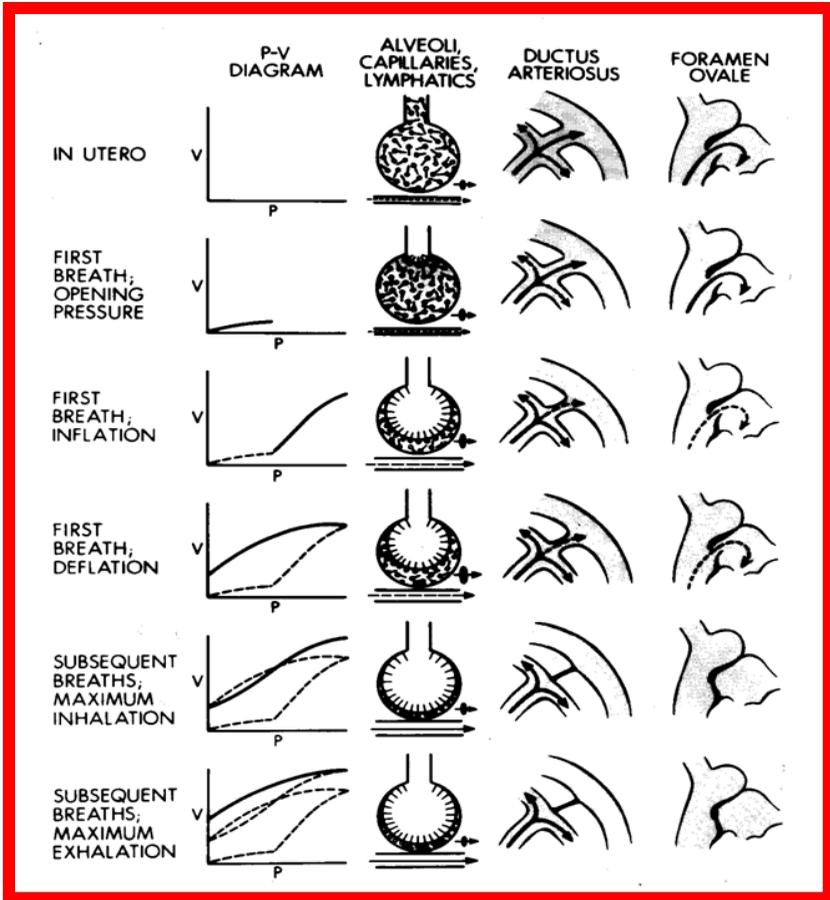
As the pulmonary vascular resistance is now lower than the systemic resistance, the blood flow in the ductus arteriosus reverses, passing from the aorta to the pulmonary trunk. The ductus arteriosus constricts at birth but there is often a small left-to-right shunt for 24 to 48 hours in a normal, healthy infant. Several events promote ductus constriction in the full term newborn. These include an increase in the arterial partial pressure of oxygen, a decrease in the blood pressure within the ductus (due to the postnatal decrease in pulmonary vascular resistance), a decrease in the circulating prostaglandin (PG) E<sub>2</sub> (due to the loss of placental PG production and increase in PG removal by the lungs), and a decrease in the number of the PGE<sub>2</sub> receptors in the ductus wall. Fifty percent of the ducts are functionally closed at the end of 24 hours, ninety percent by 48 hours and one hundred percent by 72 hours. The anatomical closure of the ductus and formation of the ligamentum arteriosum occurs by the twelfth week.

### **Transitional Pulmonary Physiology: The Science of First Breath**

It is important to note that circulatory changes that occur alone during transition do not completely explain improved oxygenation soon after birth. In order to sustain oxygenation after birth and placental separation, parallel to circulatory changes, critical changes take place in the previously dormant lung during the first few breaths of the newborn. Two major developmental changes in the lung prepare the fetal lung for extra-uterine gas exchange. 1) The lung in utero is not a completely collapsed organ; it is filled with lung fluid. The mechanisms of production and constituents of lung fluid have been well studied. A lack of production of lung fluid or loss of lung fluid from chronic leakage is associated with hypoplasia of the lung, and a consequently difficult neonatal transition; 2) Although not consequential in oxygen delivery, fetal breathing movements are considered important for the newborn to have a smooth fetal to neonatal transition. Fetal breathing movements start midway through gestation. These are intermittent breathing movements lasting for varying periods, but they occur for about 20 minutes of every hour near term. Sensory stimulation and cooling of the skin, changes in the arterial oxygen and carbon dioxide levels, and the detachment of the placenta are the

factors found to be responsible for the onset of continuous breathing after birth.<sup>15-17</sup>

In the normal fetus-to-neonatal transition, replacement of fetal lung fluid with air is an important step towards the establishment of smooth respiration. Karlberg, Vyas, Milner and their associates successfully conducted studies on newborns to understand the changes that occur with the first breath.<sup>17-19</sup> They studied air flow, pressure, and volume changes in the lung using an intra-esophageal catheter, face mask, and low resistance pneumotach. In addition, they took serial chest X-rays starting at the time of birth and initiation of the first breath, and continued to take chest X-rays during subsequent breaths until the establishment of sustained ventilation. They found that with the first inspiration the pressure generated varied from 10 to 70 cm H<sub>2</sub>O and the inspiratory volume was 20-75 ml. Expiration was passive and there was no pause at the end of inspiration. The residual volume varied from 0 to 70 ml and subsequent breaths required lower intra-thoracic pressures. The total respiratory work was equal to the square of the tidal volume. The total inspiratory work during the first three breaths showed no difference. A significant correlation has been shown between the first inspiratory volume and the FRC at the end of the first breath ( $p < 0.004$ ). Figure 9-1 shows the sequential changes that occur in the inspiratory pressure, fluid in the alveoli, ductus arteriosus, and foramen ovale during the "First Breath" and subsequent breaths. Full inflation and prolonged expiration associated with the baby's crying drives out nearly 100 ml of fluid with the first few breaths. When taking the first breath after birth, a healthy newborn exerts a negative intrathoracic pressure of approximately 50 cm H<sub>2</sub>O (0-100cm H<sub>2</sub>O) and with adequate surfactant supply will develop an FRC of approximately 5-6 ml/kg.<sup>18,19</sup> There is increased production of adrenaline by the fetus, and of thyrotropin-releasing hormone and glucocorticoids by the mother with the onset of labor; this stimulates the reabsorption of fluid by the pulmonary epithelial cells. During vaginal delivery at term, up to 35 ml of fluid is expelled from the baby's lungs by uterine contraction and passage through the birth canal. Similar findings were observed by other investigators in various experimental models.<sup>20-25</sup>



**Figure 9-1.** Sequential changes at birth. The figure diagrammatically shows the sequential changes in four physiologic parameters:

- Left vertical panel. Pressure (p) Volume (v) loop during the “First Breath” starting in the top portion to lower panel. Note that the lungs open up only after reaching a certain opening pressure. Functional residual volume is established at the end of the first breath (third panel from the top) facilitating the easier second and subsequent breaths.
- The second vertical panel from the left shows the changes in the alveoli, starting from the top. The liquid-filled alveoli open up with increasing intra-alveolar pressure, as seen in the pressure/volume (PV) curve, eventually establishing functional residual volume and the formation of an air-liquid phase with a monolayer of surfactant lining the alveoli (Bottom). Note that the horizontal lines below the alveolus depict

pulmonary vessels and blood flow. With the increase in alveolar pressure there is an increase in the pulmonary blood flow.

- The third vertical panel diagrammatically shows the changes in the pulmonary blood flow and patency of the PDA before the first and subsequent breaths. Refer to the text for details.
- The fourth vertical panel shows the changes in left atrial filling and closure of the foramen ovale prior to and following the first breath, top to bottom. Refer to the text for details.

Sequential changes with the first and subsequent breaths. Note that less pressure is required to open the alveolus with subsequent breaths, air displaces fluid from the alveolus with each breath, and the ductus arteriosus foramen ovale close.

In summary, with the first breath there is a mechanical expansion of the lungs, and fluid is pushed out from the alveoli and absorbed into the lymphatic system. With subsequent breaths, the alveoli are filled with air which contains 21% oxygen. As a result of gaseous distension and increased oxygen in the alveoli, the blood vessels in the lungs relax, the pulmonary blood flow increases, and well-oxygenated blood is pumped for the whole body. These pulmonary changes, in conjunction with improved pulmonary circulation, establish normal postnatal circulation and oxygenation. Lang et al. studied the changes in pulmonary blood flow in newborn rabbits whose lungs were partially aerated using 100% N<sub>2</sub>, air, and 100% O<sub>2</sub>. They showed that the increase in pulmonary blood flow and lung aeration immediately after birth are not spatially related and that oxygen is not the only stimulus to initiate aeration-induced changes in the pulmonary blood flow.<sup>26</sup> Further studies are required to understand the underlying mechanisms for the changes in pulmonary blood flow immediately after birth.

## **Abnormal Cardiopulmonary Transition and Oxygenation**

Compromised and at-risk newborn infants born by cesarean section, and premature infants, are prone to experiencing difficulties in establishing a normal transition at birth. The consequent burden of birth asphyxia is a major concern. Its prevention requires attention to proper resuscitation in the delivery room. It is estimated that 10-15 % of babies require resuscitation in the delivery room. At a global level it is estimated that 1 million babies may require resuscitation to establish transition and normal oxygenation for the baby, to prevent hypoxia. With this background the American Heart Association (AHA) and American Academy of Pediatrics (AAP) developed the Neonatal Resuscitation Program (NRP) to train healthcare workers to provide proper resuscitation in the delivery room.<sup>3,4</sup>

The main objective is to establish normal breathing and adequate oxygenation. Clinical observation of color is the main guide to assess neonatal oxygenation. However, clinical assessment of oxygenation in the newborn has been proven to be inadequate.<sup>5</sup> Then, an invasive method of blood gas monitoring became the standard way to precisely monitor blood PaO<sub>2</sub>. The introduction of the non-invasive method of pulse oximetry several decades ago opened the door to monitoring blood oxygenation continuously in newborns. Now pulse oximetry is a standard method of monitoring the newborn in the Neonatal Intensive Care Unit (NICU). Indeed, it is considered to be the fifth most important vital sign after heart rate, respiratory rate, blood pressure, and temperature.<sup>27</sup> The use of pulse oximetry in the delivery room to assess the degree of desaturation and guide the resuscitation of the newborn is now standard practice in tertiary care centers with trained birth attenders all over the globe.<sup>28</sup> Several investigators have demonstrated the importance of pulse oximetry in the delivery room to assess the oxygenation of the newborn after the first breath.<sup>29-42</sup> In the following pages we shall provide a review of the studies on pulse oximetry and the current knowledge of its applications in the delivery room.

## What is Pulse Oximetry?

Pulse oximetry is a noninvasive method used to measure the level of blood oxygen saturation (SpO<sub>2</sub>).<sup>43,44</sup> A pulse oximeter consists of a small light emitting diode (LED) and a photodiode which are placed opposite each other with the translucent site (eg., palm, wrist, sole, or finger in newborns) in between the two diodes. The LED transmits red light with a wavelength of 660 nm and infrared light with a wavelength of 905,910 or 940 nm which is received by the photodiode on the opposite side. The absorption of red and infrared light by oxyhemoglobin and deoxyhemoglobin present in the blood between the two diodes varies at these wavelengths, and this is calculated as the R/IR ratio and converted into the SpO<sub>2</sub> value using the look-up tables provided by the manufacturer. These tables are based on reference values obtained from healthy volunteers who were made hypoxic with saturations as low as 60-70% under controlled conditions. Therefore the accuracy of pulse oximetry is limited to oxygen saturations above 60-70%.

The signal varies with each myocardial contraction due to the surge of blood through the arteries which increases the blood volume at the measuring site. This is displayed in the waveform on the monitor. By

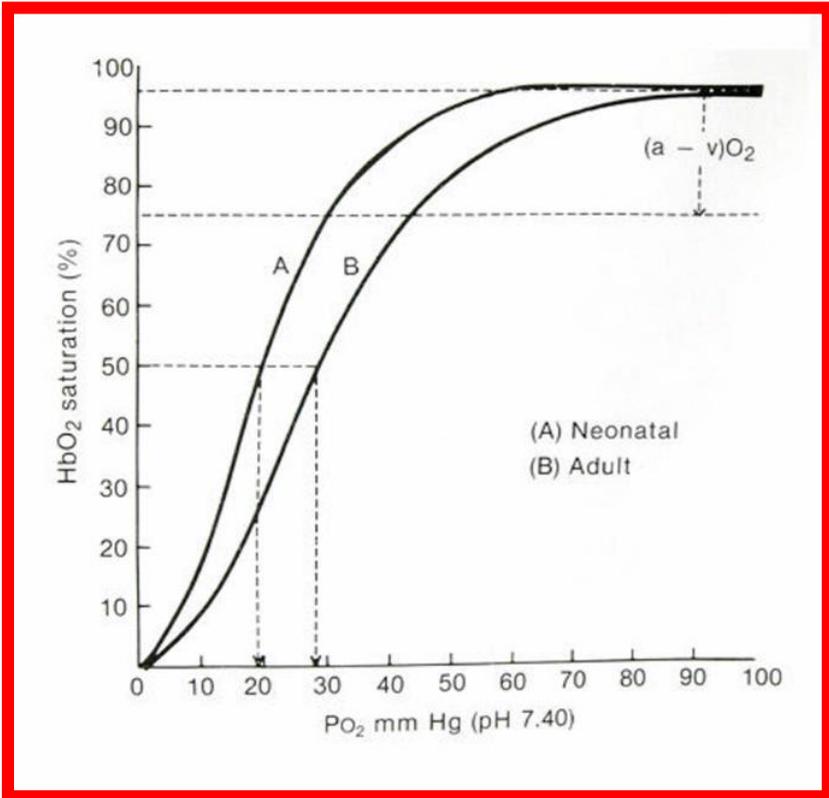
subtracting the minimum absorption (due to the constant presence of skin, soft tissue, and venous blood at the site) from the peak absorption (due to the surge in blood volume) a monitor can show only the absorption caused by the arterial blood. Hence the presence of a pulse is important for the functioning of the pulse oximeter.

The major drawbacks of conventional pulse oximetry are obtaining reliable data during movements of the limbs, and low perfusion at the measuring site. The reason for this is a difficulty in distinguishing pulsating arterial blood from moving venous blood. In 1995, Massimo introduced signal extraction technology (SET) that could accurately extract the arterial signal from the venous signals and thus overcame the problems caused by motion artifacts.

Oxygen in blood is carried in two forms: 98-99% is bound to hemoglobin (Oxyhemoglobin) and the rest is dissolved in the blood plasma ( $PO_2$ ). The combined oxygen content is represented in ml  $O_2$ /100ml of the whole blood. Tissues utilize the dissolved form of oxygen. The oxygen hemoglobin dissociation sigmoid shape curve explains the relationship between these two forms of oxygen. Oxygen bound to the hemoglobin is released into the blood's plasma and absorbed into the tissues. Each hemoglobin molecule has the capacity to carry four oxygen molecules. The oxygen saturation is the ratio of the oxygen bound to the hemoglobin to the oxygen-carrying capacity of the hemoglobin, which is expressed as a percentage. Various physiological factors in the newborn period affect the oxygen dissociation curve. Fetal hemoglobin has a high affinity for oxygen, and as such, when fully saturated, there is a high percentage of oxyhemoglobin. This shifts the curve to the left.

Hypothermia, a common neonatal problem, also shifts the curve to the left. Low pH secondary to metabolic acidosis in a hypoxic infant and a decreased amount of 2,3-DPG are other factors that can cause a shift of the curve to the left. The difference between the neonatal and adult hemoglobin-oxygen dissociation curves is shown in Figure 9-2. In normal infants, the P50 ( $PaO_2$  at 50% oxygen saturation) on day one of life is 20 mmHg, in contrast to 27 mmHg in adults. The P50 in term infants increases gradually and reaches adult values by 4-6 months of life. Further, a less than 24 hour-old infant can have saturations in the mid-90s and yet have a  $PaO_2$  of 50-60 mmHg. An infant with a  $PaO_2$  as low as 40 mmHg may appear pink despite low  $PO_2$  values because of the high oxygen affinity associated with fetal hemoglobin. Thus, it should be noted

that lower  $PO_2$  values in the newborn infant do not accurately indicate the amount of oxygen available to the tissue.



**Figure 9-2.** Oxygen dissociation curves. Oxyhemoglobin equilibrium curves of blood from term infants at birth, and adults (Ref; Fetal & Neonatal Physiology 3<sup>rd</sup> Edition, Chapter 86). The figure shows that in the fetal hemoglobin oxygen the dissociation curve is shifted to the left (A) compared to the adult hemoglobin oxygen dissociation curve (B). The figure also shows that at 50% saturation, fetal hemoglobin has a lower  $PaO_2$  (20 mmHg) than the adult hemoglobin (30 mmHg), indicating oxygen is tightly bound to fetal hemoglobin even at lower  $PaO_2$ . Most importantly, an infant with a  $PaO_2$  as low as 40 mmHg may appear pink despite low  $PO_2$  values, because of the high oxygen affinity associated with fetal hemoglobin. Thus it should be noted that lower  $PO_2$  values in the newborn infant do not accurately indicate the amount of oxygen available to the tissue. See the text for details.

Immediately after birth the presence of a large amount of fetal hemoglobin shifts the curve to the left compared to curve found in adults. In addition, the steep portion of the curve which allows the tissues to extract large amounts of oxygen with a minimal drop in the  $PO_2$  will also shift the curve to left. Consequently even a major drop in the  $PO_2$  from 80 to 40 mmHg will not affect the oxygen saturation much.

Oxygen saturation is therefore a more precise indicator of the oxygen content in blood than  $PaO_2$  and more important to monitor physiologically since it gives a complete picture of the amount of oxygen available for use. Measurements of oxygen saturation levels soon after birth also indicate the degree of interaction between ventilation and pulmonary blood flow, and thus provide a good measure of the postnatal adaptation of the newborn. This is the basis of using pulse oximetry as a tool for monitoring the newborn in the delivery room.

The use of pulse oximetry for neonatal care began in the 1980s and the earliest reported use in delivery room was in 1986 by Sendak and Harris, to monitor the changes in  $SpO_2$  immediately after birth.<sup>45,46</sup> Since then, investigators have been interested in monitoring  $SpO_2$  changes in the newborn immediately after birth, and have developed guidelines for the use of oxygen in the delivery room. The experience with pulse oximetry soon after birth in the delivery room is discussed in detail below.

### **The Need for Measuring Oxygen Saturation in the Delivery Room**

As stated earlier, birth asphyxia remains a major problem in neonatal medicine. It is one of the leading causes of death in developing countries.<sup>47</sup> Although birth asphyxia is much less of a problem in developed countries, it is still a major concern because the consequences of birth asphyxia, namely the development of hypoxemic encephalopathy and, later, neurodevelopmental delay, are serious.

Therefore, the recognition of infants at risk of developing birth asphyxia and the presence of experienced health care persons capable of resuscitating the newborn are essential primary steps in preventing the after-effects of birth asphyxia. Aggressive efforts have been taken by AHA and AAP to promote the training of healthcare personnel using a well-designed, evidence-based, physiologically appropriate Neonatal Resuscitation Program.<sup>3,4</sup> It was found that a clinical assessment of the oxygenation of the blood while undertaking resuscitation based on skin

color is not accurate enough to assess blood oxygenation.<sup>4</sup> Hence the use of pulse oximetry in the delivery room is recommended to guide neonatal resuscitation and maintain normoxia in the newborn.

As mentioned earlier, the earliest reported use of pulse oximetry in the delivery room was by Sendak and Harris et al.<sup>45,46</sup> who documented low oxygen saturation levels in healthy term infants until 7 minutes of age, even with normal Apgar scores. They suggested that the objective SpO<sub>2</sub> measurement using pulse oximetry, along with subjective clinical assessment, would be more beneficial to identifying infants at risk of hypoxemia. Since then, other studies have confirmed their observations. Several investigators have reported changes in oxygen saturation immediately after birth in newborns. Kamlin<sup>40</sup> and Rabi<sup>30</sup> and their associates showed a gradual rise in pre-ductal oxygen saturation during the first 5 to 10 minutes of life in infants of >31 or ≥35 weeks' gestational age, respectively, who received neither assisted ventilation nor supplemental oxygen. The median time to reach an oxygen saturation of 90% was 4.7 minutes in the Kamlin study and 8 minutes in the Rabi study. Kamlin et al. found the median SpO<sub>2</sub> level at 1 minute of life to be 63%, with an interquartile range of 53% to 68%, and at 3 minutes of age the lower interquartile range was still 64%. In a study of the pre- and post-ductal SpO<sub>2</sub> of 50 neonates using 2 Nellcor 300 pulse oximeters,<sup>32</sup> the pre-ductal SpO<sub>2</sub> values reached 95% by 12 minutes, compared to 15 minutes at post-ductal sites. O'Brien and colleagues attempted to monitor oxygen saturation in 90 term infants for the first 24 hours of life using the Nellcor N 200 pulse oximeter, analyzed in 6 four-hour stages. The baseline SpO<sub>2</sub> was between 89% and 100%.<sup>35</sup> Only one infant had an oxygen saturation of <80% during an apneic episode.

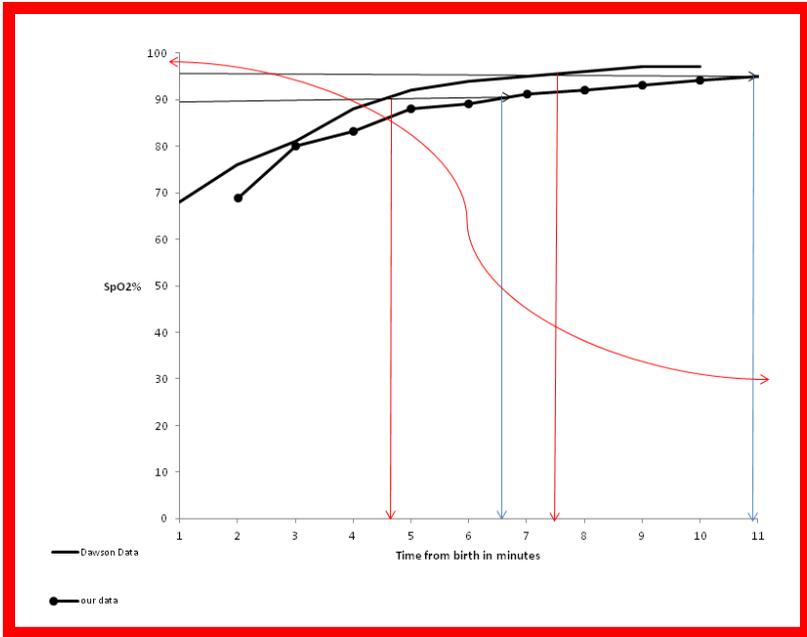
Overall, when we compare these studies, the results of sequential SpO<sub>2</sub> changes have been consistent, establishing the median SpO<sub>2</sub> at 1 minute of life at approximately 60% to 70%. Soon it was found that there was a need to establish the reference values for oxygen saturation in newborns delivered in resource-poor settings. Dawson et al. created percentile charts for SpO<sub>2</sub> changes in the first 10 minutes of life using the data of 61,650 SpO<sub>2</sub> measurements from 468 infants who did not receive any interventions other than warmth and stimulation.<sup>48</sup> The authors refer to them as "Reference" charts for changes in SpO<sub>2</sub> values in first 10 minutes of life. This study was done when immediate cord clamping was standard policy and immediate skin-to-skin contact was not routine. A study on the use of pulse oximeters on neonates delivered at home by midwife-supervised, uncomplicated vaginal births, where delayed cord clamping

(DCC) and immediate skin-to-skin contact (ISSC) are routinely done showed higher SpO<sub>2</sub> in the first minutes compared to these reference ranges.<sup>49</sup>

We studied changes in oxygen saturation in 50 healthy term infants from immediately after birth and throughout the first 12 hours of life.<sup>50</sup> We plotted a graph of the median SpO<sub>2</sub> values against time from birth, and compared it with Dawson's published data (Figure 9-3). The difference in the time taken to achieve an SpO<sub>2</sub> of 90% in our study group compared to that of Dawson's data was 2 minutes. Our cohort was further delayed in achieving an SpO<sub>2</sub> of 95%, doing so 4 minutes later than the subjects in Dawson's study. The red line in the figure depicts the drop in pulmonary vascular resistance that occurs during this period. The delayed decrease in pulmonary vascular resistance in our group due to environmental hypothermia may explain the delay in achieving >95 % saturation (7 minutes vs.11 minutes).

Rao and Ramji from India previously reported the use of pulse oximetry in the delivery room to monitor oxygen saturation in babies with birth asphyxia.<sup>35</sup> Thirty normal birth weight infants who did not receive resuscitation at birth were used as controls. The mean SpO<sub>2</sub> in the control group was 69.3%, 82.3%, 89.3%, and 93.7% at 1, 3, 5, and 10 minutes respectively. In our study, we found similar SpO<sub>2</sub> values of 69% (68-79) at 1 minute and 94% (88-97, n:45) at 10 minutes of age. Another study from Thailand, using Massimo technology for SpO<sub>2</sub> monitoring, showed the SpO<sub>2</sub> at 2, 3, 4, 5, and 6 minutes to be 77% (72-92), 84% (75-94), 88% (80-94), 90% (79-95) and 95% (85-97) respectively, which are closer to Dawson's reference ranges. These studies were limited to premature babies and the median time to record the initial reliable SpO<sub>2</sub> and HR was 160 seconds.<sup>38</sup>

Table 9-1 summarizes the studies reported so far on changes in SpO<sub>2</sub> immediately after birth in the newborn. The International Liaison Committee on resuscitation developed resuscitation guidelines for newborns in 2010 after considering these studies from different countries around the world.<sup>3</sup> (Table 9-2).



**Figure 9-3.** Changes in oxygen saturation immediately after birth. The figure shows changes in oxygen saturation during the first 11 minutes of life in two studies. The curve with the solid line is based on data from a study by Dawson et al.<sup>45</sup> and the curve with the dotted line on data from the authors' study.<sup>46</sup> The X axis shows time in minutes after birth and the Y axis shows % oxygen saturation as measured by pulse oximetry. The curved line is drawn to show the expected changes (a steady drop) in pulmonary vascular resistance with time after the initiation of the first breath. The horizontal lines intersect the dissociation curves to show levels of 90% and 95% saturation respectively.

The vertical lines show the time at which 90% and 95% oxygen saturation was reached in each study. In Dawson's study (solid line) 90% saturation was reached at 4.5 minutes and 95% saturation at 7.0 minutes. In our study (dotted line) 90% saturation was reached at 6.5 minutes and it took 11 minutes to reach 95 % saturation. (Please see the text for details.)

**Table 9-1. Studies on SpO<sub>2</sub> Changes Immediately After Birth**

<b>Author</b>	<b>Gestation</b>	<b>Technology</b>	<b>Duration</b>	<b>No. of infants</b>	<b>Site of monitoring</b>	<b>Values obtained SpO<sub>2</sub>%</b>
Kamlin <sup>38</sup>	>31 wks	Massimo	15 min/ SpO <sub>2</sub> >90%	205	Pre-ductal	63, 70, 76, 81, 90 at 1, 2, 3, 4, 5 min
Altuncue <sup>39</sup>	Term	Nellcor Oximax N-550B	Until SpO <sub>2</sub> >95%	150	Pre-ductal	71, 92, 98 at 1, 5, 15 min
Rabi <sup>28</sup>	>35 wks	Massimo	10 min	45	Pre-ductal	87, 91 at 5, 8 min
Dimich <sup>29</sup>		OhmedaBiox 3700	24 hours	100	Pre-ductal  Post-ductal	71.9, 83.3, 90.7, 95.7 at 1, 5, 10 min; 24 hours 64.4, 76.6, 87.1, 95.2 at 1, 5, 10 min; 24 hours
Toth <sup>32</sup>	Term	Nellcor 300	20 min	50	Pre-ductal  Post-ductal	73, 84, 92, 92 at 1, 5, 10, 15 min 67, 78, 89, 92, 94 at 1, 5, 10, 15, 20 min

Harris <sup>42</sup>	Term	Nellcor 100			Post-ductal	61 at 1 min
House <sup>31</sup>	All infants	Nellcor N100 /OhmedaBiox 3700	First 15 min	38	Pre-ductal	64.4, 70.4, 78.6, 80.7, 83.2, 86.4, 86.9, 87.7, 88.8, 90.4, 90.6 at each minute from 1-15 min
Dawson <sup>45</sup>	All healthy infants	Massimo	First 10 min	468	Pre-ductal	Gave reference range for SpO <sub>2</sub> from 1 to 10 minutes of birth
Mariani <sup>34</sup>	Term		First 15 min	110	Pre-ductal Post-ductal	89% at 5 min; 81% at 5 min
Rao & Ramji <sup>33</sup>	Term	Novamatrix 515A	Until 90% saturation, 1, 3, 5, 10 min	30	Pre-ductal	69.3, 82.3, 89.3, 93.7 at 1, 3, 5, 10 min
Gonzales <sup>34</sup>	Term	Nellcor N 20	1, 2, 3, 4, 5, 10, 15, 30 min; 1, 2, 8, 24 hours	131	Post-ductal	60.60 ± 1.20 ,91.10 ± 0.5%. At 1, 15 min, a plateau thereafter
Zubarioglu <sup>42</sup>	Term	Massimo	First 15 minutes	141	Pre- & Post-ductal	>90% vaginal deliveries preductal 6.9±2.8 min, post-ductal 8.4±3.2 min

**Table 9-2. Preductal SpO<sub>2</sub> Levels After Birth**

<b>Time after birth</b>	<b>Preductal SpO<sub>2</sub> levels after birth</b>
1 min	60-65%
2 min	65-70%
3 min	70-75%
4 min	75-80%
5 min	80-85%
10 min	85-95%

It is to be noted that the observations in Dawson's study and other studies to date were made primarily in high-income countries where infants were born in delivery rooms with a controlled environmental temperature. Conversely, in India and other developing countries, 70 % of deliveries take place in health facilities with limited resources and with no thermal control of the delivery room or at home, causing hypothermic stress in the newborn. Hypothermia is known to influence the microcirculation of the skin thus producing lower SpO<sub>2</sub> readings.<sup>51</sup> It is essential to obtain more data on the oxygen saturation values of babies born in such environments in developing countries. We monitored 51 healthy term infants born by the normal vaginal route after an uneventful antenatal and intranatal course in a tertiary care center in India.<sup>50,52</sup> A newer-generation pulse oximeter (Planet 55 4-channel multi parameter recorder, Mysore, India) was used to monitor the SpO<sub>2</sub> immediately after birth, throughout the first 12 hours of life. The Nellcor DURA-Y multisite oxygen sensor model D-YS reusable probe was placed on the right palm immediately after birth and then connected to the multichannel monitor. Simultaneously, we also monitored the core and peripheral temperature of the baby by placing skin probes on the right epigastrium and right sole of the baby respectively. The ambient room temperature and humidity in the delivery room and the postnatal ward (PNW) during the study period were recorded. The median interquartile (IQR) oxygen saturation level that was recorded in 9 newborns by 2 minutes of age at the teaching hospital (TCH) was 69% (range, 68 to 79). A gradual rise in SpO<sub>2</sub> was seen until it reached 95% at 11 minutes of life and plateaued thereafter. The median level of SpO<sub>2</sub> at 90% and 95% was attained at 6.5 min and 11 min respectively. The median time taken to achieve the first signal in our study was 2.9 min.

Various factors can influence clinical pulse oximetry.<sup>53-56</sup> They include: 1) technical, 2) physiologic, and 3) environmental factors. In a recently reported study by Mahindra and Bhatnagar from India, pulse oximetry was found to be useful to adjust oxygen concentration 2 minutes after birth, and the feasibility of using pulse oximetry in the delivery room as per the new NRP 2012 guidelines is questioned.<sup>52</sup>

Among the technical problems, motion artifacts are the major technical factors. Investigators have reported motion artifacts as the commonest cause, and presence of vernix, low perfusion, high ambient light, and probe malposition as other causes for delay in obtaining SpO<sub>2</sub> measurements by 1 minute of life. Massimo technology is currently being considered as the better option for use in delivery room but various studies have previously used Nellcor technology for monitoring oxygen in the delivery room and found no difference except for a delay in obtaining signals immediately after birth. The availability of pulse oximeters with Massimo technology is also restricted in resource-poor settings.

The probe application technique may also affect the SpO<sub>2</sub> record. Earlier it was recommended that attaching the sensor to the patient and then connecting it to the monitor helps in the early recognition of a signal by the pulse oximeter.<sup>54</sup> We followed this technique in our study, but we faced difficulties with fixing the sensor immediately in the presence of amniotic fluid and vernix. Further studies have shown that attaching the sensor to the oximeter first and then to the infant leads to faster recognition of the heart rate and saturations in infants of >28 weeks and this has been adopted in the recent NRP guidelines.<sup>57</sup> In our study, in spite of the quick-drying and purpose-made Velcro tape, we took 20-60 seconds to attach the sensor. It is difficult to apply the sensor to the palm as infants usually keep their hands tightly clenched, which sometimes delayed application by a few seconds. In our experience, these constraints were responsible for the delay in obtaining the first signals of saturation levels (a median time of 2.9 min). However, the team's skill and efficiency at drying the right palm and applying the SpO<sub>2</sub> sensor improves with practice.

Kamlin et al.<sup>58</sup> found the earliest time by which an accurate heart rate could be displayed on a pulse oximeter was 25 seconds, and that the Massimo technology pulse oximeter could display SpO<sub>2</sub> data by 90 seconds after birth. Toth et al. found signal detection occurred significantly faster from the hand (50% after 1.3 min, 90% after 4 min) than from the foot (50% after 3.1 min, 90% after 9 min).<sup>32</sup> Meier-Stauss obtained pulse

wave signals from the hand in 71% of cases beginning in the second minute of life and 90% of cases beginning in the fifth minute.<sup>39</sup> The median time to detect the first signal was 162.5 (range, 90-180) sec in the study by Rao & Ramji.<sup>35</sup> Our findings were within the range of delay experienced by other investigators.

Environmental factors also influence pulse oximetry. This subject has not received much attention. Such data are of paramount importance in managing infants in developing countries who require resuscitation. The most important observation we encountered was relative hypothermia in the delivery room, a common phenomenon in developing countries. During our study period the ambient temperature in the delivery room was 22-28°C. Although other investigators did not specifically mention the ambient temperature in the delivery rooms, the Indian Academy of Pediatrics and World Health Organization guidelines recommend the delivery room temperature to be maintained at 26°C.<sup>59</sup> Infants in our study were significantly hypothermic in the first 15 minutes, which could have affected the delay in picking up signals immediately after birth.

Several investigators have shown that a lower skin temperature gives lower SpO<sub>2</sub> readings, and warming improves the reading.<sup>60,61</sup> This phenomenon might explain the reason for the delay in the initial signal of the pulse oximeter, and also for consistently lower SpO<sub>2</sub> readings taken during the first 15 minutes of life in newborns in developing countries. Previous investigators have also shown that the control of peripheral circulation in the newborns, in response to the temperature of the surroundings (environment), is reflexive in nature. The circulatory thermo reflex was shown to be operative during the first day of life. These findings show that the "reference values" of SpO<sub>2</sub> in term infants not requiring resuscitation or supplemental oxygen at delivery and born in developing countries are lower than the reported values from developed countries. The clinical question is whether these findings call for early resuscitative intervention in babies born in developing countries and for clear guidelines for maintenance of the temperature of the newborn immediately after birth. Cord-clamping time also affects immediate oxygenation. The introduction of delayed cord clamping in these conditions may also add to changes in the oxygen saturation range among neonates from developing countries compared to that of the reference ranges given by NRP (7<sup>th</sup> edition). A recent study showed better oxygenation in infants with delayed clamping than those with early clamping. The oxygen saturations in this study were 18%, 13% and 10%

higher at 1 min, 5 min and 10 min respectively in babies who had delayed cord clamping, compared to the early clamping group.<sup>62</sup>

A study done in a Jordan valley at 200 m below sea level reported that the mean pre-ductal SpO<sub>2</sub> values at 2 minutes were 72 (51-95), which is higher than Dawson reference range; while at moderate altitude (1500-2500 m) Habib et al. have shown pre-ductal SpO<sub>2</sub> readings in a similar reference range in the first 15 min after birth, with SpO<sub>2</sub> > 94% achieved at 13 min after birth.<sup>63,64</sup> These studies indicate that altitude at birth may also determine the oxygen saturation immediately after birth.

## Summary and Conclusions

In summary, after birth the newborn undergoes a series of physiologic changes during the transitional phase in establishing normal extra-uterine respiration and simultaneously improving pulmonary circulation, both of which are important in the proper oxygenation of the blood. Compromised infants unable to establish normal respiration require resuscitation in the delivery room. The current reliance on a clinical assessment of the degree of oxygen desaturation (cyanosis) is found to be inadequate. The introduction of a non-invasive method of assessment of oxygenation using pulse oximetry has opened the door to much more accurately assessing oxygenation during transition. Several studies undertaken earlier have shown that it takes the newborn about 4 minutes to reach an oxygen saturation of 90% and 6 to 7 minutes to reach 95%. These studies have established the “reference values” of oxygenation at birth. More studies are required to establish the reference range in neonates with delayed cord clamping and immediate skin-to-skin contact. The routine use of the pulse oximeter in midwifery-led practice is feasible and is useful to detect hypoxemia due to non-cardiac causes, in addition to critical congenital heart disease. Reports from low- and middle-income countries indicate the feasibility of using pulse oximetry in the delivery room to monitor the status of extra-uterine adaptation.<sup>65</sup> Thus the routine use of pulse oximetry of the newborn in the delivery room will help clinicians to decide the timing of the initiation of resuscitation in the delivery room.

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# 13

## CHAPTER

# Oncology

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- 13.1 Acute Leukemia
- 13.2 Lymphoma
- 13.3 Neuroblastoma
- 13.4 Medulloblastoma
- 13.5 Pediatric Palliative Care



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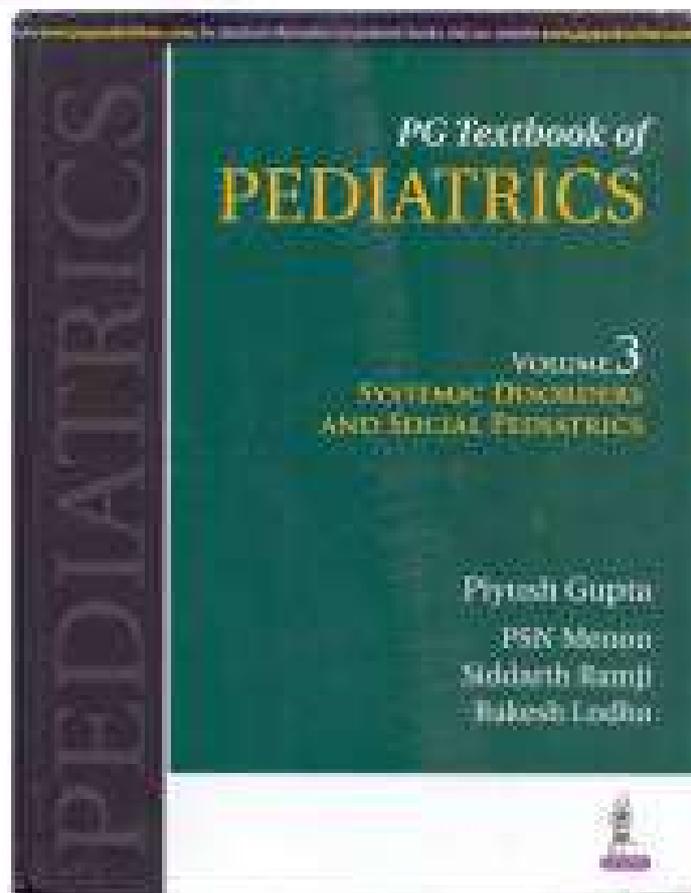
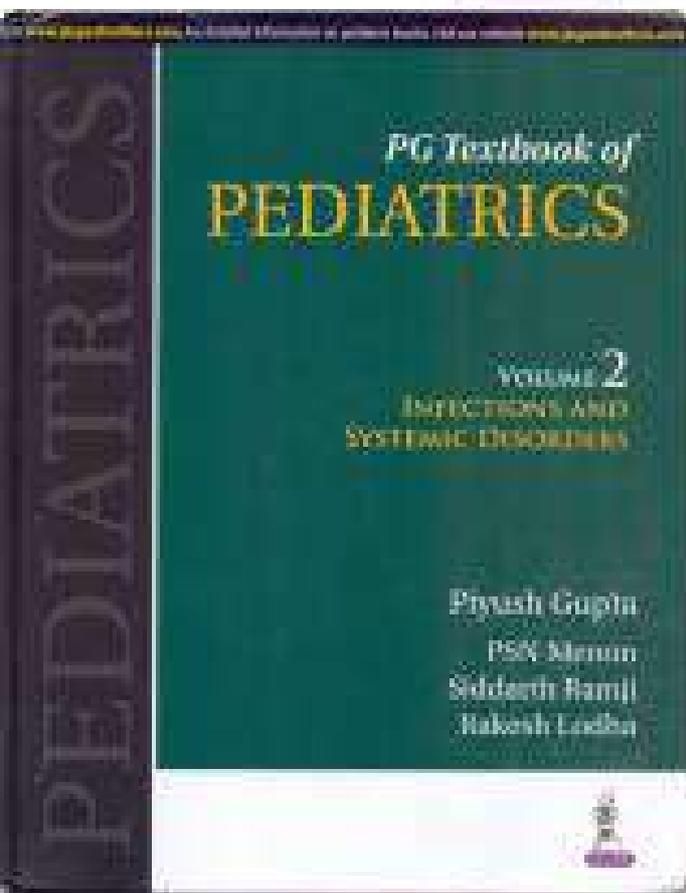
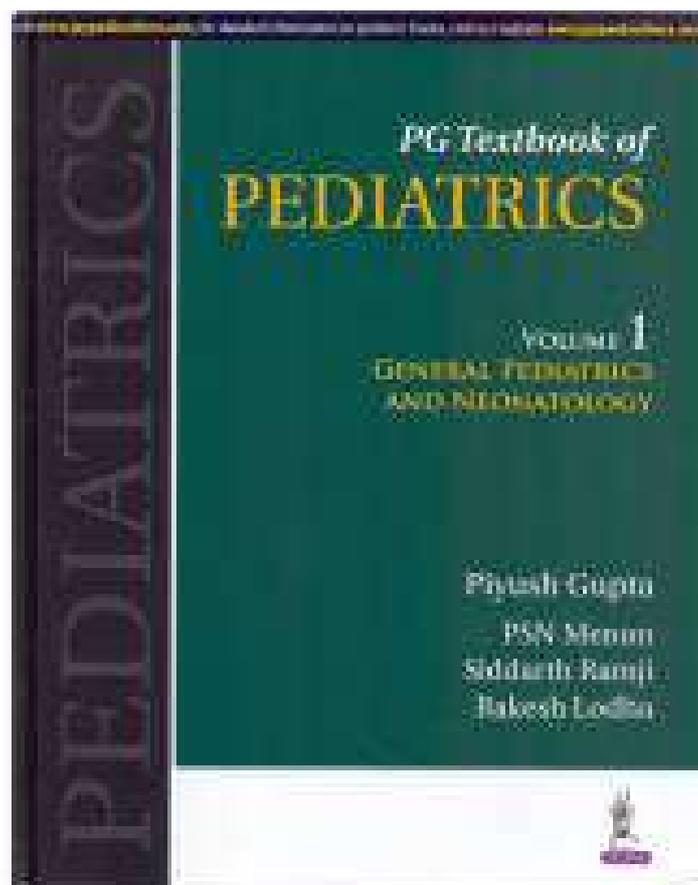
# 14

## CHAPTER

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- |      |                        |      |                  |
|------|------------------------|------|------------------|
| 14.1 | Leukemia               | 14.5 | Osteosarcoma     |
| 14.2 | Hodgkin's Lymphoma     | 14.6 | Ewing's Sarcoma  |
| 14.3 | Non-Hodgkin's Lymphoma | 14.7 | Rhabdomyosarcoma |
| 14.4 | Brain Tumors           | 14.8 | Hepatoblastoma   |





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This information aims to guide physicians in the management of children's kidney diseases and reflects current practice at the Khoo Teck Puat–National University Children's Medical Institute, National University Hospital, Singapore. Considerable care has been taken to ensure that the contents are accurate and current at the time of publication, but the reader is advised to check the drug doses, indications and precautions carefully. The authors are not responsible for any errors which may result from this publication. Application of the information in a particular situation remains the professional responsibility of the practitioner.

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# 11 Hemolytic-Uremic Syndrome

Lu L, Resontoc LP, Qader MA, Patil M, Liu ID and Yap HK

## A. Overview and Definitions

1. Thrombotic microangiopathy (TMA):
  - a. Describes a specific pathologic lesion in which abnormalities in the vessel wall of arterioles and capillaries lead to microvascular thrombosis.
  - b. TMAs are characterized by:
    - Systemic or intrarenal aggregation of platelets.
    - Thrombocytopenia.
    - Mechanical injury to erythrocytes.
2. Types of TMA:
  - a. Hemolytic-uremic syndrome (HUS):
    - i. Characterized by the simultaneous occurrence of:
      - Acute kidney injury (AKI) of varying severity.
      - Microangiopathic hemolytic anemia (MAHA).
      - Thrombocytopenia.
    - ii. Etiology is heterogeneous, which dictates management.
  - b. Thrombotic thrombocytopenic purpura (TTP):
    - i. Characterized by:
      - MAHA.
      - Thrombocytopenia.
      - Ischemic organ injury with a predilection for the involvement of the central nervous system and/or gastrointestinal tract.
    - ii. In contrast to HUS, the lungs are spared and there are minimal abnormalities for kidney function despite the presence of microthrombi in the kidney.

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<b>Automatic Determination of Harassment in Social Network Using Machine Learning</b> .....	245
Bhanu Prakash Doppala, S. NagaMallik Raj, Eali Stephen Neal Joshua, and N. Thirupathi Rao	
<b>Enhanced Performance of ssFFT-Based GPS Acquisition</b> .....	255
Harshali Mane, Matcha Venu Gopala Rao, V. Rajesh Chowdhary, and S. M. M. Naidu	
<b>Optimized Deep Neural Model for Cancer Detection and Classification Over ResNet</b> .....	267
Pavan Nageswar Reddy Bodavarapu, P. V. V. S. Srinivas, Pragnyaban Mishra, Venkata Naresh Mandhala, and Hye-jin Kim	
<b>A Steady-State Analysis of a Forked Communication Network Model</b> .....	281
Sk. Meeravali, N. Thirupathi Rao, Debnath Bhattacharyya, and Tai-hoon Kim	
<b>A Comparative Analysis of With and Without Clustering to Prolonging the Life of Wireless Sensor Network</b> .....	301
S. NagaMallik Raj, Debnath Bhattacharyya, and Divya Midhunchakkaravarthy	
<b>A Study on Techniques of Soft Computing for Handling Traditional Failure in Banks</b> .....	309
T. Archana Acharya and P. Veda Upasan	
<b>Lesion Detection and Classification Using Sematic Deep Segmentation Network</b> .....	321
Anil B. Gavade, Rajendra B. Nerli, and Shridhar Ghagane	
<b>Automatic Gland Segmentation for Detection of CRC Using Enhanced SegNet Neural Network</b> .....	337
Mohan Mahanty, Debnath Bhattacharyya, and Divya Midhunchakkaravarthy	
<b>Smart Cyclones: Creating Artificial Cyclones with Specific Intensity in the Dearth Situations Using IoT</b> .....	349
G. Subbarao, S. Hrushikesava Rao, Lakshmi Ramani Burra, Venkata Naresh Mandhala, and P. Seetha Rama Krishna	
<b>Machine Learning-Based Application to Detect Pepper Leaf Diseases Using HistGradientBoosting Classifier with Fused HOG and LBP Features</b> .....	359
Matta Bharathi Devi and K. Amarendra	
<b>Tracking Missing Objects in a Video Using YOLO3 in Cloudlet Network</b> .....	371
M. Srilatha, N. Srinivasu, and B. Karthik	



# Lesion Detection and Classification Using Sematic Deep Segmentation Network



Anil B. Gavade, Rajendra B. Nerli, and Shridhar Ghagane

**Abstract** Innovation of modern algorithms directed to development of effective segmentation and classification for liver segments. The lesion segmentation is essential in pre-operative liver surgical planning. In addition, the segmentation of liver lesions is considered as a crucial step for deriving qualitative biomarkers for precise clinical diagnosis. The aim of the research is to model an effective method that comprises of the extraction of the liver vessels and classification of liver segments for which Computed Tomography (CT) images is utilized. In classification module, the lesion detection and classification are performed using newly designed optimization algorithm named Adaptive Adam optimization algorithm along with DeepSegNet model. The proposed Adaptive Adam is designed by integrating adaptive concepts in the Adam algorithm. The liver image undergoes segmentation, wherein the tumors present in the liver are extracted based on an optimization strategy. Moreover, the accuracy is attained based on the training of the DeepSegNet using proposed Adaptive Adam algorithm. In this strategy, the probability for lesion or non-lesion is identified effectively. The performance of proposed Adaptive Adam algorithm found superior in terms maximal accuracy 0.846, sensitivity value of 0.881, and specificity value of 0.828, respectively.

**Keywords** Lesion detection · DeepSegNet · Liver vessels · Segmentation · Computed tomography (CT)

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321

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## 1 Introduction

CT is the well-known modality utilized for detecting the lesions of liver, diagnosing liver lesions, and staging of lesions. Focal liver lesions are categorized into different sets like benign lesions and malignant lesions, with substantial deviations in shape, size, location, and contrast. Precise bias between the different lesions is of great significance. Manually segmenting and classifying the liver lesions using the CT images is time consuming and leads to perplexity, which makes it a multifaceted task. Thus, the usage of automated tools assists radiologists to diagnose the liver lesions using CT images [1]. The CT images offer high spatial and temporal resolution by analyzing the pulmonary structures using three-dimensional (3-D) human thorax. Numerous techniques are devised for identifying the precise lung boundaries [2]. Computer-aided diagnostic methods are utilized for detecting the lung cancers using CT images. In CT images, it is acceptable to prohibit the pre-processing step, but the application of enhancement filter is beneficial for determining nodules in the CT images as the thresholding of the CT images may tackle the complexities [3].

Separating blood vessels from CT images and separation of liver into number of segments is essential to plan the liver transplantation [4]. Different liver segmentation algorithms are categorized into semi-automatic, automatic, and manual methods. Sketching the outline of liver manually using CT images offers more precise segmentation, but it is a burdensome and lengthy with respect to the users. The automated techniques are used for segmenting the liver without user interaction but failed to uphold accuracy [4]. In [5], an automatic segmentation method is devised based on supervoxel-based graph cuts. Then, a semi-automatic technique is applied for extracting the liver from the regions. In [6], multiregional-appearance-based approach is devised for segmenting the liver using manual initialization considering various CT slices. The vessel segmentation algorithms are mainly divided as semi-automatic and fully-automatic. In [7], region growing method was devised to segment the liver vessels by altering the thresholds. However, the method was inapplicable with smaller vessels [8]. In [9], locally adaptive region growing method was devised for segmenting the vessel trees wherein the locally adaptive analysis was performed for identifying small vessels. A level-set method was devised in [10] for segmenting the vessels using statistical histogram analysis. In [11], the thresholds are evaluated for extracting vessels in order to refine the counterfeit branches by examining the skeletonized vessel structures. In [12], a matched filter was utilized for enhancing the vessel structures and finally a generic algorithm are applied for liver lesion detection.

In this paper, we implemented a technique, called Adaptive Adam algorithm-based DeepSegNet, for detecting liver lesions and classification using CT images. Implementation is divided into three steps, which comprises thresholding, segmentation, and classification for operative liver lesion detection. Initially, the input CT images are progressed to the thresholding process, wherein the thresholding is carried out for separating pixels. After segmentation, the classification is done by the

DeepSegNet model, which is trained using the proposed Adaptive Adam optimization algorithm. Here, the proposed Adaptive Adam is developed by incorporating the self-adaptive concept into Adam algorithm. In this strategy, the probability for lesion and non-lesion is identified effectively.

This paper contributes toward the optimization algorithm, viz. Adaptive Adam, by altering the Adam algorithm and depends on self-adaptive concept. The major role of the proposed Adaptive Adam is to train the DeepSegNet for lesion detection and classification. The paper is divided into five sections, as introductory part of the liver lesion detection and classification, literature review of liver lesion classification, implemented Adaptive Adam algorithm-based DeepSegNet model, experimental results, and finally conclusion of the implementation.

## 2 Motivation

In this section, we provide overview of literature review on lesion detection, with limitation of available methods, about eight different techniques are considered and final implementation carried out.

### 2.1 Literature Review

The four existing literary techniques based on lesion detection techniques are discussed below. Yang et al. [4] developed a method named automatic seed point identification method using automated thresholding method. The method was utilized for extracting liver, hepatic vein (HV), and portal vein (PV), using the CT images. Further, a semi-automatic method was designed for separating HV and PV. Then local searching method was used to categorize the liver segments. The method was effective in segmenting the livers but failed to include other methods like geometrical analysis, graph cuts and histogram analysis. Yan et al. [13] designed a paradigm named DeepLesion for collecting the annotations of liver and then construct a huge scale lesion datasets with less manual effort. A Picture Archiving and Communication System (PACS) are radiological imagery platform they deliver cost effective storage, retrieval, managing, distribution and presentation of medical images. Hospital PACS have collected large amount of clinical annotation, meanwhile extracting, harvesting building large annotated radiological imagery datasets is a challenging process. The method poses many advantages and was considered as a widespread detector of lesions, which could determine all types of lesion in a single framework. However, this model is inapplicable with 3-D images. Diamant et al. [14] developed a technique for automating the diagnosis of liver lesions based on the CT images that enhances the image patch representation of boundary lesions. This method captured

the features of the lesion periphery using the lesion interior. The method improved the features based on visual word histograms and ROI. However, the method was unable to analyze the 3-D volumetric data. Frid-Adar et al. [15] developed a Generative Adversarial Networks (GANs) using synthetic medical images for determining the lesions by analyzing data and to improve the performance of CNN. The method synthesized improved quality liver lesion using ROI. The method was not applicable with other medical domains for enhancing the synthesis of liver lesions.

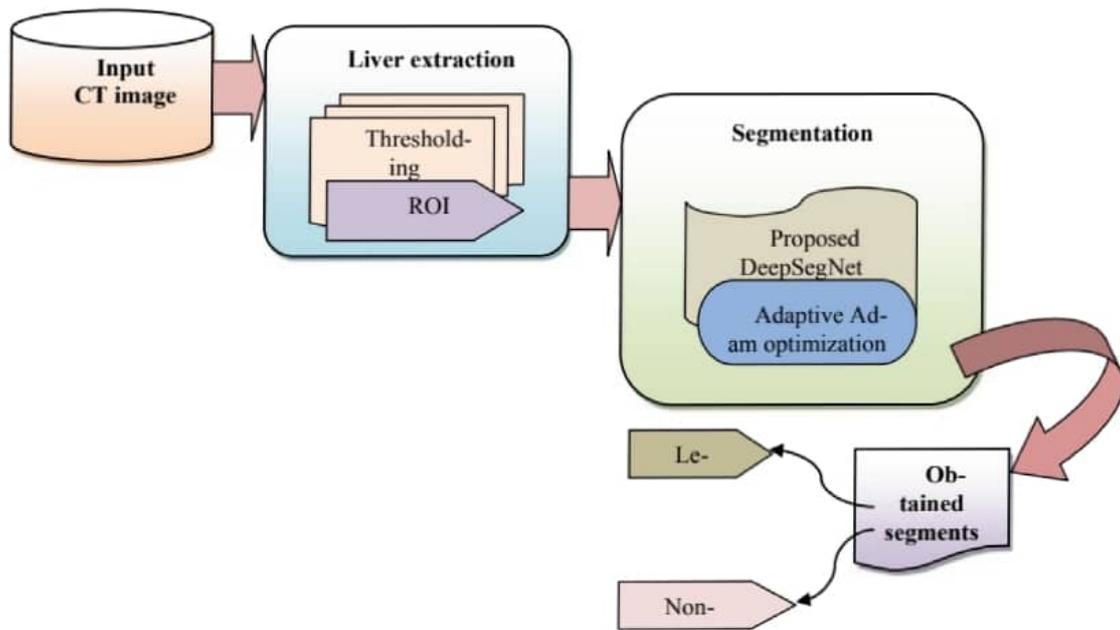
## 2.2 Challenges

The challenges of the research are deliberated below:

- In [4], a semi-automatic method is designed for distinguishing hepatic vein (HV) and portal vein (PV) using CT images. However, the recognition of PV branches using eight different liver segments is a major obstacle because of complexity in choosing a basis point for recognition of PV branches from 3-D images. In addition, this method faces complexities while dealing with local disturbances like connected structures or low contrast with intensity values.
- The major issue in the context of radiological imaging is to manage with diminutive datasets and the fewer amounts of processed samples particularly, while adapting supervised machine learning techniques that necessitate labeled data and outsized training. However, the annotations of CT images are a lengthy process and require more time for processing [15].
- Analysis of liver lesions is major challenge due to inconsistencies occurred with respect to the appearances like differences in shape of lesions, margin sharpness, size, and interior textures. In addition, the manifestation of many lesions overlaps and thereby leads to lots of variation [14].

## 3 Proposed DeepSegNet Model for Liver Lesion Detection

Figure 1 portrays the architecture of DeepSegNet model for detecting and classifying the lesion present in the CT image. The aim of implementation is to model an effective planning method that comprises of the extraction stage of the liver, extraction of vessels, and classification of the liver segments for which the CT images is employed. At first, the CT image is taken as an input, which is then fed to the liver extraction module for extracting the interesting regions from the image. The ROI from the CT image is extracted using the thresholding process. Here, the region covering the liver area is subsequently extracted from the input CT image. Once the ROI is extracted then, the extracted regions are fed to the proposed DeepSegNet model for performing deep segmentation and classification using the Adam optimization [16] algorithm.



**Fig. 1** Framework of proposed adaptive Adam-based DeepSegNet model for liver lesion detection

Based on the detected regions, the classification is done to determine whether the detected region is lesion or non-lesion.

Here,  $D$  is database with ' $f$ ' number of CT images and is given as,

$$D = \{I_1, I_2, \dots, I_g, \dots, I_f\} \quad (1)$$

where  $I_g$  represents the  $g$ th input image.

### 3.1 Thresholding to Extract the Interesting Regions

For qualitative valuation of CT image, the ROI is evaluated for estimating the noise variance. Generally, the CT images are assumed to hold additive noise along with the image. Thus, the thresholding is employed for performing ROI extraction in the CT images, wherein the pixels are normalized and set to one or zero. Thus, the thresholding result is a binary image, which can offer a mask for extracting uniform ROI. The thresholding selects the ROI on the basis of pixel intensity. The goal of image thresholding is to provide segments of the image based on typical features of the image and characteristics are devised on the basis of pixels intensity level. The thresholding process represents the image in the digital format by categorizing the image as light or dark. In order to overwhelm the changes for brightness, the thresholding is utilized that utilizes different values of thresholds for each pixel in the image. The thresholding of image offers robustness with respect to the changes in the illumination. The merits of the thresholding are that the method is simple, upfront, and result is assumed to be same, if the steps taken for the comparison are different.



### ***3.2 Proposed DeepSegNet Model for Extracting Lesions of the Liver from CT Image***

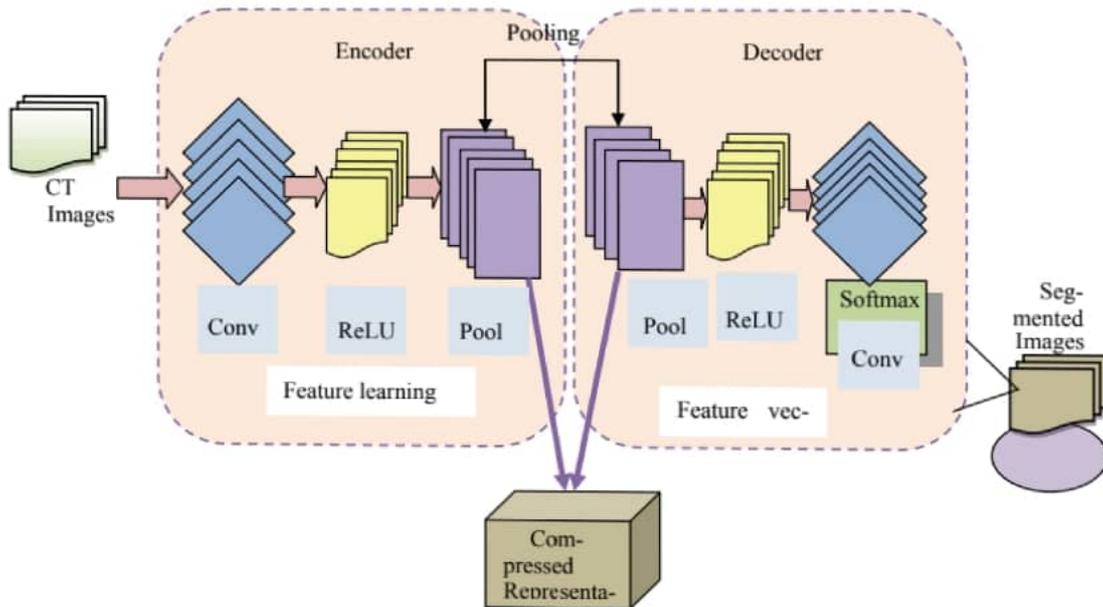
Liver lesion detection is employed for segmenting the liver to detect the unhealthy tissues for diagnosing hepatic diseases and access the medical practitioner for earlier treatment. The segmentation of liver and lesion using CT images helps the oncologists to precisely diagnose liver cancer to spot the presence of lesion. The DeepSegNet [17] model is employed for segmenting the liver lesions to detect the existence of lesion from the CT image. The DeepSegNet is an encoder-decoder network that contains a hierarchy of decoder each linking to a specific encoder. The DeepSegNet is an architecture used for performing pixel-wise semantic segmentation. The DeepSegNet is efficient with respect to computation time and memory and the DeepSegNet is flexible to implement. This section shows the DeepSegNet employed for the classification to detect the liver lesion from the CT images. The training of the DeepSegNet model is performed with proposed Adaptive Adam, wherein Adam algorithm [16] is modified using the self-adaptive concept to enhance the convergence and optimization behavior. The architecture of DeepSegNet model and the proposed Adaptive Adam algorithm is illustrated in the subsections.

#### **3.2.1 Architecture of DeepSegNet Model**

DeepSegNet is new segmentation technique, this section explains, segmenting objects by means of DeepSegNet. The CT images are subjected to the DeepSegNet [17] for the liver lesion detection. In DeepSegNet, the decision is taken for each pixel contained in the image. Semantic segmentation is defined as a method, which can understand image at its pixel level. Moreover, the model classifies each pixel according to the pre-determined class. DeepSegNet consists of decoder and encoder network and classification layer. The structural design of DeepSegNet model is demonstrated in Fig. 2.

Here, the encoder network contains convolutional layers for performing the liver lesion classification. Thus, the training process is initiated from the weights trained for classification using CT images. Each layer of encoder consists of a equivalent decoder layer for the reconstruction process. The output generated by the decoder is given to the multi-class soft-max classifier for generating the probabilities of class considering each pixel. Encoder performs convolution by means of a filter bank and generates feature maps. Then, an element-wise Rectified Linear Non-Linearity (ReLU) is applied and the resulting output is sub-sampled. ReLU is used for ensuring effectiveness, simplicity, and ReLU layers work faster while dealing with large networks. Moreover, POOL layers reduce the complication and there is no weight/bias for training rather it process the CT input images in combining the local regions in the filter. Then, the suitable decoder is employed for upsampling feature maps using the learned max-pooling indices from the corresponding encoder feature maps. Then, the feature maps are convoluted using a filter bank for generating dense feature maps.





**Fig. 2** Architecture of DeepSegNet model

The output produced by the soft-max classifier is  $K$ , where  $K$  indicates the count of classes. Thus, the DeepSegNet is responsible for generating the segments for liver lesion classification. Thus, the liver lesions are determined using the DeepSegNet module.

The segments are generated using the proposed DeepSegNet model, which is given as,

$$S^g = \{S_1^g, S_2^g, \dots, S_k^g, \dots, S_p^g\} \quad (2)$$

where  $S_k^g$  specifies the  $k$ th segment of the  $g$ th image, and ' $p$ ' refers the total number of the segments obtained from the  $g$ th image.

### 3.2.2 Proposed Adaptive Adam Algorithm for Training DeepSegNet

The proposed Adaptive Adam is utilized for training the DeepSegNet model to extract the lesion regions. In addition, the proposed Adaptive Adam is designed by integrating the merits of Adam optimization algorithm [16] along with the self-adaptive concepts. Adam [16] is the first-order stochastic gradient-based optimization that well-suits for the objective function that varies with respect to the parameters. The hitches associated with the non-stationary objectives and issues in the presence of the noisy gradients are handled effectively. This algorithm utilizes minimum memory by improving computational efficiency, the hitches associated non-stationary objectives and issues in the presence of noisy gradients are handled efficiently. Additionally, Adam witnesses the following advantages: the magnitudes of the updated parameters are invariant with respect to the rescaling of the gradient, and the step-sizes

are approximated using a hyper-parameter, which works effectively using sparse gradients and non-stationary objectives. In addition, Adam is effective for step size annealing. To obtain global optimal solutions, the Adam algorithm incorporates self-adaptive concept. The self-adaptive parameter minimizes the impacts of conventional parameters by balances the efficiency and accuracy for segmenting the liver lesions. Thus, the accuracy and the average time of the method becomes faster and higher. Generally, the adaptive parameter is utilized for making the method highly efficient and precise for solving optimization issues. Thus, the Adam optimization incorporates adaptive parameter for obtaining global optimal solution while classifying liver lesions. Moreover, the propose Adaptive Adam assists to jump out from local optimal and provides a trade-off between local and global optimization strategies. The steps of proposed Adaptive Adam are illustrated in this subsection.

### ***Step 1: Initialization***

Initialization of bias corrections is the first step, wherein  $\hat{q}_l$  is the bias corrected of first moment estimate and  $\hat{m}_l$  indicates the corrected bias of second moment estimate.

### ***Step 2: Evaluation of the fitness function***

Fitness of bias is calculated to choose optimal weights for training DeepSegNet model, fitness function is treated as error function which results global optimum solution. The function is a minimization function and it is given by,

$$J = \frac{1}{r} \sum_{k=1}^r (H_k - H_k^*)^2 \quad (3)$$

where  $r$  represents the total image samples,  $H_k$  referees output produced by DeepSegNet classifier,  $H_k^*$  indicates ground truth value.

### ***Step 3: Determination of updated bias***

Adam algorithm is employed for improving the optimization and convergence behavior, which produces smoother distinction with better computational efficiency at minimal memory utilization. According to the Adam [16], the bias is given as,

$$\theta_l = \theta_{l-1} - \frac{\alpha \hat{q}_l}{\sqrt{\hat{m}_l + \varepsilon}} \quad (4)$$

where  $\alpha$  is the step size,  $\hat{q}_l$  is the bias corrected,  $\hat{m}_l$  indicates the bias corrected second moment estimate,  $\varepsilon$  specifies the constant,  $\theta_{l-1}$  indicates the parameter at previous time instant ( $l - 1$ ). The corrected bias of first-order moment is formulated as,

$$\hat{q}_l = \frac{q_l}{(1 - \eta_1^l)} \quad (5)$$

$$\hat{q}_l = \eta_1 q_{l-1} + (1 - \eta_1) G_l^1 \quad (6)$$



The corrected bias of second-order moment is expressed as,

$$\hat{m}_l = \frac{m_l}{(1 - \eta_2^l)} \quad (7)$$

$$\hat{m}_l = \eta_2 m_{l-1} + (1 - \eta_2) G_l^2 \quad (8)$$

where,

$$G_l = \nabla_{\theta} \text{loss}(\theta_{l-1}) \quad (9)$$

While update, algorithm is made self-adaptive, by adjusting the step size without any user intervention. The standard parameter update equation of the Adam optimization is modified using the adaptive parameter for which  $\alpha$  is considered. Here, the  $\alpha$  of the Adam optimization algorithm is made self-adaptive and is formulated as,

$$\alpha = \left( 1 + \frac{(1 - n)}{1 + n_{\max}} \right) \quad (10)$$

where  $n$  is current iteration, and  $n_{\max}$  indicates the maximum iteration.

#### ***Step 4: Stopping criterion***

Optimal weights are developed in and reiterative way until final iterations is attained.

## **4 Results and Discussion**

The results of implemented Adaptive Adam algorithm devised for the lesion detection is illustrated. The effectiveness of the Adaptive Adam algorithm is estimated by varying the training data percentages with respect to accuracy, sensitivity, and specificity parameters.

### ***4.1 Experimental Setup***

The implementation is done using MathWorks MATLAB tool on Windows platform, with Titan-Nvidia GPU hardware.

## 4.2 Dataset Description

The DeepLesion dataset [18] is created in November 27, 2020, by National Institutes of Health—Clinical Center and donated by Ke Yan. The dataset comprised of certain attributes like patient\_index, study\_index, series\_index, and slice\_index. The DeepLesion dataset was collected on the basis of radiologists' annotations named as 'bookmarks.' The dataset accumulated the key slices, which comprise of the bookmarks and 60 mm contexts with extra slices above and below the key slice for enabling usage of the 3-D information.

## 4.3 Evaluation Metrics

The performance of the implementation is computed by means of three parameters accuracy, sensitivity, and measures.

- (a) **Accuracy:** Accuracy is one of the most significance parameter in classification of objects, this is the degree of familiarity of assessed value with respect to it unique value and accuracy is represented as,

$$A = \frac{(TP + TN)}{(TP + FP + FN + TN)} \quad (11)$$

where TP is true positive, TN is true negative, FP and FN denotes false positive and indicates false negative.

- (b) **Sensitivity:** Represents as ratio of the positives that are recognized appropriately.

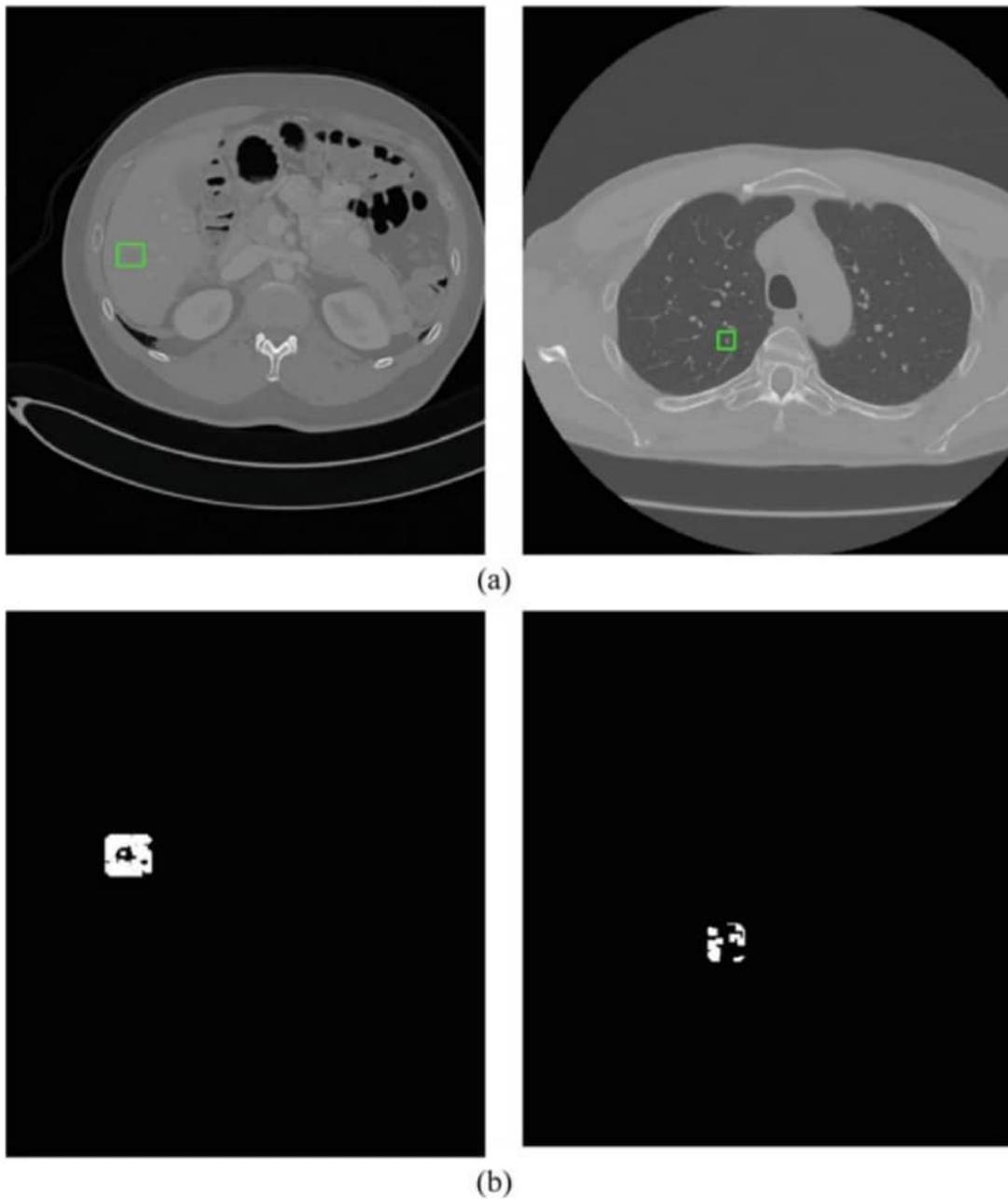
$$TPR = \frac{TP}{(TP + FN)} \quad (12)$$

- (c) **Specificity:** The specificity is utilized to produce a result which indicates that a given condition is present when it is not.

$$FPR = \frac{FP}{(FP + TN)} \quad (13)$$

## 4.4 Experimental Results

The experimental results of liver lesion segmentation using proposed Adaptive Adam-based DeepSegNet model are illustrated in Fig. 3. Figure 3a portrays the input CT images of liver disease patient, and Fig. 3b portrays the segmented CT



**Fig. 3** Results of Adaptive Adam algorithm. **a** Input image, **b** segmented image

image for detecting the presence of liver lesions. The white indicates the detected lesions whereas the black depicts the non-lesion regions.

#### **4.5 Performance Analysis**

Implementation analysis of proposed algorithm is carried by changing the convolutional layers ranging from 2 to 10, showing in Fig. 3. Figure 3a indicates the analysis

based on accuracy, with 50% training data, the calculated values for different convolutional layer 2, 4, 6, 8, and 10 are 0.603, 0.688, 0.726, 0.747, and 0.771, respectively. When the training data increased to 90% corresponding accuracies increased drastically, with convolutional layer 2, 4, 6, 8, and 10 are 0.651, 0.733, 0.774, 0.796, and 0.822, respectively. Figure 3b indicates the analysis based on sensitivity, with 50% training data, the calculated values for different convolutional layer 2, 4, 6, 8, and 10 are 0.586, 0.668, 0.705, 0.726, and 0.749, respectively. When the training data increased to 90% corresponding accuracies increased drastically, with convolutional layer 2, 4, 6, 8, and 10 are 0.648, 0.730, 0.770, 0.793, and 0.818, respectively. Figure 3c indicates the analysis based on specificity, with 50% training data, the calculated values for different convolutional layer 2, 4, 6, 8, and 10 are 0.817, 0.714, 0.686, 0.589, and 0.573, respectively. When the training data increased to 90% corresponding accuracies increased drastically, with convolutional layer 2, 4, 6, 8, and 10 are 0.891, 0.735, 0.705, 0.598, and 0.584, respectively.

## 4.6 Comparative Methods

Implemented Adaptive Adam DeepSegNet is compared with Fuzzy-c-means (FCM) [19], Adaptive threshold [20] with parameters accuracy, specificity, and sensitivity is elaborated further.

### 4.6.1 Comparative Analysis

Implementation evaluation of proposed Adaptive Adam DeepSegNet algorithm is carried using accuracy, sensitivity, and specificity metrics, represented in Fig. 4. We have observed when the training data dimension is large; we get better accuracy for classification. Figure 5a indicates the analysis based on accuracy parameter with 50% training data, obtained results of FCM, Adaptive threshold, and proposed Adaptive Adam DeepSegNet are 0.671, 0.819, and 0.797, respectively. When training data dimension is increased to 90%, corresponding accuracy are 0.81, 0.831, and 0.846 respectively. Figure 5b represents analysis based on sensitivity parameter with 50% training data; obtained results of FCM, Adaptive threshold, and proposed Adaptive Adam DeepSegNet are 0.672, 0.831, and 0.850 respectively. When training data dimension is increased to 90%, corresponding accuracy are 0.839, 0.842 and 0.881 respectively. Figure 5c represents analysis based on specificity parameter with 50% training data, obtained results of FCM, Adaptive threshold, and proposed Adaptive Adam DeepSegNet are 0.654, 0.600, and 0.676 respectively. When training data dimension is increased to 90%, corresponding accuracy are 0.800, 0.726, and 0.828 respectively.



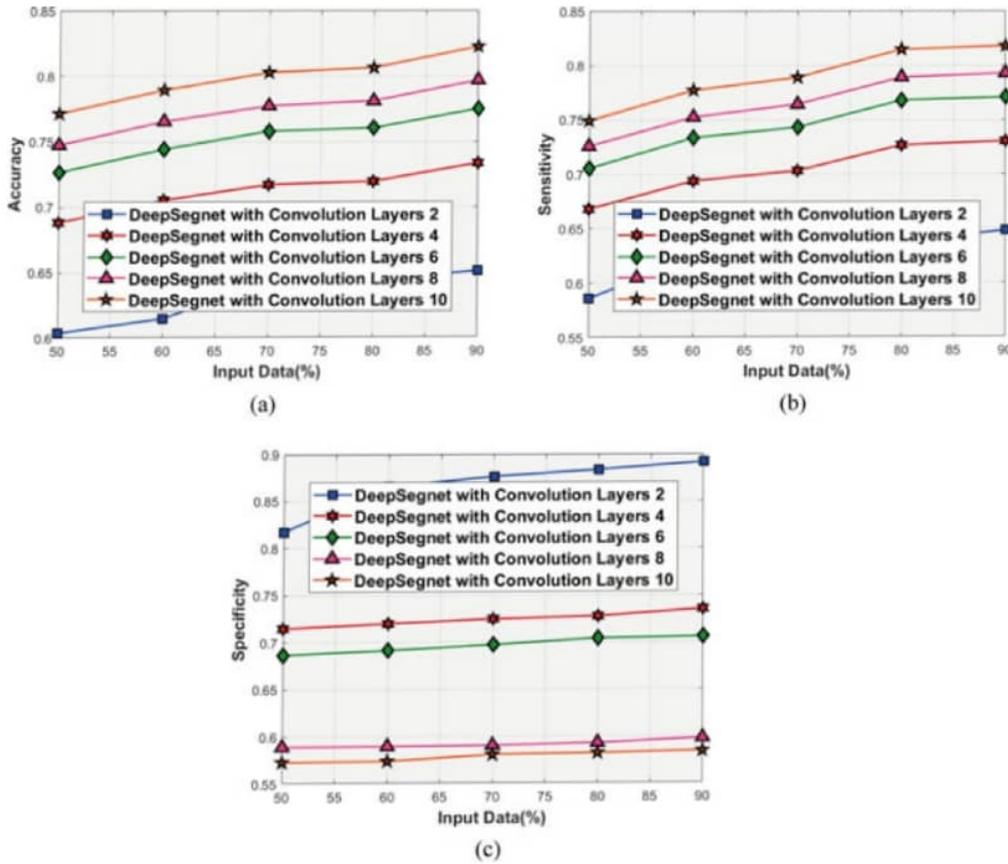
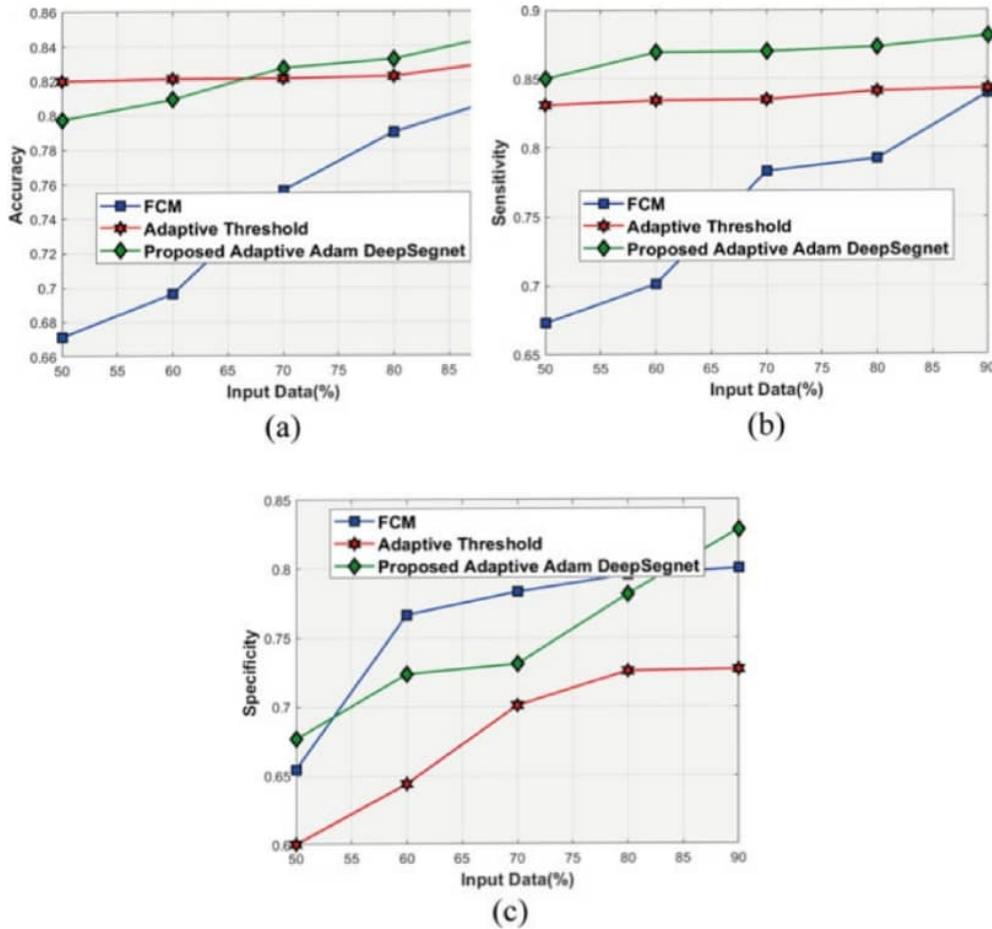


Fig. 4 Performance analysis of proposed DeepSegNet based on convolution layers with **a** accuracy, **b** sensitivity, **c** specificity

### 4.7 Comparative Discussion

Table 1 describes the comparative analysis of proposed Adaptive Adam DeepSegNet model with the available methods like FCM, Adaptive threshold. The performance analysis is carried out by the training data dimensions of 90%, with classification assessing parameters such as accuracy, sensitivity, and specificity measures matrices. The maximal performance is attained with accuracy value of proposed Adaptive Adam DeepSegNet as 0.846, whereas the accuracy values of available FCM, Adaptive threshold as 0.81, and 0.831, respectively. Similarly, for 90% training data, the sensitivity values calculated by proposed DeepSegNet as 0.881, whereas the sensitivity values of existing FCM, Adaptive threshold as 0.839, and 0.842, respectively. Similarly, for 90% training data, the specificity values computed by proposed DeepSegNet as 0.828, whereas the specificity values of existing FCM, Adaptive threshold as 0.800, and 0.726, respectively.





**Fig. 5** Analysis of methods with training data percentage with **a** accuracy, **b** sensitivity, **c** specificity

**Table 1** Comparative discussion

Metrics	FCM	Adaptive threshold	Proposed Adaptive Adam DeepSegNet
Accuracy	0.81	0.831	0.846
Sensitivity	0.839	0.842	0.881
Specificity	0.800	0.726	0.828

## 5 Conclusion

This paper proposes an effective optimization strategy for extracting the stage of the liver, vessel extraction, and classification of the liver segments for which the CT images is utilized. In the classification module, the lesion detection and classification is done, which is the goal of this paper. The liver with tumors is segmented through including the tumors to the extracted liver based on a strategy that work on the deviation of the intensity variations of the image with respect to the tumor and tumor

regions. Once the liver and vessel extraction are done, lesion detection and classification are progressed for which the DeepSegNet model is utilized. Here, the training of the DeepSegNet classifier is done by proposed Adaptive Adam algorithm. The proposed Adaptive Adam is designed by making the Adam algorithm self-adaptive. In this strategy, the probability for lesion or non-lesion is identified effectively. The performance of the proposed Adaptive Adam is superior to the existing methods with maximal accuracy value of 0.846, sensitivity value of 0.881, and specificity value of 0.828, respectively.

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the minimum effective volume of 0.5% ropivacaine required for surgical anesthesia. The minimum effective volume estimated was 15 mL of 0.5% ropivacaine. This 15 mL of 0.5% ropivacaine was found to be sufficient for adequate anesthesia for upper limb surgeries below mid humerus. Saric et al. studied the minimum effective volume of 50:50 mixture of 0.5% levobupivacaine and 2% lidocaine in elderly and middle-aged patients and concluded minimum effective volume in elderly was 16.49 mL and in middle-aged was 44.52 mL.<sup>4</sup> Diaphragmatic paralysis was a major concern in our study. This complication is because of the cephalad spread of LA and the involvement of the phrenic nerve. We assessed the diaphragmatic excursion with ultrasound in M mode preoperatively on both sides, after 30 minutes of block performance, postoperative after 6 hours of the block. Percentage of diaphragmatic paralysis decreases by decreasing volume of drug in successive patients. 17 and 15 mL of 0.5% ropivacaine were found to be safer as there was partial loss of diaphragmatic movement after 30 minutes of the block but it was not significant. Renes et al. did a study on ultrasound-guided supraclavicular brachial plexus block, using 20 mL of 0.75% ropivacaine, and found that none of the patients developed hemidiaphragmatic paresis and reduction in lung function (FEV1, FVC, PEFr).<sup>5</sup> In our study, we also assessed the diaphragmatic excursion through a portable bedside spirometer. We measured FEV1, FVC, and PEFr preoperatively as a baseline after 30 minutes of the block and 6 hours post block and compared preop values with 30 minutes after block, 30 minutes after block with 6 hours post block within groups. Also, we compared different volumes of 0.5% ropivacaine. Based on our study observations was that with higher volumes there was a decrease in pulmonary function after 30 minutes of the block. The mean difference seen was more in higher volumes than the lower volumes. **Conclusion:** We concluded, on decreasing volume of 0.5% ropivacaine, the incidence of diaphragmatic paralysis decreases significantly, and no compromise on the quality of the block.

### 3. Comparison of the Effect of Dexmedetomidine vs Fentanyl Infusion on Attenuating the Hemodynamic Responses, Bispectral Index (BIS) Changes and Cerebral Perfusion Pressure to Skull Pin Head Holder Application during Craniotomy. (Conference Abstract ID: 185)

*Shivangi Saxena, Parul Jindal, Parul Jindal*  
Himalayan Institute of Medical Sciences, Uttarakhand, India  
DOI: 10.5005/jp-journals-10071-23711.156

**Introduction:** Rigid head immobilization before craniotomy is a pivotal element of neurosurgery. As microscopic neurosurgery requires operating with smaller incisions as well as restricted surgical corridors, firm head immobilization is important to maintain the appropriate position of the head and thus, providing stabilization during the complex surgical procedures which are easily achieved by skull pin application.<sup>1</sup> Despite the adequate depth of anesthesia, insertion of skull pin for the stability of head during elective craniotomies, along with skin incision and intubation may prove to be a prominent noxious stimulus characterized by an acute sympathetic stimulation, leading to hemodynamic instability.<sup>2</sup> These noxious stimuli can lead to a sympathetic response in turn tachycardia and hypertension which may further disrupt cerebral autoregulation. **Objectives:** To compare the effect of dexmedetomidine and

fentanyl in attenuating the hemodynamic responses, BIS and cerebral perfusion pressure changes to pin placement during elective craniotomies. **Materials and methods:** Sixty patients undergoing elective craniotomy with skull pin placement were randomly categorized into two equal groups. Group I received IV dexmedetomidine 1 µg/kg over 10 minutes and group II received IV fentanyl 1 µg/kg over 10 minutes before pin insertion. Outcome variables like heart rate, blood pressure, SpO<sub>2</sub>, EtCO<sub>2</sub>, central venous pressure, cerebral perfusion pressure, condition of the brain, and the adverse side effects of the drugs were compared in both the groups at different time intervals pre, post, and during pin insertion, i.e., B0 (baseline value), I0: At the initiation of IV drug infusion of dexmedetomidine or fentanyl. I2, I4, I6, I8, I10: 2, 4, 6, 8, and 10 minutes during IV drug infusion. T0: At the completion of pin insertion. T30, T60, T90, T120, T150, T180, T300, T600, and T900: 30, 60, 90, 120, 150, 180, 300, 600, and 900 seconds, respectively, after pin insertion. **Results:** The demographic data was comparable between both the groups. No significant change in heart rate, cerebral perfusion pressure, BIS among both the groups at all the time intervals. Systolic, Diastolic, mean blood pressure and central venous pressure was significantly increased in the fentanyl as compared to the dexmedetomidine group after the pin insertion ( $p < 0.05$ ). Surgeons reported satisfactory brain condition during surgery in the dexmedetomidine group. **Discussions:** The application of skull pin head holder application used in craniotomies for rigid immobilization of the head during the procedure produces a brief, intense hemodynamic response despite an adequate depth of anesthesia, which can be deleterious to the patient as it can even lead to changes in the cerebral perfusion changes and its sequelae, these stress response can be blunted using various pharmacological agents in addition to the local infiltration with local anesthetics.<sup>3,4</sup> Based on our results from the study, we can emphasize that even though both the agents have the potential to attenuate this stress response, intravenous dexmedetomidine infusion in a dose of 1 µg/kg over 10 minutes just before the pin application has better hemodynamic stability than intravenous fentanyl 1 µg/kg over 10 minutes. Both the agents lead to comparable changes in the BIS values. Thus, this study serves as a double edge sword-albeit in a good way — by not only substantiating the intraoperative hemodynamic stability for the anesthesiologist but also by aiding in providing a good surgical field for the neurosurgeon. **Conclusion:** Based on the results of our study, we suggest IV dexmedetomidine a dose of 1 µg/kg infusion over 10 minutes is a better attenuating agent than IV fentanyl 1 mg/kg over 10 minutes for blunting the deleterious hemodynamic response to the skull pin placement.

### 4. CMAC Videolaryngoscopy vs Direct Laryngoscopy: Comparing the Mouth-to-Nose Distance between the Patient and Laryngoscopist. (Conference Abstract ID: 179)

*Surabhi Gupta, Rajesh S Mane*  
Jawaharlal Nehru Medical College, India  
DOI: 10.5005/jp-journals-10071-23711.157

**Introduction:** Tracheal intubation is a high-risk procedure for the transmission of the virus during this COVID-19 pandemic. These patients may require emergency tracheal intubation and mechanical ventilation to help recovery from illness. These patients may also present for various emergency/elective surgeries that

## ABSTRACTS CRITICARE – IJCCM2021

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may require administration of general anesthesia and tracheal intubation. Procedures involving securing and manipulation of the airway may put the laryngoscopist at great risk of exposure to the virally contaminated aerosols. Increasing the distance of the laryngoscopists face from the patient and expelled droplets reduces the direct exposure to the mucous membrane. The study aimed to determine the mouth-to-nose distance between the patient and laryngoscopist, the angle formed between the two oral cavities, and the ease of intubation. **Materials and methods:** The study was approved by Institutional Ethical Committee. A total of 104 ASA I and II patients undergoing surgery under general anesthesia were enrolled and consent was taken. They were randomly divided into two groups — one group undergoing tracheal intubation with CMAC videolaryngoscope and another group with Macintosh direct laryngoscope. The intubation procedure was filmed and the mouth-to-nose distance formed between the patient and the laryngoscopist was calculated. The angle formed between the two oral cavities were assessed using a mobile phone application. The ease of intubation was determined using a standard scoring system. Descriptive statistics reported using mean, median, and standard deviation for continuous variables and compared using Student's paired *t*-test. Categorical variables were reported using numbers and percentages and compared using the Chi-square test. **Results:** The mean mouth-to-nose distance using CMAC VL was 45.5673 and using DL was 27.6731. This was statistically significant using a paired *t*-test ( $p < 0.05$ ). The mean angle formed by the oral cavities was 49.0577 and 34.0769 with CMAC VL and DL respectively. The ease of intubation was also scored more with CMAC VL compared to DL. **Discussions:** The greatest viral load of SARS-CoV-2 is most commonly found in the sputum and upper airway secretions. Droplet spread and direct contact with the respiratory secretions is the leading mode of transmission. The aerosol spread is another mode of transmission and these particles can remain suspended in the air for longer periods. Hence, procedures, such as, endotracheal intubation, connection, and disconnection from a ventilator circuit, extubation, bronchoscopy, tracheal suctioning can cause aerosolization of the viral particles. The process of handling infected patients and performing these procedures can increase the risk of infection to the laryngoscopist. This study showed that the use of a videolaryngoscopy significantly extends the mouth-to-nose distance between the patient to the laryngoscopist compared to direct laryngoscopy and places the laryngoscopist's face above the direct line of sight to the pharynx, thus minimizing the risk of direct exposure to virally contaminated particles. It may also help reduce the time taken for intubation, thus avoiding a longer exposure to the laryngoscopist. **Conclusion:** VL significantly increases the mouth-to-nose distance between the patient and the laryngoscopist compared to DL and increases the angle formed between the laryngoscopist's face and the patients' oral cavity. Intubation is easier with VL compared to DL. Hence, this study signifies the use of a videolaryngoscope to minimize the risk of exposure of the infected viral particles to the laryngoscopist.





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# CERTIFICATE

OF PARTICIPATION

This is to certify that

*DR CHAITANYA KAMAT*

has presented a research paper in **ISA OM (One Minute) Award** category, titled

*EFFECTIVENESS OF A NEW ASSESSMENT TOOL, DIRECT OBSERVATION OF PROCEDURAL SKILLS (DOPS) AMONG ANESTHESIOLOGY POSTGRADUATE STUDENTS*

**Dr. Muralidhar Joshi**  
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Scientific Chairperson

**Dr. Heena Chhanwal**  
Scientific Secretary

the leak site was sutured at the skin level after 24h of persistent leakage. The patient was discharged home the next day completely asymptomatic. She had the suture removed 3 days later, without any recurrence of the leakage. She didn't report any symptoms during a two-month follow-up.

**Conclusions** This report presents another case of a CSF fistula after a neuraxial block and highlights the success of a conservative approach that avoided not only a blood patch, but also a surgical procedure, in an asymptomatic young woman.

## 12 FLUOROSCOPIC APPROACH TO NEURAXIAL ANAESTHESIA IN A PATIENT OF KYPHOSCOLIOSIS

S Gupta\*, R Mane. *Jawaharlal Nehru Medical College, KAHER, Belagavi, India*

10.1136/rapm-2021-ESRA.12

**Background and Aims** Kyphoscoliosis is a complex deformity of the spine resulting in lateral curvature and rotation of the vertebrae and a deformity of the rib cage. There is usually secondary involvement of the cardio-respiratory and neurologic systems.

Neuraxial block is routinely performed without the aid of imaging modalities and approached blindly for placement of epidural catheter. Kyphoscoliosis poses a remarkable challenge to administration of neuraxial anaesthesia and may result in multiple pricks and complications such as nerve injury and hematoma formation.

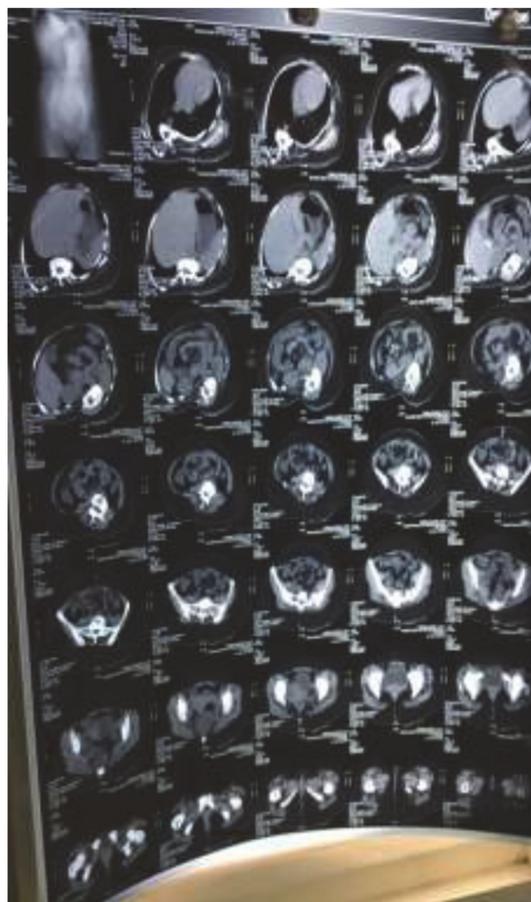
We aimed to assess the feasibility and success of using fluoroscopy guidance for administration of epidural anaesthesia in a case of severe kyphoscoliosis.

**Methods** A 18-year-old female 132 cm tall, with severe kyphoscoliosis was posted for Cholecystectomy. She had severe dextrorotatory-thoracic scoliosis [Cobb angle- 62°] and a compensatory levorotatory-lumbar curve [45°]. Respiratory examination showed restricted breathing with B/L wheeze. PFT showed a restrictive pattern. Open cholecystectomy was planned under Epidural Anaesthesia. Serial MRI films were assessed to determine the direction of placement of the epidural needle which was enhanced with the use of fluoroscopy guidance during the intraoperative period.

**Results** Intraoperative period assessed in terms of patient compliance and adequate surgical anaesthesia was satisfactory.



Abstract 12 Figure 1



Abstract 12 Figure 2



Abstract 12 Figure 3

Intraoperative use of analgesics was significantly reduced. Epidural analgesia was continued for 2 days postoperatively.  
**Conclusions** Despite various challenges, this case of severe kyphoscoliosis was successfully managed with fluoroscopy-guided epidural anaesthesia. Fluoroscopy is a well-established imaging modality and its knowledge adds to the Anaesthesiologist armamentarium and offers an opportunity to provide neuraxial anaesthesia in patients with anticipated difficulty.

**13 CONTINUOUS ERECTOR SPINAE PLANE BLOCK AS MULTIMODAL ANALGESIA AND INTRAOPERATIVE HEMODYNAMIC STABILITY IN OPEN NEPHRECTOMY FOR LIVING DONOR KIDNEY TRANSPLANT**

R Rahmi\*, RB Sukmono. *Universitas Indonesia, Jakarta, Indonesia*

10.1136/rapm-2021-ESRA.13

**Background and Aims** Open nephrectomy is associated with moderate to severe postoperative pain.<sup>1</sup> Erector spinae plane block (ESPB) provides effective analgesia for various surgical procedure but only a few reports on ESPB used for pain control in open nephrectomy.<sup>2</sup> We reported two cases of

continuous ESPB as multimodal analgesia and intraoperative hemodynamic stability in open nephrectomy for living donor kidney transplant.

**Methods** Two adult patients underwent open nephrectomy for living donor renal transplant. ESPB was performed before general anesthesia with ultrasound guided using high frequency linear probe at level of T8-T9. After transversus process and erector spinae muscle were identified, hydro dissection with 2 ml of normal saline was used to confirm the correct needle tip position. 18-gauge epidural catheter then inserted into the plane between erector spinae and transverse process. 20 ml local anesthetic 0,25% levobupivacaine was injected and spread of local anesthetic under erector spinae muscle was seen by ultrasound. For postoperative pain control, patients were administered 10 ml levobupivacaine 0,125% via catheter at the end of surgery, continuous levobupivacaine 0,125% 6



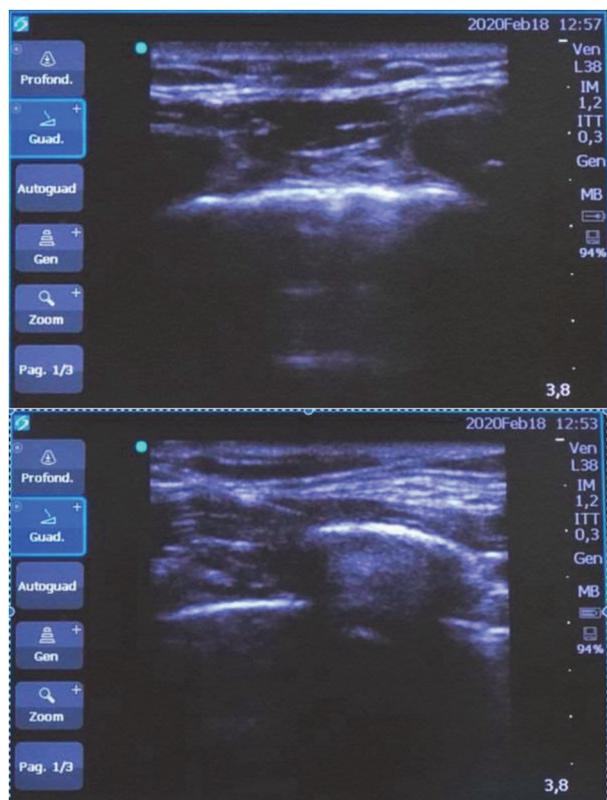
Abstract 13 Figure 1



Abstract 13 Figure 2



Abstract 13 Figure 3



Abstract 153 Figure 1

**Conclusions** In our experience we perform ultrasound-guided interfascial plane blocks with high profile of efficacy and safety in s-ICD placement also in sick patients.

**154 SELF-COILING CATHETER FOR CONTINUOUS INTERSCALENE BRACHIAL PLEXUS BLOCK AFTER SHOULDER SURGERY: THE INCIDENCE OF CATHETER TIP MIGRATION AND EFFECT ON ANALGESIA**

Y Aoyama\*, S Sakura, K Gunji, S Sakakibara, H Yamamoto, Y Saito. *Shimane University, Izumo, Japan*

10.1136/rapm-2021-ESRA.154

**Background and Aims** Continuous interscalene brachial plexus block (CISB) provides analgesia after shoulder surgery. However, when catheter tip migration occurs, pain relief is degraded. We previously reported that catheter tip migration occurred at a rate of 44.8% during CISB for 48 hours regardless of catheter insertion length change when a conventional catheter was used and this migration decreased the analgesic effects. Reducing the migration rate is required to improve postoperative analgesia. Using a catheter of a different shape, like a self-coiling catheter, may help decrease tip migration. We therefore prospectively observed the catheter tip position of self-coiling catheters using ultrasound and studied its analgesic effect during CISB after shoulder surgery.

**Methods** After receiving IRB approval and informed consent, we studied 19 consecutive patients undergoing shoulder surgery who received the posterior in-plane approach to CISB under ultrasound-guidance. A self-coiling catheter was inserted for postoperative infusion for 48 hours. Using ultrasound, catheter tip location was assessed immediately after surgery

**The Shimane University Institutional Committee on Ethics  
Evaluation Form Regarding the Research Proposal**

Study number: 4301  
Date: February 5, 2020

Applicant (Principal Investigator): **Shinichi Sakura**

Research Title: **Migration rate of the tip position of self-coiling catheter inserted for continuous interscalene brachial plexus block: a prospective, observational study**

Your research proposal submitted on November 26, 2019, has been reviewed by the Shimane University Institutional Committee on Ethics. The result is as follows:

Result:

- Approved  
 Unapproved  
 Put on hold  
 Not applicable

Administrator of the personal information concerned with this research proposal

Name: **Shinichi Sakura**

Official Title: **Professor**

Affiliation: **Operation Division**

Date: February 5, 2020

Authorized Signature

Dean of Faculty of Medicine, Shimane University  
Kazumichi Onigata M.D., Ph.D.

Abstract 154 Figure 1

and at 24 and 48 hours after block procedure. Pain scores, analgesic requirements, sensory and motor blockade were also assessed.

**Results** Under ultrasound, a catheter tip was found to be migrated in 2 patients (10.5%) including one patient with no catheter-at-skin change during CISB. Pain was well controlled for 48 hours.

**Conclusions** Catheter tip migration can occur even with a self-coiling catheter. However, since the incidence rate was almost one quarter of that with a conventional catheter, a comparative randomized study to confirm the present findings is warranted.

**155 SUPERIOR TRUNK BLOCK: AN UNORTHODOX ALTERNATIVE TO INTERSCALENE BLOCK FOR PROXIMAL HUMERUS SURGERIES IN PATIENTS WITH SIGNIFICANT PULMONARY DISEASE**

R Darshan\*, RS Mane, MC Patil. *Kaher's Jawaharlal Nehru Medical College, Belagavi, India*

10.1136/rapm-2021-ESRA.155

**Background and Aims** Proximal shoulder surgery in patients with compromised pulmonary function stipulates anaesthesiologists to look for an alternative to interscalene block. Such aforementioned challenge pioneered the initiation of use of superior trunk block to utilise distinct advantage of phrenic nerve sparing, allowing the patients to execute normal

respiratory functions perioperatively. Superior trunk of brachial plexus visualised accurately through ultrasound, steers effortless performance and achieving acceptable block characteristics.

**Methods** Here we present a case series of 8 patients aged between 40 years to 80 years with significant restrictive, obstructive pulmonary disease and post-covid patients posted for proximal humerus surgeries. The block was performed under ultrasound guidance, 23G Quincke spinal needle, 1:1 local anaesthetic mixture of 2% Lignocaine+Adrenaline and 0.5% Bupivacaine with total volume injected being 15 ml. The outcomes measured were loss of shoulder abduction, numbness of shoulder and pain relief, numbness of arm and sonographic assessment of diaphragm movement, oxygen saturation perioperatively and closed-circuit measurement of tidal volume generated

**Results** 7 patients with superior trunk block achieved complete surgical anaesthesia of proximal shoulder. There was solitary use of Dexmedetomidine for patient with severe anxiety. 2 patients required oxygen supplementation throughout the intraoperative period extending to post-operative period as well. Sonographic assessment intraoperatively and post-operatively disclosed adequate diaphragmatic excursion in all patients. Post-operative pain scores revealed satisfactory pain relief.

**Conclusions** Effective surgical anaesthesia and analgesia can be delivered considerably with Superior trunk block for surgeries of proximal humerus in patients with compromised pulmonary function by sparing phrenic nerve and it is an appropriate substitute for interscalene block

156

#### EVALUATION OF THE PERIPHERAL NERVE STIMULATOR USAGE FOR A SUCCESSFUL COSTACLAVICULAR BRACHIAL PLEXUS BLOCK

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10.1136/rapm-2021-ESRA.156

**Background and Aims** Ultrasound (US) has become standardized during peripheral nerve block (PNB). Peripheral nerve stimulator (PNS) is combined with US to avoid intraneural injection (1). Monitoring opening injection pressure with a sensor could also show intraneural injection (2). Adding PNS to US guidance did not change block success rates for different types of PNBs (3,4). There is no study in the literature that evaluate effectiveness of adding PNS to US for a successful costoclavicular brachial plexus block (CCBPB). In this randomized prospective clinical study US and injection pressure monitor (IPM) guided CCBPB is compared with US, IPM and PNS guided CCBPB.

**Methods** 60 patients scheduled for orthopedic surgery below the elbow were enrolled in the study. Ultrasound and IPM guided group called USP and US, IPM and PNS guided group called USPN. In both groups 30 ml bupivacaine-lidocaine mixture was injected when injection pressure is less than 15 psi. In Group USPN, local anesthetic was injected after visualizing the disappearance of motor movement under 0.3 mA on PNS. Motor and sensorial block levels of the radial, ulnar, median and musculocutaneous nerves were measured. Block success rate, block performance time, number of needle passes and complication rates were compared.

**Results** Block success rate, number of needle passes and complications were similar (table 1). Block performance time was longer in group USPN (figure 1).

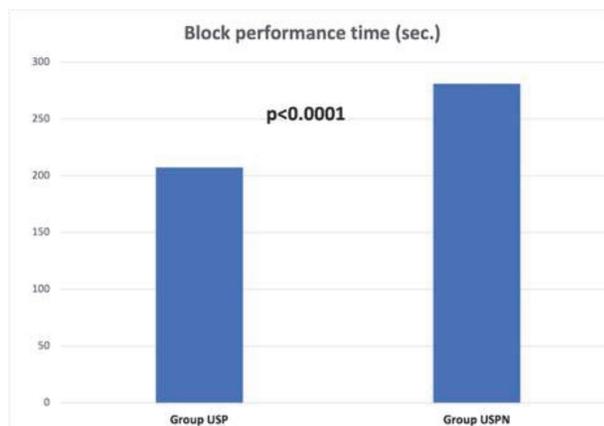
**Conclusions** Peripheral nerve stimulator is not necessary for a successful CCBPB. Using PNS increased block performance time significantly. Ultrasound and IPM are enough for a successful block with shorter procedure time in CCBPB.

Abstract 156 Table 1

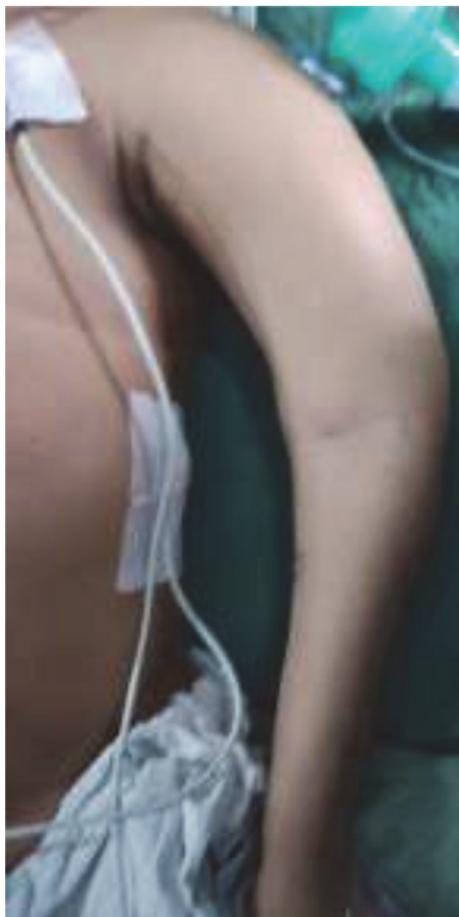
	Group USP(n=30)	Group USPN (n=30)	p-value
Block success rate (%)	90	96,7	0,612
Number of the needle passes	2,5	2,7	0,387
Complication rate (%)	6,6	10	0,628



Abstract 156 Figure 1



Abstract 156 Figure 2



Abstract 26 Figure 2



Abstract 26 Figure 3

**27 ANAESTHETIC MANAGEMENT IN PARTURIENT WITH COARCTATION OF AORTA, PATENT DUCTUS ARTERIOSUS AND ARNOLD CHIARI MALFORMATION FOR ELECTIVE CAESAREAN SECTION**

L Aishwarya\*, RS Mane, MC Patil. *Jawaharlal Nehru Medical College, KLE University, Belagavi, India*

10.1136/rapm-2021-ESRA.27

**Background and Aims** Coarctation of aorta represents 6%-8% of CHD with associated Patent ductus arteriosus. Arnold chiari malformation is characterized by prolapse of cerebellar tonsils below the foramen magnum causing compressive symptoms. The primary goal is to minimize the incidence of haemodynamic stressor response and brainstem herniation which is a possible risk with endotracheal intubation.

**Methods** A case of 24year G2P1L0 with 34weeks POG, a known case of ACM was diagnosed with COA and PDA. She was planned for elective caesarean due to uncontrolled upper limb hypertension. Examination revealed pansystolic murmur and Loud P2 with suzzman's sign positive. She had feeble femoral pulse with radiofemoral delay. Uppler limb BP : 190/100 mmhg and lowerlimb BP: 130/80 mmhg. 2DEcho revealed Large PDA with left to right shunt, dilated RA, RV. Severe COA with PPG 76 mmhg. Trivial TR with PPG 40 mmhg. No sensory and motor deficits noted. Graded epidural anaesthesia was administered.

**Results** Parturient with congenital anomalies has been successfully managed perioperatively with graded epidural doses and by providing adequate post-operative analgesia.

**Conclusions** Parturient with Coarctation of the aorta and Arnold chiari malformation presents with unique challenges to the anaesthetist and management must be tailored to avoid hemodynamic instability and associated risk of tonsillar herniation. The use of epidural anaesthesia in graded dose was successful in achieving this goal.

**28 LOCAL ANAESTHETIC SYSTEMIC TOXICITY AFTER AXILLARY BRACHIAL PLEXUS BLOCK IN AMBULATORY SURGERY – A CASE REPORT**

<sup>1</sup>GS Sousa\*, <sup>2</sup>M Oliveira, <sup>2</sup>P Esperança, <sup>3</sup>E Segura Grau. <sup>1</sup>*Centro Hospitalar Tondela-Viseu, Viseu, Portugal*; <sup>2</sup>*Centro Hospitalar Universitário São João, Porto, Portugal*; <sup>3</sup>*Anesthesiology, Centro Hospitalar Tondela-Viseu, Viseu, Portugal*

10.1136/rapm-2021-ESRA.28

**Background and Aims** Local anaesthetic systemic toxicity (LAST) is a rare but potentially fatal complication of regional anaesthesia. LAST affects two major systems, namely neurologic and cardiovascular<sup>1</sup>. The number of regional anaesthesia has been increasing and the risk of LAST, despite all the good practices, increases proportionally. Axillary brachial plexus block is reported as the most associated block to LAST events.<sup>2</sup>

We pretend to increase awareness to this rare but life-threatening entity.

**Methods** Case report and literature review.

**Results** A 55-years-old female patient, ASA II, was admitted for left hand ambulatory surgery. It was performed an ultrasound-guided axillary brachial plexus block. The left axillary artery and the branches of median, radial and cubital nerves were identified. Then 200 mg of mepivacaine and 37.5 mg of levobupivacaine were administered through an in-plane

previous history of difficult airway management with postponement of this procedure 3 days before. After patient's consent, we successfully managed the case with an ultrasound-guided IPB and a PIFB (figure 2), total local anaesthetic solution – 20 mL of mepivacaine 1,5% & ropivacaine 0,375% under light sedation. The procedure was uneventful, for patient and surgical team.

**Conclusions** IPB and PIFB successfully managed anaesthesia & analgesia of this case under light sedation, avoiding GA and management of a documented difficult airway patient. Latest evidence supports IPB as a good technique for BCS(2) and PIFB is a relatively novel block suited for inner quadrant breast surgery approach(3). RA has been a good alternative avoiding airway management on this documented difficult airway, provided excellent surgery conditions, pain relief and a high level of patient satisfaction.

Approval has been granted by the ethics committee

171

**PTERYGOPALATINE BLOCKADE IN THE ALGORITHM OF TREATMENT OF OPHTHALMIC COMPLICATIONS OF HERPES ZOSTER**

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10.1136/rapm-2021-ESRA.171

**Background and Aims** Ophthalmoplegia in herpes Zoster is quite rare. At the same time, we observed a case of relapse of herpes Zoster with the clinic of ptosis of the upper eyelid on the background of a pronounced pain syndrome without vesicular rashes as the primary clinical signs. Relief of pain syndrome against the background of antiviral therapy is one of the primary tasks. To evaluate the effectiveness of pterygopalatine blockade (PPB) in the algorithm of treatment of atypical ophthalmic herpes Zoster with severe pain syndrome and ophthalmoplegia.

**Methods** Patient 60 years old. Complaints about OS blepharoptosis, pain (VAS = 4). The edge of the OS eyelid is lowered to the upper edge of the pupil, the cornea is transparent, there are no signs of uveitis. The condition is regarded as ganglionitis n.opthalmicus of unknown etiology. The patient underwent PPB (4 mL ropivacaine 0.5%) for pain relief in herpetic ophthalmic neuralgia

**Results** 40 minutes after PPB, the pain was relieved, VAS = 0. 2 hours after PPB, the ptosis decreased. After 72 hours the patient had a draining herpetic rash on the skin in the projection of the III branch of the trigeminal nerve on the left. Further treatment of the patient was continued by an infectious disease specialist.

**Conclusions** The experience gained in the use of the PPB in the algorithm for the treatment of ophthalmic complications of herpes Zoster allowed us to achieve not only the relief of pain, but also to reduce the severity of the inflammatory reaction of extraocular muscles, ptosis.

172

**ULTRASOUND GUIDED COMBINED SCIATIC PLUS FEMORAL NERVE BLOCK IN HIGH RISK PATIENTS POSTED FOR LOWER LIMB SURGERIES**

N Adhyapak\*, R Mane, M Patil, R Kerur, P Apoorva, A Qadir Zeeshan. KAHER'S J N Medical College, Belagavi, India

10.1136/rapm-2021-ESRA.172

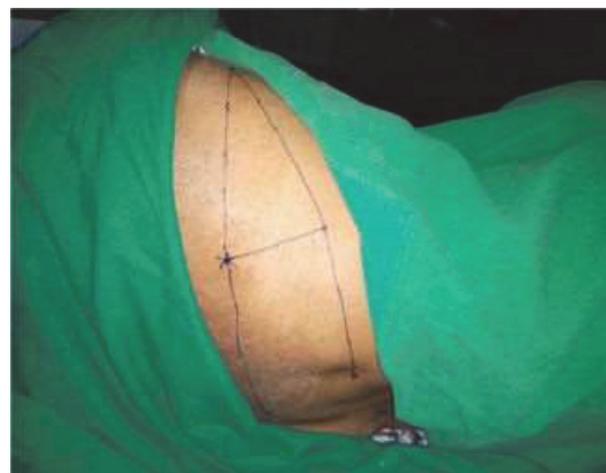
**Background and Aims** Regional Nerve Blocks are now the mainstay for high risk patients undergoing surgery where General, Spinal or Epidural Anaesthesia have poor outcome. Combined Sciatic and Femoral Nerve block given for lower limb surgeries like amputation, arthroplasty, ORIF in patients having multiple co-morbidities like Ishaemic Heart Disease (IHD), COPD, Uncontrolled DM and HTN. Ultrasound guided nerve blocks are effective, safe and have reduced incidence of neurological damage and Local Anaesthetic Systemic Toxicity (LAST).

**Methods** 5 patients undergoing lower limb surgery, in KLE's Dr. Prabhakar Kore Charitable Hospital and MRC were considered. Three of the patients had IHD with EF 40%. One had RV Dysfunction with IVC collapsibility <50%. Another had COPD and was in sepsis. A complete pre-anaesthetic evaluation was done after selecting appropriate patients. Under ultrasound guidance, with patient in sciatic and femoral nerve blocks were given with equal mixtures of 0.5% Bupivacaine + 2% Lignocaine + 2 ml of Soda Bicarbonate. Intra-operatively hemodynamics was maintained. Case 1 required rescue Epidural Anaesthesia. For case 3 i.v paracetamol was given for additional analgesia. In rest of the cases no additional analgesia/anaesthesia was needed.

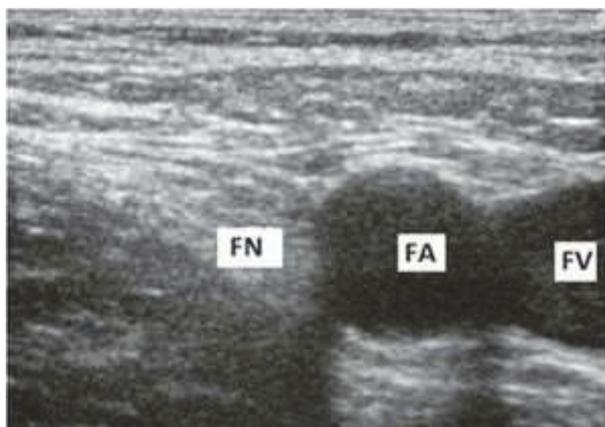
**Results**



Abstract 172 Figure 1



Abstract 172 Figure 2



Abstract 172 Figure 3

- **Conclusions** Combined Sciatic and Femoral Nerve block is an effective and viable alternative to either General, Spinal or Epidural Anaesthesia as it provides better hemodynamic stability and good post operative analgesia in high risk patients without resulting in any adverse incidents.

### 173 PERIPHERAL NERVE BLOCKS ALLOW HIP FRACTURE SURGICAL MANAGEMENT IN AN EXTREMELY FRAGILE PATIENT: NO PENG NO GAME

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10.1136/rapm-2021-ESRA.173

**Background and Aims** Hip fracture represents a frequent cause of disability in the elderly [1]. Early surgery (<48h) has been proven to be associated with lower risk of mortality and morbidity [2]. Regional anaesthesia seems to be the best option, but there is no consensus when a central block is not indicated [3]. We present a case of a multimorbidity patient under anticoagulant drug, underwent hip fracture surgical repair with peripheral nerve blocks.

**Methods** Female 84 y.o. Atrial fibrillation, PMK wearer, hypertension, renal failure, CODP, cerebrovascular disease, OSAS, confusion and psychomotor agitation.

Echocardiogram: severe systolic function reduction, estimated ejection fraction 23%.

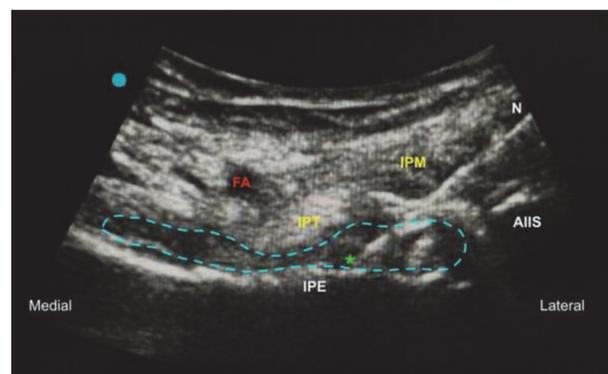
Right sub-capital hip fracture, candidates for hip endoprosthesis.

Anticoagulant therapy with apixaban with no data on last assumption; thromboelastogram showed augmented values, so a central block was not indicated. Patient's multimorbidity highly elevated the risk of general anaesthesia.

With patient consent, peripheral blocks and sedation were considered. Ultrasound guided Pericapsular Nerve Group Block (PENG) was performed (ropivacaine 0,5% 20 ml + dexamethasone 4 mg), to block femoral, obturator and accessory obturator nerves, which innervate the hip [4]. Lateral femoral cutaneous nerve was also blocked, to cover surgical incision. Moderate sedation was given, maintaining spontaneous breath.

**Results** Surgical procedure was carried out uneventfully and without pain, parameters were good and stable during and after surgery.

**Conclusions** Regional anaesthesia could be the key in fragile patients. Knowledge of anatomy and different techniques is



Abstract 173 Figure 1

FA=femoral artery; IPM=iliopsoas muscle; IPT=iliopsoas tendon; N=needle; IPE=iliopubic eminence; AIIS=anterior inferior iliac spine.

fundamental to tailor the anaesthetic plan on patient conditions and surgical approaches.

### 174 PERIOPERATIVE JOURNEY OF PATIENTS HAVING UPPER LIMB NERVE BLOCKS- A SERVICE EVALUATION AND QI PROJECT

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**Background and Aims** Regional anaesthesia (RA) improves postoperative analgesia and can contribute to a reduction in postoperative nausea and vomiting (PONV). RA can improve value of care by reducing length of stay and enhancing patient satisfaction<sup>1</sup>.

Regional nerve blocks are commonly performed for upper limb day case surgeries at our centre. We did a prospective patient survey on perioperative experience of upper limb surgery with nerve blocks.

**Methods** Patients who had regional nerve blocks for upper limb surgery were given proforma to fill after surgery with pre-stamped envelopes. We included 28 proformas returned from March to June 2019 for the survey.

**Results** All patients received anaesthetic information pre-surgery which included pre-assessment nurse (7/28), information leaflet (2/28) and both (19/28). One patient found information provided unsatisfactory. Quarter of (8/28) patients reported severe pain and PONV during first 24 hours and timings of first oral pain relief was variable with non-standardised analgesics on prescription.

Most of patients (92%) would prefer to have nerve block again.

**Conclusions** Results showed that post op pain prescription varied. Although most patients were satisfied with nerve block information but could be improved. We recommended to standardise post-operative discharge prescription. We suggested to produce patient video about the perioperative journey of nerve blocks for upper limb surgery which has been produced and will be implemented soon as delayed by pandemic.

Regular patient satisfaction surveys are needed for service evaluation and improvement.

## ABSTRACT

## Jens Andreassen Award

### 346 | Spontaneous re-eruption after severe intrusive luxation in primary teeth and following sequelae: A case report

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**Introduction:** Intrusive luxation is one of the most severe and frequent traumatic dental injuries during early childhood, which can cause sequelae in the injured tooth and disturbances in the permanent tooth germ.

**Case report:** A 1-year and seven months old boy is presented. The father reported that the child had suffered a trauma five days ago. Clinical examination revealed the absence of teeth 61 and 62 with no signs of alveolar fracture on palpation. A periapical radiograph of the region showed both teeth intruded into the alveolar bone. Treatment considered spontaneous re-eruption and monitoring. Six months later the teeth were completely erupted. However, at 21 months tooth 61 presented an abscess and the radiograph showed enlargement of the periodontal ligament space in both injured teeth; therefore, pulpectomy treatment was performed on both primary incisors. Two years and five months later, the teeth and surrounding tissues were clinically and radiographically asymptomatic, although mild discoloration was observed in tooth 61. The patient remains under observation.

**Discussion:** Intrusive luxation is a common injury in primary dentition. Most teeth that suffer this injury re-erupt spontaneously after a few weeks. Nonetheless, pulp necrosis is a frequent complication especially in severe cases. In this case root canal treatment was performed to preserve the injured teeth.

**Conclusion:** A therapeutic alternative in cases of severely intruded teeth is to allow spontaneous re-eruption, however, there is always the possibility of an unfavorable outcome. Consequently, monitoring and follow-up is essential to address possible sequelae as well as in permanent successors.

### 1745 | Avulsion and replantation of permanent central incisors in a 6-year-old boy: A case report

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**Introduction:** Traumatic injuries in young children are most common. Among them, maxillary central incisors are most commonly affected. Surface resorption, ankylosis, and/or inflammatory resorption are sequelae of replantation and pose challenges to the pediatric dentist. Delayed replantation of an avulsed tooth may result in rapid root resorption or, more frequently, dental ankylosis with subsequent bone substitution. This clinical case reports a dental trauma of a central incisor in a young boy characterized by tooth avulsion and its replantation.

**Case Report:** This clinical case reports a dental trauma of both central incisors (11 & 21) in a young boy (6) characterized by tooth avulsion and its immediate replantation. The tooth has been maintained in place for two years now.

**Discussion:** Avulsion is the most serious dental injury and may determine immediate or potential tooth loss as a consequence of root resorption. However, when possible, even a delayed replantation should be performed to maintain the crown of the traumatized tooth in place, thus preserving the space and partially the crest bone resorption. The development of ankylosis was demonstrated in the above clinical case that involved both maxillary central incisors. The characteristic percussion sound demonstrated by both the affected teeth verified the diagnosis of ankylosis within 6 months of the initial injury.

**Conclusion:** Early radiographic signs of ankylosis/replacement resorption were noted only late in the observation periods. Minimal evidence of infraocclusion was observed and the boy has yet to reach his pubertal growth period. It is anticipated that infraocclusion will become apparent and then it will be important to minimize any negative growth-related

## 1320 | Has the COVID-19 pandemic affected the incidence of paediatric intra-oral and dental trauma presenting through the emergency department?

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**Background:** The Oral and Maxillofacial Surgery team treat paediatric patients sustaining intra-oral and dental trauma. The COVID-19 pandemic resulted in fewer Emergency Department attendees; this audit aimed to identify whether the incidence, aetiology and management of intra-oral trauma varied as a consequence. It compares data collected in 2018 and 2020 at a district general hospital in South Wales.

**Methods:** Data was collected via clinical and operation notes, Myrddin and Welsh Clinical Portal from 2018 and 2020. This was recorded in an Excel spreadsheet and analysed.

**Results:** The number of paediatric patients treated was comparable in 2018 and 2020. The most common age of injury was 0-2 years in 2018 whilst in 2020 it was 3-4 years. 77.1% and 80.5% of injuries were caused by falls in 2018 and 2020 respectively. However, no sports injuries were reported in 2020. Interestingly, whilst no antibiotics were prescribed in 2018, this was not the case in 2020. The most common dental injury was subluxation in 2020 whilst in 2018 it was a combination of injuries. The labial mucosa was the most common site of soft tissue injury in both years. Patient outcomes remained comparable regarding outpatient reviews and admissions for theatre.

**Conclusions:** The incidence of intra-oral and dental trauma in paediatric patients was similar in 2018 and 2020. Interestingly however, there were areas that varied which may be related to the COVID-19 pandemic. In 2020 no sports injuries were reported, and antibiotics were prescribed more often following treatment. These findings call for further investigation.

## 1792 | The use of revascularization in the treatment of the immature maxillary lateral incisor subluxation: A case report

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**Introduction:** Dental trauma of the immature teeth is challenge for paediatric dentistry. Thus, the issue of development and testing of new methods and approaches, in particular those based on the concept of regenerative endodontics is relevant.

**Case report:** 11 years-old patient complained on tenderness on biting and mobility of the tooth 12 (4 hours after trauma). Objectively: the crown was intact, II degree of mobility, wasn't displaced, tenderness on percussion, pulp testing - negative, there was a slight bleeding from the gingival sulcus. Open apex according to X-ray. Diagnosis: subluxation of tooth 12. The biofilm removing and splinting for 14 days was performed. Pulp necrosis was diagnosed after 1 month. "Revascularization" was chosen. The root canal was cleaned (20 ml 5.25% NaOCl and 17% EDTA) and obturated (Triple antibiotic paste for 3 weeks followed 2 weeks with Ca(OH)<sub>2</sub>). The next visit the root canal was irrigated (5 ml 17% EDTA), blood clot was formed and covered with MTA/GIC. Postendodontic restoration was performed. After 1 year the completion of the root formation, root walls thickening and narrowing of its lumen were revealed. No complaints, percussion - painless, pulp testing - negative.

**Discussion:** The "revascularization" and apexification with MTA were the treatment options in this case. Despite all advantages of apexification, technically sensitivity and increased risk of the root fracture requires the development the alternative approaches. Thus "revascularization" was chosen in this case.

**Conclusion:** This clinical case demonstrates the possibilities of "revascularization" in immature teeth treatment after dental trauma.

## 1783 | Impact of traumatic dental injuries on oral health-related quality of life of preschool children

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**Background:** Traumatic dental injuries (TDI) in primary dentition may lead to consequences for the children and their families. The purpose of the study was to evaluate the parental perceptions of the impact of TDI on the oral health-related quality of life (OHRQoL) of preschool children.

**Methods:** 83 children aged 1-5 years who suffered TDI and were attended at the Center of Dental Trauma in Primary Teeth, University of São Paulo were selected. Complete information related to TDI was collected. Parents answered the Brazilian version of Early Childhood Health Impact Scale (B-ECOHIS) to assesses their perception of their child's

OHRQoL. To evaluate the association between the OHRQoL and possible independent variables, Multilevel Poisson regression analyses were conducted.

**Results:** 157 primary teeth suffered TDI, and children aged  $\leq 3$  years old were the most affected (61;73.5%). Intrusion and avulsion were the most prevalent types of TDI, which were suffered by 22 (26.5%) and 16 (19.3%) children, respectively, and the majority of the B-ECOHIS were answered by the child's mother (85.5%). Children who took 1 month to seek treatment after TDI (Prevalence ratio-PR=1.33; 95%CI=1.09 to 1.62) and suffered high-severity TDI (PR=1.31; 95%CI=1.02 to 1.68) presented higher prevalence for greater B-ECOHIS scores than those who sought treatment  $\leq 1$  month and suffered low-severity TDI. TDI in children aged 3 years was a protective factor for higher B-ECOHIS scores.

**Conclusions:** Severe dental trauma and delayed seek for treatment have a negative impact on child's OHRQoL; however, the parental perception of oral health problems decreases in older children.

Funding: CAPES

## 505 | Management of an extrusive luxation injury complicated by apical infection-related resorption: A case report

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**Introduction:** Extrusive luxation is a periodontal ligament (PDL) injury characterized by partial displacement of the tooth from its socket. Prevalence is 7% with repositioning and flexible splinting the treatment of choice. Pulpal necrosis is a possible sequelae and root canal treatment may be complicated by the need for apexification when apices are resorbed.

**Case Report:** A 14-year-old girl presented following extrusive luxation of UL1, which had been repositioned and flexibly splinted 2 weeks previously. Medical history was non-contributory. Clinical and radiographic examination revealed a caries-free late-mixed dentition. UL1 presented with completed root development and closed apex. It was of normal colour and mobility and was reliably positive to sensibility testing. There was no evidence of infection. The splint was removed, and a regular review protocol implemented. On review, 10 months later, UL1 presented with loss of vitality with periapical pathology and infection related resorption apically. Pulpal extirpation was performed with calcium hydroxide dressing. One month later, an MTA apical barrier was placed. Obturation was completed using injectable thermoplasticised technique (Obtura).

**Discussion:** The optimal treatment goal for extruded teeth is to facilitate revascularisation and PDL fibers reorganisation via repositioning and flexible splinting. However, healing is significantly reduced in teeth with closed apices and may lead to subsequent pulp necrosis and infection related resorption.

**Conclusion:** Regular clinical and radiographic review is imperative following traumatic dental injury to allow early identification of pulpal and periodontal sequelae. This will facilitate timely management and optimal long-term outcomes in the growing child.

## 754 | Unexpected sequelae following dental trauma: A case report

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**Introduction:** Alveolar bone fractures account for 5.5% of traumatic dental injuries. Inadequate fixation can cause mobility of fractured segment(s) and subsequent sequestrum, resulting in loss of supporting bone. This case aims to explore the differential diagnoses, investigations, treatment options and challenging management of atypical bone loss in a young patient.

**Case Report:** A 15 year-old anxious patient was referred to the Paediatric Dentistry Department with a provisional diagnosis of acute necrotising ulcerative gingivitis. On examination, 32 and 33 were mobile, with localised gingival inflammation, and unusual hard tissue inter-proximally which remained immobile during scaling. A thorough history revealed that dental trauma had been sustained several months earlier; resulting only in gingival tenderness and slight mobility of the teeth, thus no treatment was sought. Radiographic examination and cone beam computed tomographic (CBCT) analysis revealed a radiolucency consistent with pathology adjacent to 32, which was investigated and curetted under general anaesthesia.

**Discussion:** Histopathological investigations of the hard tissue sample showed bony sequestrum, likely to have developed from an alveolar bone fracture due to the dental trauma. Following necrotic bone removal, 32 became considerably mobile and required extraction with the provision of a temporary auto-bridge. Multi-disciplinary liaison was fundamental to discuss replacement options in view of the significant alveolar bone defect.

**Conclusion:** Early recognition of clinical and radiographic signs of localised alveolar bone fracture is essential in cases of dental trauma. Consequent appropriate management is critical to prevent further complications such as tooth loss; as late presentation may reveal subsequent necrosis of surrounding bone, requiring invaluable multi-disciplinary liaison.

## 1883 | Traumatic injury to the soft tissues of the temporomandibular joint in a child: A case report

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**Introduction:** Initial signs of soft tissue injuries to the TMJ include pain, tenderness, restricted opening, midline shift and haemotympanum. A haemarthrosis or joint effusion with late development of disc displacement and TMJ ankylosis may result.

**Case report:** An 8-year-old boy in the mixed dentition phase was referred to the National Maxillofacial Unit following an impact to the chin on a trampoline one day prior. Symptoms included pain and tenderness over the left temporal region, trismus, deviation of the lower dental midline to the right and bleeding from the left ear. Orthopantomogram and mandible x-rays revealed no fracture. Assessment by ENT surgeons revealed no acute otic injury. Following clinical examination, he was diagnosed with a left sided TMJ effusion.

**Discussion:** Plain imaging x-ray films are of limited use in these cases. Injury to the chin can result in damage to the condyle or to the temporal surface with bleeding into the joint from trauma to the bone, disc or tearing of the retrodiscal and lateral capsular tissue. Formation of an intra or extra-capsular haematoma restricts TMJ movement, leading to pain or tenderness on palpation of the TMJ. These signs may be missed or dismissed in children, especially when the only clinical sign is ecchymosis or chin laceration. Home physiotherapy to restore range of mandibular function is the focus of treatment.

**Conclusion:** Soft tissue TMJ injuries are easily misdiagnosed and should be considered in the differential of chin trauma. These patients need specialist follow-up and monitoring to minimize long-term sequelae.

## 1153 | Treatment of young permanent tooth with root fracture, 6-year follow-up: Case report

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**Introduction:** Root fractures involving dentin, cementum and pulp are a type of trauma that can compromise the dental element, and if not properly diagnosed and treated, can lead to extraction of the fractured element

**Case Report:** The objective is a clinical case of trauma in young permanent teeth, with a poor prognosis, with a 6-year follow-up. Male patient, 11 years old, went to the CEC Specialization Clinic in 2014, complaining of mobility and pain in teeth 11 and 21 after a week of trauma to these teeth. Before, he sought out other professionals, where they indicated that the best treatment would be the extraction of teeth. When performing the clinical and radiographic examination, tooth 21 was observed with a root fracture in the middle third and the root of tooth resorption 11. Due to the patient's young age, conservative treatment was chosen, teeth were split, followed by endodontics at 21 and follow-up at 11. The endodontic treatment performed managed to pass through the root fracture. Over time, root fracture consolidation occurred. Tooth 11 remains with pulp vitality, despite the aspect of root resorption and all teeth are firm and without painful symptoms

**Discussion:** The treatment of this type of fracture is complex and depends on many variables such as the level of the fracture and its proximity to the gingival sulcus. Conservative treatment is indicated in young patients

**Conclusion:** Conservative treatments should always be attempted with clinical and radiographic monitoring by a specialized multidisciplinary team in order to prevent premature tooth loss

## 642 | Blueprint of regeneration for root completion in newly erupting maxillary central incisor after severe luxation injury-a 5 years follow up

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**Introduction:** Injuries of tooth-supporting structures is most common in newly erupting maxillary central incisors. Treatment of still erupting permanent maxillary-incisor having a developing wide-open apex with luxation injury is one of the most difficult to manage.

**Case report:** A newly erupting upper-right permanent incisor in a seven-year-old male patient was luxated in palatal direction, resulting in crossbite. It was digitally manipulated into the correct occlusal position and splinted. Apexification was attempted when the tooth developed an abscess after three months and a 24-month follow-up was done Continuing root formation was observed and the tooth developed pulp sensibility. Clinically, the teeth became firm and the radiographic results showed uneventful healing and a successful independent root formation over

a period of five years. The root formation was observed almost comparable to adjacent normal left maxillary incisor independent of attempted apexification at the half root level.

**Discussion:** Procedures that preserve the remaining dental pulp stem cells and mesenchymal stem cells of the apical papilla can result in intracanal revascularization and continued root development. The regeneration of these teeth is based on the concept that vital stem cells in the apical papilla can survive pulpal necrosis, even in the presence of periapical infection, because the open apex provides good communication to the periapical tissues.

**Conclusion:** The present case report evaluated the long-term prognosis of root formation in the luxated immature tooth, with the aim of providing reliable evidence for the regeneration.

### 183 | Reimplantation of avulsed primary anterior teeth: A report of three cases

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**Introduction:** Prevalence of avulsion injuries in primary teeth varies between 5.8% - 19.4% of all types of traumatic injuries to primary dentition. Commonly encountered in 2–4 year old children and primary maxillary central incisor being the most commonly involved tooth. The primary causes of avulsion of primary teeth are falls, fights and child abuse.

**Case Report:** This poster presents replantation of avulsed primary maxillary incisors in three patients aged 3.6 – 4 years. The patients reported with the primary incisors in an appropriate storage media, avulsed due to trauma. The extra oral dry time ranged between 10 minutes – 19 hours. Treatment was completed with endodontic management and reimplantation. The teeth were stabilized for 2 weeks and clinical/ radiographic follow up were done until exfoliation of primary reimplanted teeth and eruption of the permanent successor in one patient. Average follow up time ranged from 18 – 33 months. During the review periods the patients remained asymptomatic.

**Discussion:** Treatment options available for the management of avulsed primary teeth include either no treatment or replacement with prosthesis. This poster describes reimplantation procedure as a treatment option for the management of avulsed primary teeth. Reimplantation of avulsed primary teeth is contra-indicated due to possible damage to the underlying successor or ankylosis of the reimplanted teeth. However in the following cases, no unfavorable outcomes were observed.

**Conclusion:** The case reports show successful management of avulsed primary anterior teeth with reimplantation. Further research to advocate reimplantation as a treatment option for avulsed primary teeth is required.

### 168 | Success of a delayed partial pulpectomy with biodentine™ in an immature permanent incisor with a complicated crown fracture: A 32-month follow-up case report

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**Introduction:** In a complicated crown fracture tooth, partial or coronal pulpotomy is usually recommended. Ideally, treatment should be provided as early as possible. However, this case report presented the success of a delayed partial pulpectomy in an immature incisor with long duration of pulp exposure.

**Case Report:** A 9-year-old boy with a complicated crown fracture on immature maxillary lateral incisor presented for treatment 26 days after trauma. The tooth responded positively to cold test. Pre-operative radiograph showed a large root canal with open apex. Partial pulpectomy was performed by gradually removing necrotic tissue; however, slow and minimal pulpal bleeding was observed. After hemorrhage control, Biodentine™ was placed in the canal and the tooth was restored with resin composite. High-strength bis-acryl resin (LuxaCrown; DMG America) crown was custom-made and cemented on the tooth a month later. At 32 months follow-up, the tooth had favorable pulpal and restorative outcomes and continued its root formation.

**Discussion:** Although it had already been 26 days after trauma, this case report highlighted the regenerative potential of vital pulp tissue left at the apical part, when using Biodentine™, in a traumatized immature tooth. The semi-permanent crown used in this case also demonstrated an economical solution with long-term esthetic, functional, and biological successful restoration.

**Conclusion:** Preserving pulpal vitality should be an ultimate goal of treatment in immature permanent incisors. Partial pulpectomy, the unusual type of vital pulp therapy, can be

performed successfully in these immature teeth with the use of bioactive cement and good coronal seal.

### 1035 | Dental traumatic injuries in 2-year-old Brazilian babies

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**Background:** The study evaluated the occurrence of traumatic dental injuries (TDIs) in 2-year-old babies in Brasília, Brazil.

**Methods:** Data were collected from a birth cohort study of babies that were borne from August 2017 to July 2018 at the University Hospital of Brasília. During the 2 years follow-up appointment, a questionnaire about oral health and TDIs information was applied to the parents. Clinical examination was also performed to assess signs of TDIs in primary teeth. Data were tabulated and a descriptive statistical analysis was performed.

**Results:** The mean age ( $\pm$  SD) of the babies was 24.18 ( $\pm$  0.61) months. Of the 130 children evaluated, 50.8% were girls and 76.2% had some oral trauma. The prevalence of TDIs was 39.4%, a total of 56 teeth were affected. The upper right and left central incisors (60.7%) were the most affected teeth. Regarding the clinical findings affecting teeth and supporting tissues, enamel fracture (41.1%) and concussion (33.3%) were the most prevalent, respectively. The majority of TDIs occurred at home (80.8%) caused by fall from own height (72.7%). Regarding dental care-seeking, only 6.1% of mothers reported to seek dental care.

**Conclusion:** The prevalence of TDIs was high and most of the mothers reported did not seek dental care.

### 860 | Rising like a phoenix: 36 months of pan speciality management of delayed consequences of early childhood dentofacial trauma

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**Introduction:** Dentofacial trauma in early childhood with unmet needs can lead to a plethora of complex long-term sequelae affecting the growth and development of the orofacial region.

**Case Report:** 3 years ago, a 13-year-old boy reported to Exclusive pediatric dental practice with a chief concern of acute unbearable pain. Past history highlighted pan-facial and dental trauma during the first two years of life. Immediate medical care was done but dental care was largely unmet due to lack of access of care & awareness. Long-term sequelae led to severe dilacerations, hypomineralization, and Turner's hypoplasia in all maxillary and mandibular anterior. OPG revealed impacted 12 along with a supernumerary tooth in the same affected region. Extraction of needful by an oral surgeon along with regenerative endodontics in 11 and 22 was done by pediatric dentist concomitantly followed by strip crowns and restorative build-up as transient treatment. Cleft orthodontist employed the AltRamec technique to correct the Class III skeletal discrepancy followed by fixed mechanotherapy with a facemask to align the teeth in the best possible profile. Finally, a cosmetic dentist has done smile designing to camouflage and give the final esthetic outcome by veneering.

**Discussion:** After 36 months of multispeciality approach, not only the adolescent is transformed aesthetically but also his psychosocial morale has risen like a phoenix.

**Conclusion:** Dentofacial trauma management is not a one-time approach. It is inclusive of preventive, interceptive, and corrective approaches in pan specialty ways. Anticipatory guidance can definitely minimize possible long-term sequelae.

## 1227 | Prevalence of dental trauma and its relationship with dental caries among preschool children in Lattakia City, Syria

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**Background:** Dental caries has been underestimated when studying the epidemiology of dental trauma in primary teeth. However, dental caries is a significant public health problem and if it is present, it may affect the outcome of dental trauma.

**Methods:** This cross-sectional study involved 2039 children (1054 males and 985 females) aged between 3 and 5 years in 24 private kindergartens in Lattakia city. Intraoral examinations were obtained and the injury was recorded according to the field screening classification of Andreasen et al. The presence of dental caries in the anterior teeth was recorded as well. Data were analyzed using the chi-square test with  $P < 0.05$ .

**Results:** The prevalence of dental trauma in primary teeth was 7.45% and it was 1.5 times greater in male children than that of females with no statistical significance ( $P = 0.015$ ). Age had no significant effect statistically as well. Enamel-dentin fractures were the most common (31.4%), followed by fractures with pulpal involvement (25.6%). The prevalence of dental fracture associated with caries was 17.4%. Fractures with pulpal involvement were the most common 29.5%, followed by Enamel-dentin fractures (22.2%) and enamel fracture (9.8%) with no statistical significance ( $P = 0.077$ ).

**Conclusion:** Dental caries increases the likelihood of enamel and dentin fracture in primary teeth due to trauma. Moreover, the outcome could be more complicated if the tooth was compromised due to caries as it more likely to have pulp injury.

## 1840 | Treatment outcomes in permanent immature non-vital traumatized teeth: A retrospective clinical report

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**Introduction:** Trauma of an immature permanent tooth can result in loss of pulp vitality, arrest of root development and possible root fracture. There has been a transition in the treatment of traumatized immature young permanent teeth with necrotic pulps. Modalities range from traditional procedures such as apexification to newer regenerative protocols.

**Case reports:** Healthy children in the age group of 7 -10 years had been treated for immature necrotic maxillary incisors, following dental trauma. All treatment procedures had been carried out as per the institution's patient protocol

guidelines and with written parental consent. Choice of treatment for each tooth was based on clinical and radiographic criteria. In four teeth, apexification had been done using either calcium hydroxide or MTA or Biodentin. Revascularization/Regeneration endodontic procedure had been carried out in seven teeth. Triple antibiotic paste had been used in five teeth, and a scaffold of Platelet Rich Fibrin had been placed in the canals of two teeth. Clinical and radiographic outcomes of treatment were monitored at regular intervals. The average follow-up period was 13.5 months (range= 9 – 21 months). All cases had been supervised by a single operator.

**Discussion:** There was resolution of clinical signs and symptoms. Digital radiographs showed increase in root length, thicker dentinal walls and narrowing of apical foramen in five teeth.

**Conclusion:** Following trauma, proper case selection and therapeutic protocols are important to achieve successful treatment outcomes in immature non-vital permanent teeth.

## 1012 | Regeneration of pulp-dentin complex of immature permanent tooth by auto-transplantation of deciduous tooth pulp: A case report

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**Introduction:** Traumatized non-vital young permanent tooth presenting with immature apex is usually an endodontic challenge. Regenerative endodontics has been developed as an array of biological procedures based on the concept of tissue engineering. Tissue engineering approaches comprises of three central components: stem cells, scaffolds and induction of growth factors. Deciduous tooth pulp satisfies the criteria for an ideal scaffold and also contains undifferentiated stem cells (SHED) and growth factors in a natural microenvironment. This case report describes the management of a nonvital young permanent tooth by auto-transplantation of deciduous tooth pulp

**Case report:** An 8-year-old child reported non-vital permanent central incisor with immature apex and periapical radiolucency. Endodontic access preparation, irrigation with 5.25% NaOCL was done followed by 3 weeks of triple antibiotic paste dressing. Pulp from deciduous second molars were harvested and placed in the canal along with Rosuvastatin followed by placement of Nanohydroxyapatite. Follow up visits at the end of 2,4,6,8 and 12 months revealed continued root development, return of vitality with absence of periapical pathologies

**Discussion:** In this case deciduous tooth pulp was used as the scaffold and source of stem cells(SHED), rosuvastatin as the

material to induce angiogenesis and nanohydroxyapatite as a stimulator for dentinogenesis. Successful clinical and radiographic outcomes were seen at the end of follow up period.

**Conclusion:** This case report shows the successful management of a nonvital young permanent tooth by the novel method of autotransplantation of deciduous tooth pulp which could be a viable method in the future regenerative endodontic procedures.

### 805 | Global status of knowledge for the prevention and emergency management of traumatic dental injuries among non-dental healthcare professionals: A systematic review and meta-analysis

Nitesh Tewari<sup>1</sup>; Immaculate Jonna<sup>1</sup>; Vijay Mathur<sup>1</sup>; Shubhi Goel<sup>1</sup>; Priyanshi Ritwik<sup>2</sup>; Morankar Rahul<sup>1</sup>; Partha Halder<sup>3</sup>; Kalpana Bansal<sup>1</sup>; Ravindra Pandey<sup>4</sup>

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**Background:** This Systematic Review was conducted to evaluate the global status of the knowledge of prevention and emergency management of traumatic dental injuries among non-dental healthcare professionals (NDHCP).

**Literature Review:** The protocol was designed as per PRISMA and registered in PROSPERO (CRD42020192381). A broad-based search using text-words and MeSH terms was performed in established databases as per a predefined strategy without any limitation of language and year of publication. Studies without details of questionnaire, knowledge-score, validity and reliability were excluded. Data extraction was performed and risk of bias assessment was done using the Joanna Briggs Institute's critical appraisal tool and a meta-analysis was performed.

The qualitative synthesis included 14 studies between 2009-2020 with nine of them from Asia. Majority of the studies had low risk of bias and reported poor overall level of knowledge. Less than 40% of the NDHCP had received a dental trauma first aid training in six of the 10 studies and majority of the participants (50%) believed that dental trauma training was required in five studies. Less than 36% of the participants were adequately aware of the correct approach towards management of avulsed permanent tooth in five studies.

**Conclusions:** The knowledge of non-dental health care professionals regarding the emergency management of traumatic dental injuries was insufficient or low in the majority

of studies and the knowledge about prevention was not evaluated. There was a paucity of studies from the countries of Europe and Australia, with wide variability in the study methods, categories of the participants and questionnaire characteristics.

### 1181 | Avulsed and replanted maxillary central incisors, obturated with calcium silicate-based cement (Biodentine<sup>®</sup>): 18 months follow-up

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**Introduction:** Avulsion of permanent teeth is one of the most serious dental injuries and a prompt and correct emergency management is very important for the prognosis. The treatment prognosis is multifactorial such as storage of the teeth, extraoral time, oral hygiene.

**Case Report:** This case report describes multiple trauma lesions which involves alveolar fracture and avulsion of both maxillary permanent central incisors of a 10 year old male and 18 months follow-up. The central incisors were avulsed, remained 2 hours dry extraorally and was replanted after repositioning the alveolar fracture. Reimplantation and the Flexible splint were applied for 4 weeks. The endodontic treatment was started 10 days after and Calcium hydroxide (CaOH) was used as a root canal medicament for 4 weeks. Calcium Silicate-Based Cement (Biodentine<sup>®</sup>) was utilized as a novel endodontic treatment. After 18 months post-injury, the teeth were asymptomatic. Clinical and radiographic follow-up showed evidence of healthy periodontium.

**Discussion:** According to the IADT guidelines, reimplanting a tooth is almost always the correct decision even if the extraoral time is more than 1 hour. In this case, after CaOH usage for 4 weeks, the roots were fully filled with Biodentine as the roots were completely affected by external resorption. Biodentine is easy to prepare and handle also has shorter setting time than other silicate-based cements. The favorable clinical and radiographic outcome in this case demonstrated that Biodentine may be an efficient alternative to the Mineral Trioxisit Agregat (MTA).

**Conclusion:** The present case represents a success of reimplantation, despite inappropriate storage conditions and late reimplantation. Thus, the findings will encourage dentists to attempt this procedure to restore function and esthetics in patients with avulsed teeth.

## 580 | Complicated crown fracture in a patient with Marfan syndrome: Case report

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**Introduction:** Complicated crown fracture involves the following: enamel, dentin, pulp exposure as well as injury to adjacent structures. It represents 0.9% - 13% of dental trauma. In traumatic pulp exposure that is not treated immediately, inflammatory reaction is proliferative and extends no more than 2 mm into pulp tissue, even after 9 days. Cvek recommends that removal should not be greater than 3 mm in order to expose healthy tissue, placing an odontoblast stimulating bioactive agent and thus, preserving pulp vitality.

**Case report:** 8-year-old female with Marfan Syndrome without heart disease, controlled epilepsy, arrives to the emergency room with a complicated coronal fracture of DO 11, mobility Grade III DO 11, 21 and 22; subluxation of DO 21 and 22. Treatment: Partial pulpotomy of DO 11 is performed, disinfection (chlorhexidine 0.12%), direct pulp coating (Tricalcium silicate); replacement of DO 21-22 and splint for 20 days. Clinical and radiographic follow-up for 1 year post-trauma, observing notable improvement of the periodontium and formation of the dentin bridge of DO 11.

**Discussion:** In this case, the coronal fracture involved the pulp exposure of an immature DO in a medically compromised patient. The tricalcium silicate which is a bioactive ingredient stimulated the formation of a dentine bridge, maintaining pulp vitality and inducing apical closure. During follow-up, these DOs remain vital and without mobility data.

**Conclusion:** This case shows the success of managing multiple DO trauma that required strict and meticulous follow-up in a medically compromised patient, avoiding permanent DO loss as well as its consequences.

## 411 | Multiple crown-root fractures in primary molar teeth secondary to chin trauma: A case report with one-year follow-up

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**Introduction:** Dental trauma of primary molar teeth is unusual yet may be seen due to chin trauma. Crown-root fracture of primary molar may be seen with 0.8% incidence of all injured primary teeth. This situation generally results in extraction of the tooth, if the fracture line extends vertically to the root.

**Case report:** The present case report describes the management and one-year follow-up of multiple crown-root fractures in primary molars caused by chin trauma in a 27-month-old girl. The pediatric dental patient referred to Yeditepe University, Faculty of Dentistry, Department of Pediatric Dentistry two days after the trauma. Extra-oral examination demonstrated sutured chin laceration. Intra-oral examination showed sublingual multiple hematomas and crown fractures on mandibular primary molars. Both radiographic and detailed intra-oral examinations revealed teeth fractures on upper left primary molars, and vertical crown-root fractures of lower right and left primary molars. The dental rehabilitation of the patient was performed under general anesthesia due to lack of cooperation. The patient is rescheduled for dental check-ups every 3-months for one year.

**Discussion:** Crown-root fractures may be overlooked in emergency dental examination. The main symptom is pain in mastication. In this case, the patient referred to the dental clinic two days after trauma. A space maintainer is crucial for normal development of dentition.

**Conclusion:** This report shows the diagnosis and treatment of crown-root fractures in primary molars after chin trauma. Follow-up is considered the key point in these type of trauma cases.

## 650 | An innovative approach in managing complicated crown-root fracture with subgingival margin: A case report

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**Introduction:** A subgingival crown-root fracture presents the clinicians with a restorative dilemma, mainly due to the location of the fracture line and the needs to maintain a good periodontal health. Extraction and extrusions are among the treatment options available in managing such case.

**Case report:** We present a case of a 11-year-old girl who had a fall at an ice-skating ring. She sustained a complicated crown-root fracture of tooth 11 with subgingival margin and complicated crown-fracture of tooth 21. Cvek's pulpotomy

was performed on tooth 21, followed by a resin composite restoration. However, the tooth become non-vital and root canal treatment was carried out. Tooth 11 underwent root canal treatment, obturated up to 5 mm from the apex. A 2 × 4 orthodontic appliance was used to extrude the tooth 11, using a modified everStick post as an anchor. Following successful extrusion, tooth 11 was restored with a composite crown.

**Discussion:** A subgingivally located fracture line needs to be brought supragingivally prior to any restorative procedure in order to preserve the biological width and maintain the periodontal health. The flexibility of everStick post allowed us to modify its shape and use it in assisting the orthodontic extrusion of the tooth. The use of 2 × 4 orthodontic appliance provides a fast extrusion rate under a well-controlled force. This treatment modalities avoid the need for dental extraction and maintain patient's aesthetic.

**Conclusion:** The use of simple orthodontic appliance combined with an everStick post can be an alternative option in managing subgingival crown-root fracture.

The histopathology marks a strong base for diagnosis. It widely deals with many cellular and nuclear altered structures. These are either intracellular or extracellular structures, appear within the nucleus, cytoplasm or in both. Commonly associated with the name of the scientist who first described them. One of the interesting and important features is the observation of various histopathological bodies. These typical bodies are unique and an important diagnostic-aid in identifying the underlying disease. Therefore here we present histopathological bodies characteristic of various diseases.

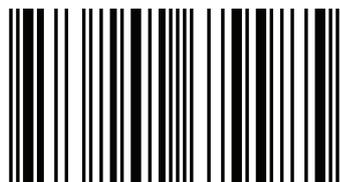


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## Histopathological bodies- A Diagnostic clue



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# **HISTOPATHOLOGICAL BODIES**

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## **INTRODUCTION**

**Inclusion bodies** are nuclear or cytoplasmic aggregates of stainable substances, usually proteins. These show peculiar presentation which denotes the morphologic alterations in a highly specific pattern. Inclusion bodies can also be hallmarks of diseases.

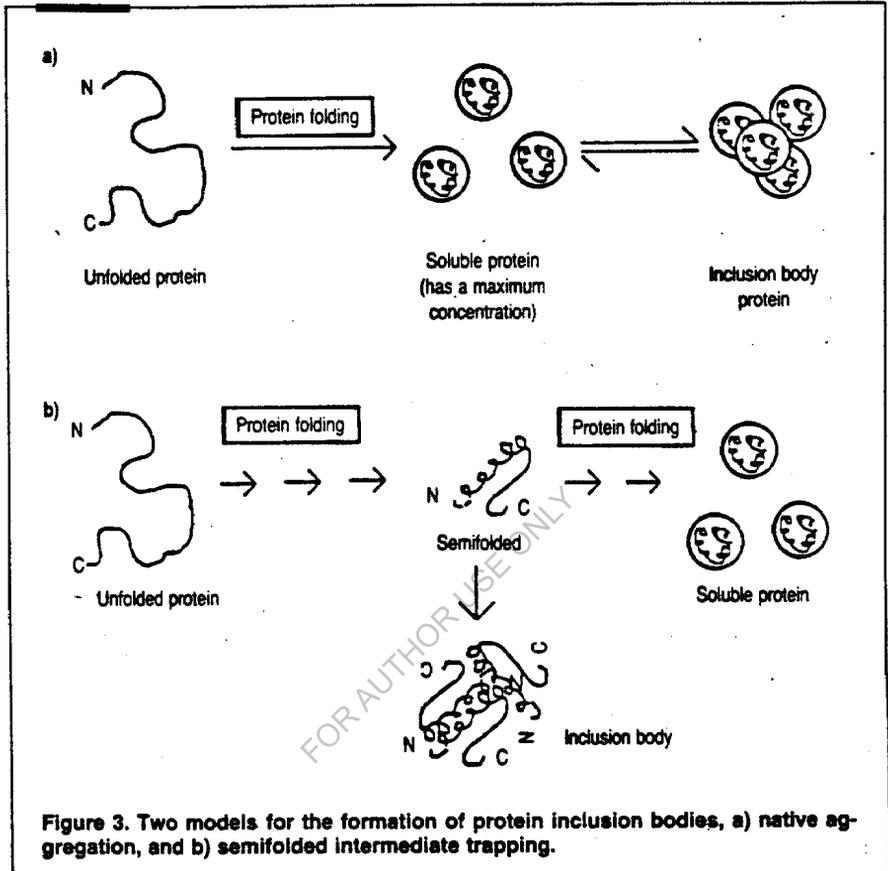
### **MECHANISM OF FORMATION:**

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Basically there are two general explanations for inclusion body formation.

Firstly, the overproduction of certain proteins results in concentrations that exceed the solubility limit for the cytoplasm. Excess protein thus precipitates from solution, leaving a constant maximum concentration of protein in the cytoplasm; this model assumes equilibrium between soluble and insoluble forms of the proteins.

A mutation in single amino acid creates a hydrophobic surface patch that acts as a site for molecular contact, resulting in a fiber. The mechanism that best fits the available data requires at least two alternative protein folding pathways one which leads to a soluble native form of protein and the other to an inactive precipitated form.<sup>1,2</sup>



- a) Native Aggregations
- b) Semifolded intermediate trapping

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## CLASSIFICATION

<b>I. Inclusion bodies in blood dyscrasias</b>	<b>5</b>
<b>II. Viral inclusion bodies</b>	<b>10</b>
<b>III. Bacterial inclusion bodies</b>	<b>19</b>
<b>IV. Inclusion bodies in autoimmune diseases</b>	<b>25</b>
<b>V. Inclusion bodies seen in cysts</b>	<b>29</b>
<b>VI. Bodies in neoplasm.</b>	<b>33</b>
<b>SUMMARY</b>	<b>38</b>
<b>REFERENCES</b>	<b>39</b>

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## **INCLUSION BODIES IN BLOOD DYSCRASIAS**

### **HOWEL JOLLY BODIES**

#### **INTRODUCTION:**

It is named for William Henry Howell and Justin Marie Jolly.

Howell –Jolly bodies are histopathological findings of basophilic nuclear remnants (clusters of DNA) in circulating erythrocytes. During maturation in the bone marrow, erythrocytes normally expel their nuclei, but in some cases a small portion of DNA remains.

#### **MORPHOLOGY:**

This DNA appears as a basophilic spot on the otherwise eosinophilic erythrocyte on a standard H&E stained blood smear. These inclusions are normally pitted out by the spleen during erythrocyte circulation, but will persist in individuals with functional hyposplenia or asplenia.<sup>3</sup>

#### **OCCURENCE:**

- Asplenia
- Splenectomy
- Autsplenectomy caused by sickle cell anemia
- Coeliac disease
- Radiation therapy
- Haemolytic anemia
- Myelodysplastic syndrome.

**SPECIAL STAIN:** Stain reddish-blue with Wright stain

---

## **BASOPHILIC STIPPLING**

### **INTRODUCTION:**

Represents the spontaneous aggregation of ribosomal RNA in the cytoplasm of erythrocytes. It is an abnormal collection of nucleic acid in dots throughout the cell and indicates the presence of disease. These aggregates stain, and hence are visible with routine haematological stains.

### **MORPHOLOGY:**

This stippling is either fine or coarse, deep blue to purple staining inclusion that appears in erythrocytes on a dried Wright stain.<sup>4</sup>

### **OCCURENCE:**

- Sideroblastic anemia
- Lead poisoning (microcytic anemia)
- Arsenic poisoning
- Beta thalassemia
- Alpha-thalassemia.

**SPECIAL STAINS:** Wright stain.

## **PAPPENHEIMER BODIES**

### **INTRODUCTION:**

Pappenheimer bodies are first described by Pappenheimer in 1945, these are abnormal granules of iron found inside red blood cells on routine blood

---

stain. They are a type of inclusion bodies formed by phagosomes that have engulfed excessive amounts of iron.

**MORPHOLOGY:**

They appear as dense, blue-purple granules within the red blood cell and are usually only one or two, located in the cell periphery.

**OCCURENCE :**

Sideroblastic anemia

Hemolytic anemia

Sickle cell disease.

They can interfere with platelet counts when the analysis is performed by electro-optical counters.<sup>5</sup>

**SPECIAL STAINS:** Wright and/or Giemsa stain.

Perls' Prussian blue stain: for confirmation of non-heme iron in the granules

Romanowsky stains: because of co-precipitation of ribosomes

Cells containing Pappenheimer bodies can be confused with late reticulocytes. Prussian blue stain, which is not taken up by reticulocytes, is helpful in differentiating the two.

**HEINZ BODIES ( HEINZ-EHRLICH BODIES)**

**INTRODUCTION:**

---

Robert Heinz (1865-1924), a German physician who in 1890 described these inclusions in connection with cases of hemolytic anemia.

Oxidation of exposed sulfhydryl (SH) groups on hemoglobin causes formation of disulfide bonds and distortion of the tertiary structure of the hemoglobin molecule. The result is precipitation of hemoglobin, which may then coalesce to form intracellular inclusions called Heinz bodies (HB).

Damaged cells are attacked by macrophages in the spleen, where the precipitate and damaged membrane are removed, leading to characteristic "bite cells". The denaturing process is irreversible and the continual elimination of damaged cells leads to Heinz body anemia.<sup>6</sup>

There are several pathways leading to the hemoglobin damage.

- In  $\alpha$ -thalassemia, lack of  $\alpha$  subunits causes  $\beta$  subunits to form tetramers which precipitate out of solution, creating Heinz bodies.
- G6PD (Glucose-6-Phosphate Dehydrogenase) deficiency brought on by administration of oxidant drugs (e.g., primaquine, dapsone, quinidine) also can result in Heinz bodies.
- Heinz bodies can also be found in chronic liver disease.

## **MORPHOLOGY:**

Heinz bodies appear as small, irregular, deep purple granules in red blood cells due to damage of the haemoglobin molecules.<sup>6,7</sup>

## **SPECIAL STAINS:**

- 1) Crystal Violet
- 2) Wright's Stain

---

3) Appear more clearly when supravitaly stained (e.g., with New methylene blue or bromocresyl green

4) When stained with Romanowsky dyes they may appear as projections from the cell.

**OCCURENCE:**

- Glucose-6-phosphate dehydrogenase deficiency following administration of oxidant drugs, e.g. primaquin.
- Hereditary haemolytic anaemia,
- $\alpha$  Thalassaemia

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## **VIRAL INCLUSION BODIES**

### **NEGRI BODIES**

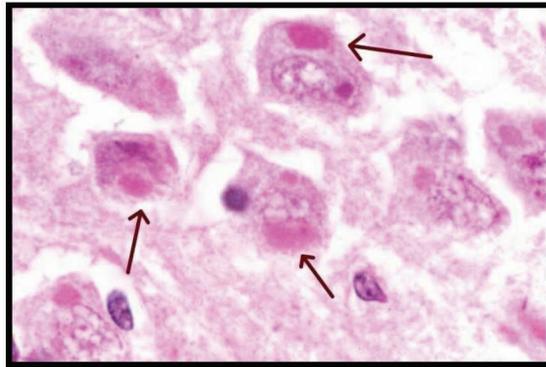
#### **INTRODUCTION:**

Negri bodies were first described by Adelchi Negri in 1903, an Italian microbiologist. The presence of Negri bodies are pathognomic for rabies.<sup>8</sup>

**Negri bodies** are eosinophilic, sharply outlined, pathognomonic inclusion bodies (2–10  $\mu\text{m}$  in diameter) found in the cytoplasm of certain nerve cells containing the virus of rabies, especially in Ammon's horn of the hippocampus and purkinje cells of cerebellum.<sup>9</sup>

#### **MORPHOLOGY:**

Negri bodies appear as eosinophilic inclusions. They are round or oval in shape. 0.25 $\mu\text{m}$  to 0.27 $\mu\text{m}$  in size. The inner structure show basophilic staining granules.<sup>10</sup>



Negri bodies: Eosinophilic sharply outlined inclusion body measuring about 0.25 to 27  $\mu\text{m}$ .

**SPECIAL STAINS** : Mann's stain

Seller stain

Giemsa stain

**OCCURRENCE:**

- Rabies: Rabies is severe encephalitis transmitted to humans by the bite of rabid animal.<sup>11</sup>

## **BORRELL BODIES/ BOLLINGER BODIES**

**INTRODUCTION:**

Bollinger bodies are named after German pathologist Otto Bollinger (1843-1909). The most important feature of a pox virus infection in the skin and

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mucous membranes is hyperplasia of the epithelium and enlargement of cells, with associated inflammatory changes and characteristic eosinophilic cytoplasmic inclusion bodies i.e. Bollinger bodies.<sup>12</sup>

### **MORPHOLOGY:**

Relatively large, spheroid or ovoid, usually somewhat granular, acidophilic, intracytoplasmic inclusion body observed in the infected tissues of birds with fowlpox virus; when body are ruptured large numbers of fowlpox virus particles are released.

### **PATHOGENESIS:**

Particles of fowlpox virus; aggregates in infected cells result in formation of bollinger bodies or granules.

**OCCURRENCE:** Fowlpox Virus Infections.

## **COUNCILMAN BODIES**

### **INTRODUCTION:**

Councilman bodies are named after American pathologist William T. Councilman (1854-1933), who discovered them.<sup>13</sup>

### **STRUCTURE:**

Councilman bodies refer to acidophilic inclusion bodies in the cytoplasm of hepatocytes, which also show shrinkage or swelling (ballooning degeneration).

### **ELECTRON MICROSCOPE:**

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Councilman bodies found in hepatic cells, naturally infected with yellow fever virus, are identified with the electron microscope. At the fine structure level, these bodies show no limiting membrane or internal vacuole membrane. The only constituents found are particles of different sizes presenting different osmium affinity. There are no lipid droplets or membranous components present within the bodies.<sup>14</sup>

### **PATHOGENESIS:**

It represents a hepatocyte that is undergoing apoptosis (controlled cell death). Necrotic cells finally undergo coagulation, with the formation of characteristic eosinophilic Councilman bodies which correspond to apoptotic cells. Viral antigen is identified initially in Kupffer cells and appears later in hepatocytes, Councilman bodies.

### **OCCURRENCE:**

- Viral Hepatitis (Acute Viral Hepatitis): Viruses that causes viral hepatitis are Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, and Hepatitis E.
- Yellow Fever:
- Viral Hemorrhagic Fever.

## **HENDERSON- PATERSON BODIES/ MOLLUSCUM BODIES**

### **INTRODUCTION:**

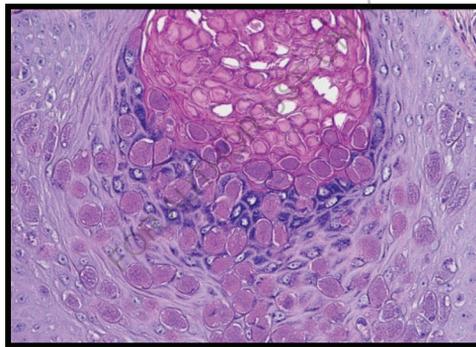
These are inclusion bodies described by Henderson and Patterson in 1891, these are viral particles which develop about and within the cytoplasmic

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vacuole which are regarded as the cellular response to the presence of living foreign body. These are made of nuclear or cytoplasmic aggregates usually proteins, they typically represent site of viral multiplication usually in capsid protein.

### **MORPHOLOGY:**

Large, round cytoplasmic inclusions within the enlarged cells of epidermis, which push the nucleus to the periphery. They present as minute, ovoid eosinophilic structures in the cells of stratum malphigi. At the level of wide poorly defined granular layer the staining reaction of molluscum bodies change from eosinophilic to basophilic.<sup>15,16,17.</sup>



Molluscum bodies: large cells with cytoplasmic, eosinophilic inclusions that displace nuclei and contain viral particles. ( Courtesy: Jerad M Gardener, MD, University of Arkansas for Medical Sciences, USA.)

### **SPECIAL STAINS:**

Phopshotungstic acid hematoxylin

Carbol aniline fuschin after mordanting with potassium permanganate

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## INTRANUCLEAR BODIES

### OWL'S EYE INCLUSION BODIES

#### INTRODUCTION:

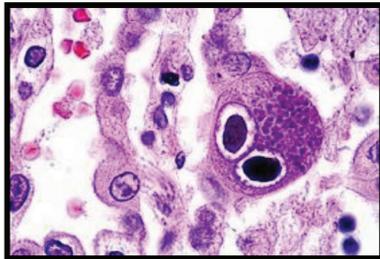
Owl's eye appearance of inclusion bodies, are highly specific for cytomegalovirus infection.<sup>18</sup>

#### MORPHOLOGY:

They are large, intranuclear viral inclusion bodies with eosinophilic nucleolus and thick nuclear membrane where chromatin is distributed at cell periphery.

#### PATHOGENESIS:

Cytomegalo virus (CMV) is a lytic virus that causes a cytopathic effect in vitro and in vivo. The pathologic hallmark of CMV infection is an enlarged cell with viral inclusion bodies. The microscopic description given to these cells is most commonly an "owl's eye," depicted in the image below. Owl's eye appearance is considered diagnostic for cytomegalovirus infection.<sup>18</sup>



Owl's eye inclusion bodies: Enlarged cell with nuclear and cytoplasmic inclusions. Nuclear inclusions appear as owl's eye and cytoplasmic inclusions appear basophilic and granular. Courtesy: Danny L Wiedbrauk, PhD, Scientific Director, Virology & Molecular Biology, Warde Medical Laboratory, Ann Arbor, Michigan.

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## **OCCURRENCE:**

Cytomegalo Virus Infections: Cytomegalic inclusion diseases

Hodgkin's Lymphoma

## **COWDRY TYPE- A INCLUSION BODIES**

### **INTRODUCTION:**

Cowdry in 1934. discovered Cowdry-A type inclusion bodies. These are intranuclear eosinophilic amorphous or droplet-like bodies surrounded by a clear halo, with marginations of chromatin on the nuclear membrane. They occur in diseases as herpes simplex infection or yellow fever<sup>19</sup>

### **MORPHOLOGY:**

Droplet-like masses of acidophilic material surrounded by clear halos in sections stained with haematoxylin and eosin, located within the nuclei of neurons, viruses.

By electron microscopy, Cowdry type-A inclusion bodies contains tubular structures typical of nucleocapsids of viruses. Within nuclei, with margination of chromatin on the nuclear membrane.

### **PATHOGENESIS:**

Hemorrhagic necrosis with intranuclear aggregates of herpes simplex viruses, presumably of nonspecific protein, are responsible for the granular appearance of the inclusion body called Cowdry type A inclusion body, formed by fusion of these aggregates; and these can be seen in the epidermal cells.<sup>19</sup>

---

## **OCCURRENCE:**

- Herpes simplex virus infection: like gingivostomatitis, keratinoconjunctivitis, and skin lesions
- Varicella zoster virus infection: chickenpox

## **COWDRY TYPE –B INCLUSION BODIES**

### **INTRODUCTION:**

Cowdry type-B inclusion bodies first described by Dr. E.V Cowdry in 1934.<sup>18</sup>

Intranuclear eosinophilic amorphous or droplet-like bodies surrounded by a clear halo, without other nuclear changes during early stages of development of the inclusion. They are seen in neural cells.<sup>19</sup>

### **MORPHOLOGY:**

Intranuclear eosinophilic amorphous or droplet-like bodies surrounded by a clear halo, without other nuclear changes during early stages of development of the inclusion. They are seen in neural cells.<sup>20</sup>

### **OCCURRENCE:**

- Adenovirus: Pharyngoconjunctival Fever and Epidemic Keratoconjunctivitis.
- Poliovirus infections: Poliomyelitis.

---

## **LIPSCHUTZ BODIES**

### **INTRODUCTION:**

Eosinophilic, intranuclear inclusions most often seen in herpes simplex or zoster infections are known as Lipschutz bodies.

### **MORPHOLOGY:**

Eosinophilic, nuclear inclusions with enlarged nuclei and clear halo.

### **PATHOGENESIS:**

In early stages of herpes simplex virus infections there is intercellular edema and ballooning and vesiculation of keratinocytes due to intercellular edema. This leads to intraepithelial vesiculation, nuclei become enlarged and occasionally basophilic or eosinophilic nuclear inclusions with a clear halo; called as lipschutz bodies.<sup>21</sup>

### **OCCURRENCE:**

- Herpes simplex infections: These causes gingivostomatitis, keratoconjunctivitis, meningitis etc.
- Herpes zoster infections: It involves the face by infection of the trigeminal nerve. Unilateral painful vesicles are seen in buccal mucosa, tongue, uvula, pharynx and larynx.

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## **BACTERIAL INCLUSION BODIES**

### **DOLHE BODIES**

#### **INTRODUCTION:**

Dohle bodies are named after German pathologist, Karl Gottfried Paul Dohle (1855-1928) they are light blue-gray, oval, basophilic, leukocyte inclusions located in the peripheral cytoplasm of neutrophils. These bodies are commonly seen in bacterial infections such as tuberculosis, diphtheria, typhus etc.<sup>22,23</sup>.

#### **MORPHOLOGY:**

The bodies are usually round or oval shaped and have a diameter from just visible size to approximately 1 to 2 $\mu$ . They are found most often at the periphery of the cell cytoplasm of the neutrophil leucocytes.

Some of the cells contain one Dohle body, others may contain up to three or even four. They are always discrete and clearly separated by normal stained cytoplasm.

#### **PATHOGENESIS:**

The presence of Dohle bodies in mature and immature neutrophils on a blood smear can be normal if they are present only in small numbers. Dohle bodies are intra-cytoplasmic structures composed of agglutinated ribosomes; they will increase in number with inflammation and increased granulocytopenia. If there are many neutrophils in the bloodstream containing Dohle bodies, these can be referred to as toxic neutrophils. Toxic neutrophils

---

can also correspond to neutrophils that possess a more basophilic cytoplasm, basophilic granulation (infrequently observed), or cytoplasmic vacuoles in addition to one of the preceding cytoplasmic changes..

### **SPECIAL STAINS:**

Leishman-Giemsa

Romanowsky stains.

They are a sky blue to grey blue colour and are easily distinguished from the pinkish stained cytoplasm of the neutrophil leucocytes.<sup>22,23.</sup>

### **OCCURENCE:**

Bacterial Infections – Typhus

Diphtheria

Tuberculosis

Physical trauma- Patients with Burns

Wissler's disease

May-Hegglin anomaly

Chédiak-Steinbrinck-Higashi's syndrome

Chronic thrombocytopeni

---

## **DONOVAN BODIES**

### **INTRODUCTION:**

Donovan in 1905 described inclusion bodies named as Donovan bodies. The characteristic Donovan bodies are clusters of blue-space or black-staining organisms with a “safety pin” appearance in the cytoplasm of large infected mononuclear cells of granuloma inguinale. Granuloma inguinale is a progressive, chronic, infectious, granulomatous disease caused by bacilli, *Calymmatobacterium granulomatis*. Lesions may occur in oral cavity such as the lips, buccal mucosa, palate and appear as ulcerative, exuberant and cicatricial.<sup>24,25.</sup>

### **MORPHOLOGY:**

The Donovan bodies, clusters of blue or black-staining organisms with a “safety pin” appearance in the cytoplasm of large mononuclear cells. Intracellular in the vacuoles of the cytoplasm in a large number of cells, cells have pilli like projections on the surface.<sup>24</sup>

These bodies are tiny, elongated, basophilic and argyrophilic rods and are present in profuse numbers within macrophages.

The pathognomonic feature of granuloma inguinale is a large infected mononuclear cell, 25 to 90 µm in diameter, that contains many intracytoplasmic cysts filled with deep-staining donovan bodies<sup>24,25.</sup>

### **SPECIAL STAINS:**

- Warthin–Starry

- 
- Giemsa preparation

## **OCCURRENCE:**

Granuloma inguinale ( donovanosis)

## **ASTEROID BODIES**

### **INTRODUCTION**

Asteroid bodies are intracytoplasmic stellate inclusions within giant cells exhibiting 30 or more rays radiating from a central core. They probably represent functionally obsolescent cell organelles. Asteroid bodies have been reported in from 2 to 9% of tissues from patients with sarcoidosis. They may also be encountered in foreign body granulomas and rarely in other granulomatous conditions.

Asteroid bodies are 10-25 $\mu$  in diameter, occur only intracellularly within giant cells and multinucleated myeloma cells.

asteroid body is comprised primarily of multilaminar membranes typical of complex lipids, especially phospholipids, and is associated with calcium-phosphate complexes.<sup>26</sup>

### **MORPHOLOGY:**

By light microscopy, the asteroid bodies appeared as 3- to 80- $\mu$  irregular spheres and small spheroidal aggregates They often had a linear spoke like pattern.

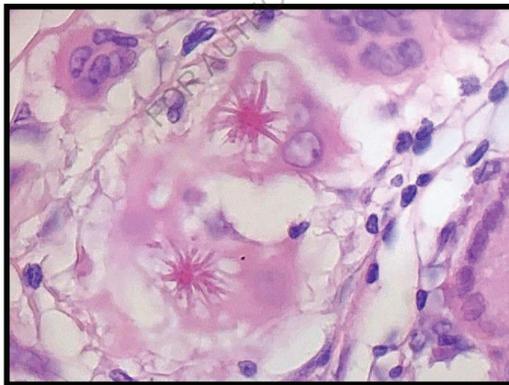
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## **PATHOGENESIS:**

In case of acute fungal infections formation of cigar bodies takes place; bud elongates, forming classical cigar bodies with an associated diffuse acute inflammatory reaction too extensive to be designated a microabscess. In some cases the cigar body rounds off and forms a double contour to produce the classic large hyaline spore with two forms of tissue reaction-

(a) The formation of microabscess; and

(b) Classical radiating material which is considered to be tissue and not fungal in origin. In chronic skin involvement, the asteroid body will be formed associated with *S. Schenckii*. In addition, spores with multiple budding, spores with budding and filament formation, cigar bodies clumped within the asteroid itself, and typical filamentous clumping of *S. Schenckii* <sup>26,27,28</sup>.



Asteroid bodies: Seen in the cytoplasm of epithelioid or giant cells as eosinophilic, stellate, or spider like inclusions. (Courtesy: Jerad M Gardener, MD, University of Arkansas for Medical Sciences, USA.)

**OCCURENCE:**    Sarcoidosis

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Tuberculosis  
Foreign body granuloma  
Blastomycosis  
Sporotrichosis  
Cryptococcosis.

### **SCHAUMANN'S BODIES (CONCHOIDAL BODIES)**

These are large, concentrically lamellated, calcified structures that are usually present within the cytoplasm of giant cells.

Rupture of the cell membranes of Schaumann's body-containing giant cells may result in their extrusion into the extracellular space.

The majority of Schaumann's bodies have birefringent crystals, mostly composed of calcium oxalate, associated with them. It has been suggested that these crystals may serve as a nidus for their formation.

Iron- and calcium-containing, red to brown, laminated inclusion bodies found in the cytoplasm of giant cells in sarcoidosis and other granulomatoses (berylliosis often containing refractile calcium oxalate crystals. Although usually intracytoplasmic they may, if numerous or very large, be extruded into the extracellular space.<sup>29,30</sup>

**OCCURENCE:** Sarcoidosis

Chronic beryllium disease, tuberculosis.

Hypersensitivity pneumonitis,

Other granulomatous diseases

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## **BODIES IN AUTOIMMUNE DISEASES**

### **CIVATTE BODIES / COLLOIDAL BODIES**

#### **INTRODUCTION:**

Eosinophilic spherical body's seen in or just beneath the epidermis, particularly in lichen planus, formed by necrosis of individual basal cells.

#### **FORMATION:**

Basal cell liquefaction degeneration and vasodilatation in upper dermis inside the massive band like infiltrate, disrupted basement membrane, Hypergranulosis causes formation of eosinophilic civatte/colloidal bodies. Civatte bodies are derived from tonofilaments of keratinocytes.

#### **MORPHOLOGY:**

##### **LIGHT MICROSCOPY AND ELECTRON MICROSCOPY:**

Civatte bodies are present in the lower part of the epidermis and/or in the upper dermis of the lesions of all patients. In the epidermis civatte bodies composed of wavily arranged fine filaments and entangled melanosomes, desmosomes and other cell organelles. In the dermis Civatte bodies transform into net-like or more amorphous masses. Melanosomes, desmosomes and other cell organelles within them, although in small numbers.

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Dermal components containing collagen fibrils merged into the rims of Civatte bodies in the dermis. And these Civatte bodies appeared to incorporate the adjacent dermal components and transform into amyloid-like filament masses.

#### IMMUNOHISTOCHEMISTRY:

By electron microscopy colloid bodies have been shown to be derived from epithelial cells. It has been suggested, however, that connective tissue cells or components from the basement membrane zone contributed to the formation of colloid bodies.

Colloid bodies show positive staining for keratin, whereas vimentin never found in colloid bodies. Laminin and collagen type IV are occasionally seen in their periphery probably owing to adherence of basement membrane fragments during apoptosis. Fibronectin is frequently seen at the entire periphery of colloid bodies which may facilitate their elimination by macrophages. In conclusion, connective tissue cells or basement membrane components do not seem to contribute to the formation of colloid bodies in oral Discoid lupus erythematosus.

Direct immunofluorescence shows diffuse granular deposition of IgG, IgM, C3 and weak deposition of IgA along the dermoepidermal junction with deposition of immunoreactions on cytooid bodies.<sup>31,32,33,</sup>

#### OCCURANCE:

Lichen planus: civatte bodies are of diagnostic importance in lichen planus lesions of a short duration only.

Discoid lupus erythematosus

Riehl's melanosis

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## ASCHOFF'S BODIES

### **INTRODUCTION:**

**Aschoff bodies** are nodules found in the hearts of individuals with rheumatic fever. They result from inflammation in the heart muscle and are characteristic of rheumatic heart disease. These nodules were discovered independently by Ludwig Aschoff and Paul Rudolf Geipel, and for this reason they are occasionally called **Aschoff-Geipel bodies**.<sup>34</sup>

### **PATHOGENESIS:**

Aschoff bodies are granulomatous lesions believed to be pathognomonic of rheumatic fever.

There are three phases in the development of the Aschoff body :

1. Early (exudative, degenerative) phase:
2. Intermediate (proliferative or granulomatous) phase:
3. Late (fibrous or healing) phase:

In the granulomatous stage of the lesion the Aschoff body is identifiable and is regarded as pathognomonic for rheumatic carditis.

The early phase of the life cycle of the Aschoff body occur upto the fourth week of acute rheumatic fever is represented by exudative degenerative and fibrinoid changes in the collagenous tissue.

In the intermediate phase which is evident during the fourth to the thirteenth week of the disease swelling and fragmentation of collagen fibres and fibrinoid change are present in the nodule, but cellular proliferation is the main feature. There is accumulation of Anitschkow cells.

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## **MORPHOLOGY:**

Microscopically, Aschoff bodies are areas of inflammation of the connective tissue of the heart, or focal interstitial inflammation. Fully developed Aschoff bodies are granulomatous structures consisting of fibrinoid change, lymphocytic infiltration, occasional plasma cells, and characteristically abnormal macrophages surrounding necrotic centres. Some of these macrophages may fuse to form multinucleated giant cells. Others may become Anitschkow cells or "caterpillar cells", so named because of the appearance of their chromatin<sup>35,36</sup>.

## **OCCURRENCE:**

Aschoff's bodies or nodules are characteristic lesion of acute rheumatic fever. These are usually located in the interstitial tissue of the heart, specially in the myocardium and the endocardium often close to small blood vessels. Occasionally, they are present in the pericardium. These have been described in the adventitia of the aorta.

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## INCLUSION BODIES IN CYSTS

### RUSHTON/ HYALINE BODIES

**INTRODUCTION:** are first discovered by Deway (1918)

Rushton bodies may show up in examination of the gross specimen as small, white, dome shaped swellings measuring up to 0.1 mm on the epithelial surface and protruding into the cyst cavity. In microscopic sections, they appear as eosinophilic, linear, straight or curved or hairpin shaped, circular or polycyclic forms, often with a granular core and sometimes concentrically laminated. These are found almost always within the epithelial lining and only rarely in the fibrous capsule.

HBs are hyaline concretions of linear, curved, or circular shapes, often in a double strip as if an oval has been completely flattened with a little granular material at its centre, or like a hairpin, measuring about 0.1 mm in length and found in the lining epithelium of odontogenic cysts.<sup>37,38.</sup>

#### **Ultra structural findings:**

##### **Two forms:**

**Lamellated:** alternate electron dense and electron lucent layers ( 2-15).

Electron dense layers: homogenous , sometimes fine granular or mottled.

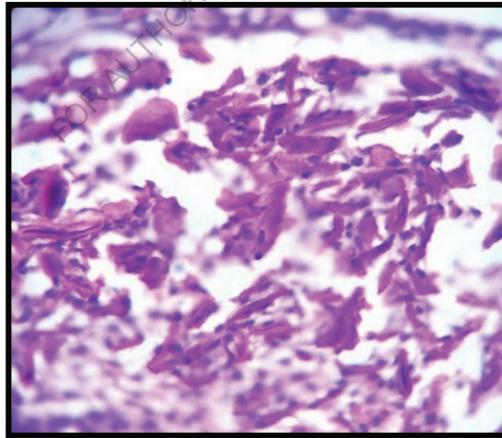
Electron lucent: granular or meshwork structures.

**Homogenous:** homogenous electron dense bands surrounding various structures like granular material, mineralized masses, cholesterol clefts.

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ORIGIN: There are several theories for formation of rushton bodies

- Keratinous or of hematogenous origin
- Elastotic degeneration or that it was the product of a cellular reaction to extravasated serum.
- Because of their sole occurrence in odontogenic cysts, the odontogenic epithelium has been strongly implicated in the genesis of Rushton bodies.
- RB are a secretory product of odontogenic epithelium deposited on the surface of particulate matter like cell debris or cholesterol crystals<sup>37</sup>



Rushton bodies. Eosinophilic, hyaline, linear and curved structures.

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**SPECIAL STAINS:** Orcein,

Mallory aldehyde fuchsin,

Papanicolaou

Gomori

**OCCURENCE:** Odontogenic cyst

Radicular cyst

Dentigerous cysts.

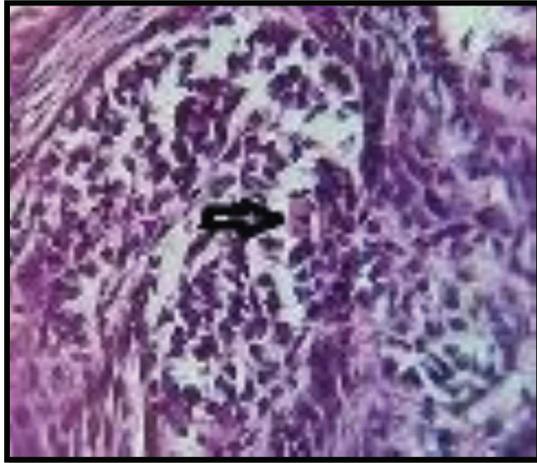
### **RUSSELL BODIES**

First described by William Russell in 1890

**RUSSELL BODIES** Russell bodies are fuchsinophilic, electron-dense homogeneous material found within distended endoplasmatic cisternae in plasma cells and also extracellularly in chronically inflamed tissues, consisting of aggregates of immunoglobulin.

Histological, immunohistochemical, and TEM studies have recently related their formation to hyperactivation of the immune system and hyperproduction of immunoglobulins, modulated and sustained by bacteria, such as gram negative anaerobes. These immunoglobulins are thought to accumulate in the intracisternal spaces of the plasma cells and form these bodies.<sup>39</sup>

The Russell body is characteristic of the distended endoplasmic reticulum. These are relatively common within plasma cells and follicle centre cells at sites associated with high antigen load within neoplastic lymphoid cells.<sup>40</sup>



Russell bodies: Round eosinophilic, refractile bodies devoid of nuclei.

**SPECIAL STAINS:** Safranin and Fucsin

Mallory trichrome and Mayer hematoxylin-Safranin  
O -Light green.

**OCCURENCE:** Periapical infections

Plasmacytoma  
Multiple myeloma  
Gastritis,  
Ulcerative colitis,  
Tonsillitis, cysts,

---

## **BODIES IN NEOPLASMS**

### **DUTCHER BODIES**

#### **INTRODUCTION:**

**Dutcher bodies** were described by Dutcher and Fahey in 1959 in patients with Waldenström's macroglobulinemia. Dutcher bodies are intranuclear inclusions of immunoglobulin protein droplets. They thought that the inclusions developed in the nucleus and were extruded through a ruptured nuclear membrane into the cytoplasm. It is now known that Dutcher bodies are actually cytoplasmic inclusions.

They commonly occurs in multiple myeloma which is a neoplasm of skeletal system and malignancy of plasma cells.

#### **MORPHOLOGY:**

Dutcher bodies which resemble nuclear inclusions are actually invaginations of cytoplasm into the nucleus. Eosinophilic intranuclear pseudoinclusions,.

Ultrastructurally, the nuclear pseudo inclusions are formed by a cytoplasmic invagination into the nucleus. They are smooth, membrane-bound, and surrounded by clumped chromatin. The pseudo inclusions are thought to result from the accumulation of immunoglobulin in the perinuclear cistern.<sup>41</sup>

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## **SPECIAL STAINS:**

- 1) Periodic Acid-Schiff-Positive
- 2) Wright-Giemsa

## **OCCURRENCE:**

- Diffuse large B-cell lymphoma
- Multiple myeloma
- Chronic synovitis
- Waldenstrom macroglobulinemia,

## **PSAMMOMA BODIES**

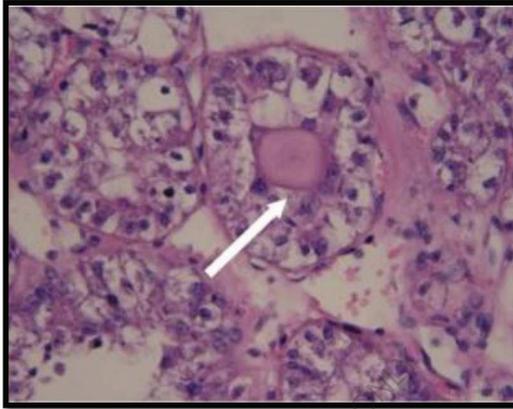
Psammoma bodies (PBs) are concentrically laminated calcific spherules that occasionally appear cracked (psammos [“sand”] oma [“tumor”]). They often are observed surrounded by cells and often appear either acidophilic or basophilic on Papanicolaou stain with a concentric appearance. PBs usually are associated with papillary neoplasms of various organs as well as a variety of benign conditions such as the use of intrauterine devices, oral contraceptives, endosalpingiosis, endometriosis, endometritis, and many others.<sup>42,43..</sup>

## **PATHOGENESIS:**

Psammoma body formation is due to necrosis followed by consequence of dystrophic calcification associated with ischemia.

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Psammoma bodies consist of laminated deposits of calcium salts with a proteinaceous matrix. This calcific nidus is then surrounded by a whorl of tumour cells of varying thickness.<sup>42,43,44.</sup>



Psammoma bodies: acellular, concentrically laminated calcifications.

## **OCCURRENCE:**

They are found in benign and malignant epithelial and connective-tissue tumors.

Psammomatoid Juvenile Ossifying fibroma

Psammomatous melanotic schwannoma

Cystadenocarcinoma

Nanobacteria promote crystallization of psammoma bodies in ovarian cancer.

Endometrial Papillary Carcinoma

Diffusely Sclerosing Variant of Papillary Thyroid Carcinoma

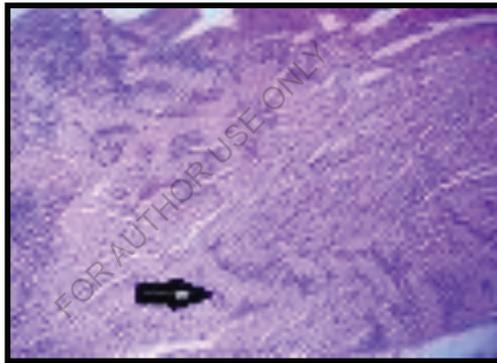
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## **VEROCAY BODIES**

Dr. Jose Verocay, Uruguayan physician in 1910 first described verocay body and considered diagnostic of schwannoma.

### **MORPHOLOGY:**

A typical Verocay body consists of a stacked arrangement of two rows of elongated palisading nuclei that alternates with acellular zones made up of cytoplasmic processes of the Schwann cells.



Verocay bodies: Elongated two rows of palisaded nuclei with a acellular zone.

### **PATHOGENESIS:**

The pathogenesis of the formation of this structure is explained by the overexpression of laminins in the cells that make up the Verocay body. Laminins are large glycoproteins that promote cell-cell adhesion and are normally found in the basement membranes of several types of cells including Schwann cells. Cell adhesion is an important function of Schwann cells and it

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facilitates myelination of axons and repair of nerve injury. Possibly the overexpression of laminins causes the alignment of nuclei of cells into a tight pattern of rows separated by acellular material in between. It has been hypothesized that such an arrangement of nuclei may be an adaptive response to maintain cell-cell interaction which may otherwise be disrupted due to increased matrix deposition of laminin and phospholipids like lysophosphatidic acid (LPA) which *in vitro* has been found to induce cluster formation in Schwann cells.

Striking formation of Verocay bodies in large areas of cutaneous neoplasms has been referred as “Rippled pattern”.<sup>45</sup>

OCCURENCE: Schwannoma

Rippled pattern seen in : Sebaceoma

Trichoblastoma

Fibrohistiocytic lesions.

Leiomyoma.

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## **SUMMARY**

Histopathological/inclusion bodies represent peculiar cytoplasmic or nuclear alterations. They also exhibit characteristic staining properties. As these are pathognomic for certain diseases, knowledge about the morphology and the occurrence of these bodies provides an excellent clue to the diagnosis of the disease.

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## ABSTRACT

## Behaviour Guidance

### 573 | Passive smoking and behavior and anxiety in dental clinics among children in Jeddah, Saudi Arabia

Manal Al Malik<sup>1</sup>; Heba Sabbagh<sup>2</sup>; Ghadeer Sharton<sup>2</sup>; Jumana Almaghrabi<sup>2</sup>; Narmin Helal<sup>2</sup>  
<sup>1</sup>Dental, Kfafh, Jeddah, Saudi Arabia; <sup>2</sup>Dental, KAU, Jeddah, Saudi Arabia

**Background:** Passive smoking has been linked to behavioural problems, but up to our knowledge no study assessed passive smoking relationship with dental anxiety. Therefore, this study aims to assess the relationship between passive smoking and both behavioural problems and dental anxiety among children.

**Methods:** The sample of this study was collected from two centers in Jeddah city, Saudi Arabia. Inclusion criterion is 5- to 16-year-old healthy children, attending their first dental visit with no emergency complain. The questionnaire including child's general information, environmental smoking exposure, child's anxiety assessment using Abeer Children Dental Anxiety Scale (ACDAS) and dental behaviour assessment using Frankl behavioural rating scale.

**Results:** From 500 children, 337 (67.4% response rate) answered the questionnaire with 201(59.6%) having being exposed to passive smoking compared to 136 (40.4%) who were not exposed. Exposed children had a statistically significantly higher tendency to develop anxiety ( $p = 0.002$ ) and uncooperative behaviour ( $p = 0.006$ ). Generalized Linear Mode and binary regression analysis suggested a statistically significant effect of passive smoking on children's dental anxiety and behaviour ( $p = 0.05$ )

**Conclusions:** Children exposed to passive smoking reported statistically significantly higher anxiety levels and showed uncooperative behaviour in the dental clinic compared to those who were not exposed.

### 293 | Acceptance of behavior guidance techniques utilized in pediatric dentistry in Khartoum locality

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**Background:** The study investigated the acceptance of behavior guidance techniques utilized in pediatric dentistry in Khartoum locality and compared these by age, gender and dental anxiety.

**Methods:** A total of 280 children aged 8-12 years participated in this study, 140 from private clinic (A) and 140 from public clinics (B). Each child was asked to fill a questionnaire for measurement of dental anxiety using the modified childhood dental anxiety faces version and then they watched six videos of behavior guidance techniques which included tell-show-do, positive reinforcement, modeling, enhancing control, protective stabilization and voice control. After watching the videos, children were asked to express their feeling toward each technique by drawing a line of favor. Spearman rank correlation test and chi-square test were used to test behavior guidance techniques acceptability rating by age, gender and dental anxiety.

**Results:** For the two study groups, positive reinforcement was the most accepted technique (86.4%), while protective stabilization was the least accepted technique (35%). There were statistically significant differences between the two groups regarding enhancing control, modeling, protective stabilization and voice control, with higher acceptability by children from private clinics ( $p = 0.007$ ,  $p = 0.002$ ,  $p = 0.001$ ,  $p = 0.001$  respectively).

Statistical analysis showed no effect of age, gender or dental anxiety upon behavior guidance techniques acceptability ( $p = 0.05$ ).

**Conclusions:** Children age 8-12 years were generally positive about the dentist's utilization of behavior guidance techniques. Positive reinforcement was the most accepted technique, while protective stabilization was the least accepted technique.

## 601 | Parental acceptance of different dental behaviour management techniques and its relation to dental fear, attitudes and family-related factors

Rana M. A. M. S. Alkandari; Gillian H. M. Lee; Cynthia K. Y. Yiu

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**Background:** Dental fear and anxiety might lead to avoidance of dental care and behaviour management problems. Various behaviour management techniques (BMTs) are used to reduce children's fear and anxiety (DFA), encourage positive behaviour and provide high-quality dental care. This study aimed to investigate the relationship between parental dental anxiety and the acceptance of behavior management techniques.

**Methods:** A total of 121 children 2-6 years old and their parents were recruited from the University affiliated dental clinic in Hong Kong. Online self-completed structured questionnaire was used to collect information. The questionnaire includes five parts: Parenting Style and Dimension Questionnaire (PSDQ), Corah Dental Anxiety Scale (CDAS), Children Fear Survey Schedule-Dental Subscale (CFSS-DS), parental acceptance to different BMTs used in paediatric dentistry, and sociodemographic information. Parents rated their preferences to after watching a video demonstration on the BMTs. Chi-square tests and Fisher's Exact Test were used for statistical analysis. The significance level was set at P0.05.

**Results:** Over half (57%) of the parents had low dental anxiety level, while 80.2% of children had DFA. Most common parenting style of the parents was training style (52.9%), followed by authoritative (27.3%), authoritarian (16.5%) and permissive (3.3%). Parents preferred non-invasive BMTs. Positive reinforcement (100.0%) and distraction (98.3%) were the most accepted BMTs. General anesthesia was the least preferred. The parenting styles were associated with the levels of preferences for audiovisual distraction ( $p = 0.036$ ).

**Conclusions:** Parents preferred non-invasive BMTs such as positive reinforcement and distraction for their children. Parenting style should be considered when choosing BMTs.

## 541 | Pain catastrophizing in pediatric dentistry

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**Background:** Catastrophizing is described as an exaggerated negative orientation to a painful stimulus. Catastrophic individuals are defined as individuals who have

difficulty magnifying or exaggerating the danger or distracting. Determining the catastrophic individual provides the prevention or reduction of pain during treatment by behavioral management and appropriate drug selection.

**Literature Review:** The patient is the best reporter of pain, and this may be difficult to understand for the dentist, who tends to establish a relationship between the level of pain and the level of tissue damage. In recent years, it has been focused more on children's perception of pain because their pain cannot be predicted and treated successfully.

Various techniques are used in dentistry to guide the child's behavior. These are divided into primary and advanced behavior guidance techniques. Basic behavior guidance techniques are voice control, silent communication, presence or absence of parents, distraction, positive encouragement, tell-show-do, reinforcement technique, desensitization, and typification. Appropriate approaches should support communication with the child's structure to establish a strong bond with the child. It was reported that catastrophic individuals had difficulty directing their attention to something other than pain during the treatment. It was reported that catastrophic individuals experienced less concern when discussing their treatment experiences during dental hygiene treatments.

**Conclusions:** Prior knowledge of the patient's catastrophic thinking level ensures that treatment plans, as well as other variables related to pain, are planned more individually.

## 1456 | COVID-19 pandemic impacts in child maltreatment: The role of pediatric dentists

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**Background:** Child maltreatment is a world-wide social problem that needs attention. During the pandemic, COVID-19 authorities have reported an increase in violence against the most vulnerable populations, such as children. The dentist, especially the pediatric dentist, has an important role in the diagnosis of these cases. After the diagnosis of maltreatment, the professional must report the case to the competent authorities, if he has the knowledge and adequate training to do so.

**Literature review:** The social isolation determined by the pandemic contributed to an increase in family conflicts, and domestic violence against children, which was already prevalent, intensified throughout the world, including in Brazil. The victims were left without the supervision of persons outside of the family due to the closure of schools. Therefore,

it is necessary to know the forms of care and attention being given to signs of violence. After pediatricians, pediatric dentists are often the ones who have the opportunity to identify a child abuse victim.

**Conclusions:** It is concluded that health professionals and educators have an important role in the observation of cases of child abuse. Pediatric dentists are important in identifying the oral health issues that can be associated with child abuse victims and have a legal obligation to report these cases.

### 1676 | Parental acceptance of behavior guidance techniques in two different countries of residence

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**Background:** The aim of this study was to compare the difference in Behavior Guidance Techniques (BGTs) acceptance between Mexican-born individuals living in Mexico and Mexican-born individuals living in the USA.

**Methods:** English- or Spanish-speaking subjects born in Mexico were recruited based on their child's age (3-8 years old) and their child's medical history (healthy). Subjects were parents of patients of record at UCLA School of Dentistry affiliated dental clinics or UADY dental clinics. Parents completed a questionnaire to establish demographics and determine their approval ratings of BGTs on a 7-point Likert scale for scenarios describing 15 BGTs recommended by the AAPD. This study examined three groups: Mexican-born individuals living in Mexico (MexAmSpan), Mexican-born individuals living in the US using Spanish as their primary language (MexAmSpan), and Mexican-born individuals living in the US using English as their primary language (MexAmEng). The means and standard deviations were calculated for each BGT. The Kruskal-Wallis test for non-parametric data was performed to test statistical significance.

**Results:** 71 parents answered the questionnaire. There was statistically significant ( $p < 0.05$ ) in tell-show-do (TDS), non-verbal communication (NC), voice control (VC), parental absence (PA), IV General Anesthesia (IVGA) and OR General Anesthesia (ORGA). The acceptance of TDS, distraction, positive reinforcement, positive imagery, modeling, ask-tell-ask, and memory restructuring was shown in all groups. However, Mexican group disapproved IVGA and ORGA,

MexAmSpan group nitrous oxide, ORGA, VC, PA and MexAmEng group PA and protective stabilization.

**Conclusions:** Results suggest that country of residence should be considered when BGTs are selected.

### 1853 | Dental anxiety and intelligence quotient among 10-year-old Indian children: A cross-sectional study

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**Background:** Cognitive ability and intelligence of children play a major role in determining their behaviour and attitudes. The aim of this study was to assess the association between dental anxiety (DA) and intelligence quotient (IQ) among 10-year-old Indian children.

**Methods:** This cross-sectional study was carried out among 202 children in Karur district, western Tamil Nadu, India. DA and IQ levels were measured using the Children's Fear Survey Schedule - Dental Subscale (CFSS-DS) and Raven's Coloured Progressive Matrices (RCPM), respectively. Chi-square test was used to analyse the differences in the categorical variables related to DA and IQ. Spearman rank order correlation test was used to assess the correlation between the two variables.

**Results:** Seventy-five (37%) girls and 127 (63%) boys participated in this study. Children with higher IQ scores expressed less anxiety. However, there was no statistically significant correlation between IQ and DA ( $p = 0.19$ ). Gender-based comparison revealed that there was no significant difference in IQ scores ( $p = 0.74$ ) and DA levels ( $p = 0.29$ ).

**Conclusion:** This study found no statistically significant correlation between children's IQ and DA scores.

### 1342 | Evaluation of dental students' perceived and dental environmental stress levels during the COVID-19 pandemic period

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**Background:** COVID-19 is a newly discovered infectious Coronavirus that became a pandemic disease. The objective of this study is to assess perceived and dental environmental

stress levels of dental students during COVID-19 pandemic period.

**Methods:** This cross-sectional study was conducted between June and July on dental students at Istanbul University Dentistry Faculty, Istanbul, Turkey. A total of 303 preclinical and clinical students (Female:203, Male:100) answered an online questionnaire that consisted of their socio-demographic information, 14 questions of perceived stress scale (PSS) and 22 questions of dental environmental stress scale (DES). Statistical analysis was performed using Chi-square test, Mann–Whitney *U* test, Kruskal–Wallis test, independent *t*-test and one way ANOVA.

**Results:** According to the PSS, the preclinical students felt more stressed during the pandemic period than the clinical students ( $p = 0.05$ ). According to DES, the clinical students are more stressed than the preclinical students regarding confidence in themselves to be a successful dentist ( $p = 0.016$ ), not having the possibility to pursue a postgraduate programme ( $p = 0.001$ ), the difficulty of manual dexterity ( $p = 0.001$ ), postponement of marriage or engagement ( $p = 0.001$ ) and personal health ( $p = 0.045$ ). Clinical students are more stressful about the faculty administration ( $p = 0.008$ ) and preclinical students about the workload ( $p = 0.001$ ). DES scores of female students are higher than males ( $p = 0.005$ ).

**Conclusions:** The COVID-19 pandemic has affected the stress levels of dental students. Stress management programs and online counseling services can help reduce the stress sources of dental students.

### 1093 | An anxiety reduction program for reducing the need for dental treatment under general anesthesia

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**Background:** To investigate the efficacy of a systematic Anxiety Reduction Program (ARP) using progressive desensitization to reduce anxiety in children to a level allowing dental treatment to be comfortably accomplished in-office and minimizing the need for general anesthesia (GA).

**Methods:** In this retrospective pilot study, we examined records of 227 patients who underwent ARP during 2017-2019. Inclusion criteria included healthy children who came to our office directly or had been referred by dentists who were not successful at performing in-office treatment due to the child's high level of anxiety. Data were collected for patients

age, gender, referring specialty, anxiety level at first visit, age at 1st ARP, number of ARP's and whether treatment was provided in-office or with GA.

**Results:** Preliminary data show that significantly more patients (205 of 227; 90%) were able to proceed with in-office treatment than had to undergo treatment under GA (chi-sq;  $p = 0.001$ ). Furthermore, patients were able to successfully complete in-office treatment regardless of their initial level of anxiety (median Frankle Behavior Rating Score = 1; logistic regression;  $p = 0.1$ ). Some patients recommended for GA at another office came on their own for a second opinion due to parental fear of GA, or the expense. Most of those children successfully completed in-office treatment after their ARP visit (108/118; 92%; chi-sq;  $p = 0.001$ ). Of the patients, 55% of patients referred to our office, 26% were referred by a general dentist and 26% were referred by a pediatric dentist. Also, children were equally successful across ages (range 2.1-15.3 years) at undergoing in-office treatment after their ARP visits (logistic regression;  $p = 0.7$ ). Boys and girls were equally successful at undergoing in-office treatment after ARP (logistic regression;  $p = 0.8$ ) with the majority of children needing only a single visit of ARP at 88% and 9% needing 2 visits and 3% needing 3 visits.

**Conclusions:** Our data suggest that when pre-operative programmed systematic desensitization is carried out by either support staff or dentist, it allows most children to have successful in-office outcomes without the need for restraints, quiet rooms or GA. This greatly reduces the costs and risks associated with GA, increases parental satisfaction, and more importantly reduces long-term adverse memories of traumatic experiences.

### 482 | Parenting styles impacting the child behaviour and oral health

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**Background:** According to AAPD, all children vary in their response to dental experience. Parents and caregivers teach the kids to deal with aversive situations. It is further interesting to study the role of parents in a dental setting. A cross-sectional observational descriptive study was planned to evaluate the relationship between parenting style, sociodemographic data, caries status, and child's behaviour during the first dental visit.

**Methods:** Total 140 Parents/Caregivers of new patients coming to OPD in age group of 3-6 years completed the Parenting Styles and Dimensions Questionnaire (PSDQ) and

also a 15-question demographic survey. On the first visit, oral prophylaxis and assessment of child behaviour was performed using the Frankel Rating scale (inter-examiner reliability 92%). Then, children were examined for presence of dental caries. Statistical analysis was performed using SPSS 22.0.

**Results:** Children with authoritative parents exhibited more positive behaviour ( $p$  0.001) and less caries ( $p$  0.001) compared to children with authoritarian and permissive parents. Children attending school exhibited more dental caries and positive behaviour compared to children who did not ( $p = 0.03$ ). Association of age with dental caries was not statistically significant whereas association of age with child behaviour was statistically significant.

**Conclusions:** Authoritative parenting was associated with less caries and better behaviour followed by authoritarian and permissive styles. School and age also have a definite impact on child behaviour.

### 1482 | Evaluation of child and parent characteristics on dental fear ratings in children using the children's fear survey schedule: Dental subscale

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**Background:** Dental fear can be challenging among children and often results in avoidance of dental treatment and deteriorating oral health. Data regarding dental fear in children are scarce in Ibadan, Nigeria. The aim of this study was to assess children's fear and compare children's self-rated fear and parent-reported children's fear.

**Methods:** This cross-sectional study was conducted among 206 child-parent pairs visiting the Paediatric Dentistry clinic of the University College Hospital Ibadan, Nigeria. Data were collected using the Children's Fear Survey Schedule-Dental Subscale (CFSS-DS). Data were analyzed using Students  $t$ -test, Spearman's test, and Chi-square test

**Results:** A total of 206 parent-child dyads participated in the study. The mean age of the child and accompanying parent was  $9.36 \pm 3.12$  years and  $42.08 \pm 6.69$  years, respectively. Children's self-reported fear showed that a majority of children (77.2%) fell into the low fear category, while the parent's rating showed that (80.6%) had low dental fear. The three most feared items reported by the children were injections, the sight of a dentist drilling, and the dentist drilling. There were no significant differences in the fear scores

regarding the ages and gender of the children ( $p$  0.05) with both self-rated and parent-rated scores.

**Conclusions:** Majority of the children had low dental fear. Children's self-rating and parents-rating of their children's dental fear were similar. Children were most afraid of injections and the dentist drilling. Options of injection and dental drill-free dentistry should be explored.

### 938 | Comparative evaluation of effect of two relaxation breathing exercises on anxiety during buccal infiltration anaesthesia in children aged 6-12 years: A randomized clinical study

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**Background:** The study evaluated dental anxiety using Pin Wheel Breathing Exercise and Diaphragmatic Breathing Exercise without Pin Wheel during buccal infiltration anesthesia in children aged 6-12 years.

**Methods:** 60 children in the age group of 6-12 years with Frankel's behavior rating score of 3 who required buccal infiltration local anesthesia were selected. Subjects were divided randomly into two groups i.e., Group A: Children who performed Pin Wheel Breathing Exercise and Group B- Children who performed Deep breathing exercise without Pin Wheel. The level of anxiety of patients was recorded using an animated emoji scale by asking child to choose one of the animated emojis on the electronic display (laptop) that best matched their feelings at that moment. The data were analyzed using IBM SPSS version 20 software with paired  $t$ -test and chi-square test.

**Results:** There was significant reduction in dental anxiety score from Score 1 (Before the anesthetic procedure) to Score 2 (After the anesthetic procedure) in both the groups. On intergroup analysis, children who performed Pin Wheel Breathing Exercise (Group A) showed higher values than children who performed Deep breathing exercise without PinWheel (Group B).

**Conclusion:** Pinwheel breathing exercise as well as Diaphragmatic breathing exercise proved to be significantly effective in reducing dental anxiety during local anesthesia. Whereas, Pinwheel breathing exercise had shown greater reduction in dental anxiety when compared to Diaphragmatic breathing exercise.

## 1121 | Community health service: Internship of French dental students

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**Background:** Since September 2018, the National Health Service is mandatory for French healthcare students. This is 6 full-time weeks dedicated to health promotion and integrated into the university curriculum. In our institution, we manage 1 year of theoretical courses for 3rd-year students and then activities on the field (oral health education sessions: OHES). Every student's group should design their own activities (content and tools). OHES began in October 2019. We present the results of this first year of fieldwork.

**Methods:** We worked on the student's reports. We selected reports on OHES with a children's audience (65%). Reports contain quiz and narrative sections. We propose quantitative and qualitative analysis according to the part of the report.

**Results:** 26 working groups (65 students) choose OHES targeting children, from pre-school to high school. The knowledge activities are multiples but quiz and dinette come up very often (28 and 22%). Most of the practical activities rely on mouth macro models (60%) and teeth brushing (24%). Students report progress on communication skills (31%), capacity to adapt their language to children (60%), developed team's work (36%), and project management (30%). Student's satisfaction focuses on the feeling of « being useful » (26.5%) and being able « to transfer of knowledge to children » (32%). 25% realized the need for dental health information for children.

**Conclusions:** This first year of OHES shows that dental students are both capable to develop and implement health preventive activities with children. It makes them feel legitimate as actors of community dental health.

## 639 | Function of the family unit, oral hygiene rules and attitudes to dental health in children during first-wave 2020 COVID-19 lockdown

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**Background:** To examine whether general and dental health and habits of families were affected by the first-wave

lockdown due to COVID-19, and whether these habits were related to family functioning, resilience and stress.

**Methods:** A cross-sectional study using an online survey disseminated among families with kindergarten and primary school-aged children during the lockdown of March and April 2020.

**Results:** A total of 361 respondents completed the survey. Most respondents adapted well to the changes imposed by lockdown and reported that they and their children had low anxiety levels and high mental resilience. Family functioning and behavior were positively correlated with nutrition habits and hygiene. General hygiene was positively correlated with oral hygiene. Respondents who reported requiring dental care had difficulties gaining access to it. Most respondents perceived that it is important to improve patients' digital access to pediatricians and dentists during crises.

**Conclusions:** The study showed that better family functioning was associated with better family hygiene and nutrition, parental resilience and lower mental stress among children.

## 1201 | Prevalence of dental fear in children between 5 and 14 years old in Medellin, Colombia

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**Background:** Dental fear (DF) has been associated with dental avoidance leading to an epidemiological impact on the oral health of the population, and more specifically in children, thus making its diagnosis and management most relevant. The objective of this study was to evaluate dental fear (DF) in children in the city of Medellin, Colombia.

**Methods:** The validated Spanish version of the Dental Subscale of the Child Fear Survey Schedule (CFSS-DS) was applied to 250 parents of children between 5 and 14 years old who attended 18 randomly selected public and private dental clinics in Medellin, Colombia. A statistical analysis was completed using the STATA<sup>®</sup> version 12 software program in order to estimate the prevalence of DF as well as the associated factors.

**Results:** Overall average DF score was 28.5 (SD 11.4) according to the CFSS-DS scale (15-75) with a score above or equal to 32 considered to be indicative of DF; moreover, a prevalence of 30.4% in the population was observed. No significant differences were observed between DF and age, gender, socioeconomic level, age of parents or school grade.

**Conclusions:** Results indicate that the average DF score was low and that the prevalence of DF in Medellín was comparable to those reported in similar studies in other cultures.

No differences were observed between possible associated factors and dental fear.

## 712 | Translation and validation of “Dental Discomfort Questionnaire” (DDQ) instrument into Chilean population

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**Background:** Pain is a subjective perception and children often do not have the ability to explain it. In Chile, there are no validated instruments that assess dental pain in preschoolers. This study aimed to adapt cross – culturally the existing DDQ into the Chilean language and culture.

**Methods:** A focus group with Pediatric Dentists was conducted to analyze DDQ components. Two independent bilingual translators, whose native language is Chilean Spanish, did a conceptual translation of DDQ, which were compared to identify differences and reach an agreement to obtain a single translation of the instrument. This was back-translated into English by native speakers, analyzed and approved by research team together with the author of the original DDQ and a methodology expert. This final version was tested on 30 people, using a digital questionnaire. Research team assessed results and comments to set up a final questionnaire.

**Results:** Participants indicated that the questionnaire items were clear and no more than 10 minutes were required to respond. They proposed including some new questions.

In general, there was a tendency to answer the option "never", so no variability was collected due to the low number of answer options. Reliability (ordinal alpha) was 0.95.

**Conclusions:** For the DDQ to be applied in the Chilean population, it is necessary to reformulate items and response options, incorporating questions related to the comments provided by the parents. A comprehensive adaptation process is required to achieve results that allow valid instruments to be obtained for the target.

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## 808 | The effect of multiple adverse childhood experiences (ACEs) on oral health in children and adolescents: A scoping review

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**Background:** This review was conducted to explore the effect of multiple ACEs on oral health in children (0-10 years) and adolescents (11-18 years), from the existing literature.

**Literature Review:** ACEs are defined as, ‘the types of abuse, neglect, and other potentially traumatic experiences that occurred to people under the age of 18’. ACEs are associated with anxiety, anger, fear and depression. To cope with these situations, individuals may use health risk behaviours such as smoking, alcohol, overeating, drug abuse or sexual behaviours, causing adverse health and social outcomes. As there is little evidence on the effect of ACEs on oral health, we conducted a scoping review. Scoping reviews are more flexible and iterative; therefore, we were able to change our research questions and search strategy based on the existing evidence. Majority of the review studies found graded association between multiple ACEs and dental caries. Especially in neglected and abused children and adolescents, higher risk of dental caries was observed.

**Conclusions:** This review and the current evidence suggest higher risk of dental caries and other adverse oral outcomes in children and adolescents experiencing 2 or more ACEs. However, due to the limitations of the review, further investigation is suggested. A longitudinal study is suggested to examine the long-term consequences of ACEs on oral health at various stages of life through follow-ups with the participants. The findings from this review can help us to develop better oral health policies and interventions to identify and prevent poor oral health caused due to ACEs.

## 357 | Preference of essential oils among children: A cross sectional study

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**Background:** The therapeutic use of essential oils, popularly known as aromatherapy, is documented to decrease the dental anxiety in children.

The aim of the present study is to determine the preference of essential oils among children and additionally appreciate the influence of age and gender.

**Methods:** A convenience sample of 1000 healthy school going children in the age range of 7 to 15 years were recruited in to the study. The participants were presented with blotter

strips dipped in four undiluted essential oils; Sweet orange, Lavender, Peppermint, and Spearmint. The preference of all the children was recorded. The data were tabulated and analyzed statistically.

**Results:** The preference of essential oils was sweet orange followed by peppermint, lavender and spearmint. The difference in the preference of oil among age groups was not significant ( $p = 0.183$ ). However, gender had a statistically significant influence, with most girls preferring sweet orange and least opting lavender ( $p = 0.001$ ).

**Conclusion:** This study demonstrates that children do have scent preferences for essential oils and that these preferences may vary with gender. It supports the fact that the response to essential oils is a complex process affected by multiple variables including gender, cultural exposure to specific odors, and/or individual experiences that create either pleasant or unpleasant memory associations

## 1862 | Application of virtual reality in pediatric dentistry: A review of literature

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**Background:** Virtual reality refers to “a technology that superimposes a computer-generated image on a user’s view of the real world, thus providing a composite view.” Different digital technologies are becoming common in the field of pediatric dentistry. Virtual reality (VR) is an emerging technology which can be used to address challenges innovatively.

**Literature Review:** Distraction is a commonly used non-pharmacologic pain management technique. VR helps in distracting patients from fears provoked by objects and situations in a well-controlled, computer-generated virtual environment until their fears and anxieties disappear. These benefits may be related to more immersive images due to the occlusive headsets that project the images right in front of the eyes of the user and block out real-world stimuli. The child’s attention is focused on what happens in the virtual world rather than on the surrounding environment. The application of VR distraction is based on the assumption that pain perception has a large psychological component and that pain attracts a strong attentive response causing anxiety.

**Conclusion:** The findings of various studies confirm the efficacy of VR distraction in the dental setting. It has a positive effect on pain, anxiety and behaviour due to a combination of the audio, visual and kinaesthetic sensory modalities in VR. It also reduces operatory stress on the pediatric dentist. Hence, this technique can be utilized in routine pediatric practice as an adjunct to other behaviour management techniques.

## 774 | Impact of COVID-19 pandemic on behavior management strategies in paediatric dentistry

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**Background:** COVID-19 pandemic has caused difficulty in management of patients in every healthcare unit so behaviour management techniques won’t be exception for it. Many changes are in queue to strategize the use of behaviour management techniques effectively.

**Methods:** A validated close-ended questionnaire consisted of 26 questions was prepared on behavior management of children and paediatric practice before the COVID-19 pandemic and after release of lockdown and then sent to paediatric dentists in India. Their data of responses were collected. The data were then entered in an excel spreadsheet and statistically analysed to draw inferences.

**Results:** There was no significant difference observed for the use of behavior management strategies before the COVID-19 pandemic and after release of lockdown. Previously, only non-pharmacological behaviour techniques were preferred but after the release of lockdown pharmacological techniques are also being preferred along with nonpharmacological techniques by paediatric dentists in India. The use of modeling as behavior management technique has been increased after release of lockdown.

**Conclusions:** The potential of use of behavior management strategies has been changed because of the COVID-19 pandemic for decreasing the risk of cross-infection. Along with this, children’s coping skills with paediatric dentists wearing personal protective equipment (PPEs) have also been affected. Paediatric dentist should make himself a compatible candidate for use of the behavior management strategies for better treatment plan in the pandemics like the COVID-19 pandemic.

## 442 | Does your child patient accept your new look and practicality of using behaviour modification techniques in COVID times?

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**Background:** The coronavirus has challenged health care professionals and dental professionals play a pivotal role in preventing transmission of COVID-19. This study aimed to evaluate knowledge, attitude, skills, preparedness of pediatric dentist in managing a pediatric case in COVID times.

**Methods:** A cross-sectional questionnaire survey was conducted in September 2020 on 52 pediatric dentist in India to assess their knowledge, awareness and skills. Data were subjected to appropriate statistical measures and analyzed.

**Result:** 52 dentists 23.08% were having an experience of 3 years and more. 100% of pediatric dentist were aware that its pre requisite to screen the patients and attendants for temperature and use of pre procedural 1% hydrogen peroxide is mandatory. 80.77% suggested using child's favourite coloured PPE and animated masks and face shield to reduce procedural anxiety. 92.31% agreed preferring Halls technique, lasers, remineralizing agents and silver diamine fluoride rather than drilling in multiple carious lesions.

**Conclusion:** A knowledgeable pedodontist should follow latest guidelines in managing children in dental operatory as behaviour modification technique are hampered due to use of PPE in cases requiring urgent dental care.

## 562 | Ions that anesthetize

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**Background:** Aim was to compare and assess the efficacy of deep Topical Anesthesia [with 15% Lidocaine spray] infused via Iontophoresis and Local Anesthesia [Infiltration of 2% Lignocaine solution] for dental procedures among 4-12-year-old patients.

**Methods:** A Randomized Clinical Trial with sample size of 110 primary teeth among patients of 4-12 years age group. The subjects were randomly divided into 2 groups. In the First group, topical anesthesia was achieved by 15% Lignocaine HCL topical spray applied by Iontophoresis and second Local infiltration of 2% Lignocaine solution, where the procedure for extraction and pulpectomy of primary teeth were performed. Digital Iontophoresis unit with indicator for intensity and duration of application was utilized. Subjective assessment was performed immediately after anesthesia with WBFPRS.

**Results:** Study established that mean value of current intensity was  $9.43 \pm 0.95$  for Extraction procedure and duration of application was  $1.85 \pm 0.80$ . For Pulpectomy procedure, mean value of current intensity was  $9.07 \pm 1.34$  and duration of application mean value at  $2.40 \pm 0.74$ . In Intergroup comparison of WBFPRS, scores were lower in Iontophoresis group ( $1.96 \pm 1.64$ ) compared to Local Anesthetic group ( $3.62 \pm 1.11$ ) which was statistically highly significant with a  $p$  value of 0.001.

**Conclusions:** Iontophoresis as noninvasive technique for topical anesthesia was more acceptable over the Local Infiltration among the pediatric patients.

## 1434 | Vibrate and inject: Diminished pain local anesthesia delivery

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**Background:** Pain is an unpleasant sensory or emotional experience. The administration of local anesthesia (LA) is the key to controlling pain during dental procedures. Effective pain control during LA administration in pediatric patients is the foundation of successful behaviour management.

**Literature review:** Gate control theory explains the alteration of pain perception through counter pressure applications. Methods like vibration stimulate A-beta fibres carrying non-noxious motion signals and block the conduction of A-delta fibres carrying acute pain signals which are triggered by LA injection.

**Conclusion:** Vibration as a counter-stimulatory method on subjective pain (pain perception) reduces pain reaction during LA administration and thus gains child's cooperation.

## 1747 | Music distraction: A contrivance juxtapose to non pharmacological behaviour guidance techniques: A review of literature

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**Background:** Behaviour Guidance forms the mainstay of successful treatment to pediatric dental patients. Due to the changing trend where the use of aversive techniques of behaviour guidance is not acceptable to the parents, Music Distraction becomes a useful non pharmacological means of behaviour guidance that can help in providing effective behaviour guidance for children undergoing dental treatment.

**Literature Review:** The use of music distraction can be a useful tool in pediatric dentistry to provide effective dental treatment in children. Music is shown to increase the release of Dopamine which is a feel good chemical that can allay and soothe the anxious mind also music can be utilized to regulate mood. Because of its rhythmic and repetitive aspects, music engages the cortex of our brain, which calms us and reduces impulsivity Literature review has shown that music can have a soothing effect on the children and also help in reducing the anxiety of the child. Many authors have used music in various forms like nursery rhymes, the music of child's preference, film songs (Hollywood/ Bollywood), folk music etc and have shown promising results.

**Conclusions:** The literature review carried out concluded that music distraction is a tangible and cost effective method of behaviour guidance that can be used by pediatric dentist to provide effective dental treatment to children.

## 1799 | Oral self-mutilation in children

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**Introduction:** Self-mutilation is defined as a form of destruction or tissue damage intentionally caused in the body, which can affect any individual and requires the attention of the pediatric dentist for its identification and diagnosis (Hildebrand et al., 2011; Limeres et al., 2013).

**Case report:** This work presents three clinical cases of children without syndromes or diseases, attended at the Pediatric Dentistry Clinic of the Ribeirão Preto School of Dentistry, who presented self-mutilating behavior: Case 1: Male patient, 6 years and 4 months old, practices onychophagy, object biting and self-mutilation, biting the cuticles around the nails; Case 2: Male patient, 7 years and 2 months old, the presence of unilateral lesion in the free gingiva adjacent to the buccal surface of tooth 54, caused by scratching was observed; Case 3: Female patient, 9 years old, the patient tightened the mucosa of the lower lip and the mucosa of the cheek with her fingers, causing injuries and bleeding.

**Discussion:** The diagnosis of this condition is complex and becomes a challenge for health professionals due to the numerous clinical presentations of oral lesions. A differential diagnosis is necessary to classify an injury as self-mutilation (Hildebrand et al., 2011; Limeres et al., 2013; Cannavale et al., 2015; Stoica et al., 2020).

**Conclusion:** Health professionals should be aware of signs of self-mutilation in their patients. Treatment strategies are individual and require the attention of a multidisciplinary team.

## 1144 | Development of an evaluation form for the assessment of the best therapeutic process in paediatric dentistry: A pilot study

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**Background:** In paediatric dentistry, there is a lack of studies focusing on predicting the most suitable therapeutic process after the first dental visit. The aim of the study was to develop an objective evaluation form, based on three indexes (psychological index, family support index, dental therapies complexity index), able to identify, from the first dental visit, the best therapeutic process for each child (outpatient procedure, inhalation conscious procedure, pharmacological sedation, general anaesthesia).

**Methods:** A total of 30 children underwent a first dental visit. One dentist carried out the visit, chose the best therapeutic process, without the aid of the evaluation form, and scheduled dental therapies, while the other one observed the dental visit and filled in the evaluation form. After dental treatments, the value obtained from the evaluation form was compared with the therapeutic procedure actually carried out to observe if there was a concordance, assessed through Cohen's Kappa. Finally, Fisher test was performed for the statistical analysis.

**Results:** The overall concordance between the results obtained from the evaluation form and the therapeutic procedure actually carried out turned out to be 73.30%. Within the indexes, a statistically significant association was detected between the family support index and the psychological index ( $p = 0.02$ ), but not between dental therapies complexity index and both family support index ( $p = 0.30$ ) and psychological index ( $p = 0.63$ ), respectively.

**Conclusions:** The evaluation form was able to help clinicians to better direct the child towards the most appropriate therapeutic dental process.

## 1496 | Say no to pain, and save time!! Use of chemomechanical caries removal agent or smart burs

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**Background:** The study evaluated the pain reaction and the time taken for caries excavation with newer chemomechanical agent (Brix 3000) and smart burs (SS White polymer burs) in deciduous molars.

**Methods:** The selection of patients was done according to inclusion criteria and the selected patients were randomly chosen for one of the two procedures, i.e., Group A- chemomechanical agent (Brix 3000) OR Group B- smart burs (SS White polymer burs). Application of Brix 3000 and use of burs was done according to the manufacturer's instruction. The pain reaction of the child was recorded by a constant observer with help of SEM scale during the procedure, and the total time taken for both the procedures was monitored with timer.

**Results:** The results were calculated using Mann-Whitney U test, with significant difference seen between group A and B. Group A (Brix 3000) showed superior results compared to group B (Smart burs) with Brix 3000 taking less time and showing minimal pain reaction.

**Conclusions:** We can conclude that the newer chemomechanical agent (Brix 3000) can be an effective alternative to other minimally invasive techniques.

## 1718 | Evaluation of the effectiveness of dietary counseling in preschool children, in relation to caries and consumption of a healthy diet

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**Background:** A dietary counseling in preschool children allows us to see the feeding problems and work as a team with parents to solve the situation to prevent or stop not only caries lesions but other diseases related to dietary consumption. Therefore, the aim of this study was to assess the efficacy of dietary counseling in children with early childhood caries (ECC).

**Methods:** The sample consisted of 113 preschool children with early childhood caries attended at the Pediatric Dentistry Clinic of the University of Chile. A diet diary was requested to evaluate the food consumed during one week; the children

studied were grouped according to their initial weight in: underweight, normal weight, overweight and obesity. The dietary counseling focused not only on dietary advice in relation to caries, but also in relation to a healthier diet, to reduce the intake of sugars, carbohydrates and foods rich in fat, indicating a balanced diet, based on the four food groups.

**Results:** The results showed that there were changes in the weight of the children studied. It was observed that 25% of the children presented positive changes in relation to the initial weight, extreme values of underweight and overweight had improved their state migrating towards normality. Statistical analysis showed a significant difference with respect to weight distribution in the study sample ( $p$  0.0167).

**Conclusions:** The results showed that dietary counseling can be favorable for the children not only for the prevention of caries, but also to maintain and regulate their weight, determining healthier values.

## 1967 | Effectiveness of teleadaptation on pediatric patient return during COVID-19 pandemic

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**Background:** Teleadaptation arised to adapt the pediatric patient to the safe return to the dental office and to achieve positive behavior during dental treatment in response to physical and dental environment restrictions imposed by COVID-19 pandemic. The pediatric patient is the "bi-unit" guardian/child we considered at the time we established assertive styles of communication according to each one in order to favor their adaptation to a safe physical and mental return.

**Methods:** To evaluate the effectiveness of this protocol on pediatric patients return who were undergoing Functional Orthopedics, Rehabilitation and Prevention treatments started before the pandemic, a descriptive study was carried out with a sample of 74 patients between 4 and 21 years of age of both genders taking into account a Frankl scale before pandemic and after return. We applied two styles of communication, one for guardians and another one for children that consisted in detailed written digital content sent during and after lockdown and videoconference to the guardians prior opening, pre-filmed playful videos for each dental procedure that were watched by children prior to each kind of treatment as a complement to behavior management techniques and colorful textiles/barriers/signs as a main tool of non-verbal communication.

**Results:** 95.95% effectiveness was obtained in the return of patients, and 96.9% of the children showed positive behaviour after treatment according to Frankl scale.

**Conclusion:** Teleadaptation acted positively to adapt the pediatric patients to a safe return to the dental office, to achieve positive behavior during treatments and to follow them on a regular basis in this unstable current pandemic.

## 255 | Dental phobia among the Kenyan Asian population

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**Background:** The study investigated dental phobia among the Kenyan Asian population.

**Methods:** A descriptive cross-sectional study was carried out at a community-based center, the Jaffery Islamic Centre, Nairobi. A total of 79 Kenyan residents of Asian descent were interviewed using a self-administered questionnaire (open-ended and close-ended questions). Dental anxiety was measured using the Modified Dental Anxiety Scale.

**Results:** 40(50.6%) of the participants were females, and 39(49.4%) were males. Most of the participants belonged to the 18-35 years age category 51(64.56%). The majority 71(89.9%) had been to a dentist before, most 25(35.2%) having visited for fillings or root canal treatment. The procedure associated with the most discomfort was fillings and RCT 29(40.8%) followed by extraction of teeth 22(30.99%). Administration of injection was found to be the major source of anxiety 45(16.4%). 16(20.25%) had previously missed a dental appointment. The prevalence of dental phobia was 16.46%, females reporting a higher incidence 9(22.5%) than males 4(10.3%). The highest prevalence was found in 18-34 years (76.92%). 5(31.3%) who had missed an appointment were dental phobics ( $p = 0.045$ ).

**Conclusion:** The prevalence of dental phobia amongst the Kenyan Asian population was 16.46%. Age was inversely proportional with dental phobia, and females had a higher prevalence of dental anxiety; however, this was statistically insignificant. The most common source of anxiety was associated with administering an injection. The study showed that dental phobia led to missing dental appointments and this relationship was found to be statistically significant ( $p = 0.045$ ), suggesting that dental phobia led to avoidance of dental visits.

## 698 | Assessment of preferred cartoon character for dentist attire and its effect on dental fear in pediatric patients

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**Background:** The aim of the study is to evaluate the preference of cartoons for dentist attire and to assess its effect on dental fear in pediatric patients using Children's Fear Survey Schedule-Dental Subscale (CFSS-DS).

**Methods:** Children in the age group of 5-7 years were selected based on the inclusion and exclusion criteria and were divided into three groups with 30 children in each group. Parental consent was taken prior to the study. A pre-survey questionnaire was given to assess the preference of cartoons. Clinical examination and oral prophylaxis were done wearing the attire with selected cartoons printed on it. Dental fear was assessed using CFSS-DS.

**Results:** On comparison of fear score, white apron had statistically significant higher fear score as compared to cartoon printed apron and without apron, respectively ( $p 0.05$ ). But, no statistical significant difference was found in relation to fear score on comparison between cartoon apron and without apron ( $p 0.05$ ). Highest fear score was found in white apron followed by without apron and least in cartoon apron.

**Conclusions:** Use of child friendly attires could be useful in fearful children for better practice management. It can help in establishing a good relationship with children during their treatment. This study helps pediatric dentists to choose child friendly attire that are better received by childrens.

## 1545 | Thaumaturgic aids for behaviour management in pediatric dentistry

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**Background:** A young child's emotional and behavioural response to dental treatment is a matter of serious concern to paediatric dentists and researchers as it may impede the efficient delivery of dental care. If not adequately resolved, a persistent negative response pattern may emerge. Hence, it is very important for paediatric dentists to know about the old as well as new techniques of behaviour management.

**Literature Review:** American Academy of Paediatric Dentistry has described basic behaviour guidance techniques such as communication, tell show do, positive reinforcement

and Distraction techniques like audiovisual aids. A new technique i.e. Thaumaturgy has become popular nowadays. It is a tool that distracts and relaxes the child by using and helps the dentist to perform necessary treatment. It is also known as magic trick. It not only relaxes the child but also build a friendly rapport between the child and dentist. Specific magic tricks seem to be effective in specific age group.

**Conclusions:** Thaumaturgy plays important role in shaping the behaviour of a child in paediatric dentistry. The age and cognitive development of child dictates the technique to be used. It can be used as an alternative to visual aids as nowadays, children are already exposed to increased screen time due to restrictions on outdoor activities and 'online' schooling.

### 1091 | Comparative evaluation of low level laser therapy and acupressure in controlling gag reflex during dental procedures in children: An experimental study

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**Background:** Comparative evaluation of Low Level Laser Therapy (LLLT) and in combination with acupressure in controlling gag reflex in children undergoing impression making procedure.

**Methods:** A total of 90 children (10.1 + 2.6) years were divided into three groups depending upon the strategies used. Group A received LLLT whereas group B received LLLT with acupressure and group C was placebo group. Each patient underwent two impressions to record GSI and GPI scores for all groups.

**Results:** Mean values of GSI and GPI scores for each group were calculated at three different stages. The mean values revealed least gagging with LLLT as compared to LLLT with acupressure and placebo group at stage 1 ( $p=0.001$ ) and stage 3 ( $p=0.000$ ) which was statistically significant. Mean values of GPI score were less than GSI score at all three stages for all the groups except for stage 1 in group C, which was not statistically significant.

**Conclusions:** LLLT and in combination with acupressure was effective in controlling gag reflex in comparison with acupressure in children undergoing impression making procedure.

### 1741 | Adaptation and emotional support: Keys for the treatment of the patient who suffers bullying: A case report

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**Introduction:** Children frequently come to dental office with bad experiences in their daily environment and consequently in the dental chair, making their attention difficult. The WHO reports 15% of the population that has fear of the dentist due to negative experiences during childhood. The pediatric dentist plays an important role in the development of strategies that allow patients to receive multidisciplinary treatment under appropriate behavior.

**Case Report:** Patient 6 years 2 months, Frankl 3. First phase mixed dentition, o.c.o.d 7, generalized gingivitis induced by dental biofilm, inactive fistula 5.5, multiple caries, premature loss 6.4. Bottle sucking, lingual interposition and alteration in phonemes.

School bullying.

Treatment focused on developing preventive stages together with a dedicated adaptation, allows successful rehabilitation and multidisciplinary intervention with orthodontics, speech therapy and psychology.

**Discussion:** A patient who suffers from school bullying develops low adherence to dental care, presenting little capacity for cooperation, distrust and bad personal perception, generating the necessity to consult only in case of pain. An adequate treatment plan responds to all the health needs of the patient; focusing not only on rehabilitation, but also on adaptation, functional alterations and biopsychosocial problems through a multidisciplinary team that supports and accompanies.

**Conclusion:** A comprehensive treatment needs collaboration of both pediatric patient and family. Due to this, it is essential as dentists to establish a relationship of trust and support with the patient, improving not only the behavior of pediatric patients in dental office, but also favoring their daily relationship with others.

## 1417 | Evaluation of therapy assisted by dogs in the control of children's anxiety in dental treatment

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**Introduction:** Children usually have anxiety in varying degrees during dental care, creating obstacles to good and suitable treatment. The main aim of this case report was to evaluate the applicability of therapy assisted by dogs to control anxiety during dental care.

**Case report:** Four children were divided into two groups CT ( $n = 2$ ): children attended by usual methods in a children's dental clinic and TAC ( $n = 2$ ): children that were in contact with a therapist dog, first in reception and then inside the dental room. The therapist dog stayed with the child and next to the child's chair during the proceedings. To evaluate anxiety, heart frequency and Corah's Scale were used. The results were analyzed in Programa Biostat 5.0. The heart frequencies were submitted to the ANOVA test, with a level of significance of 5%.

**Discussion:** There was a reduction of heart frequency after treatment in the group that used the dog ( $p = 0.0388$ ). In the Control Group, there was an increase in heart rate. After Corah's Scale was applied, a reduction of anxiety levels was observed with the Therapy Assisted by Dogs, but there was increased anxiety in the Control Group.

**Conclusions:** It is possible to conclude that the Therapy Assisted by Dogs can be an alternative for the reduction of anxiety during children's dental care.

## 1133 | Assessment of dental anxiety levels in children treated with conventional composites versus Colored Compomers

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**Background:** Colored "Compomers" for children are available in various colors which permits the child a sense of control to choose the color of their choice thus reducing disruptive behavior and enhance a positive attitude during dental treatment. The aim of this study is to evaluate and assess the dental anxiety levels in children receiving restorative

treatment with multicolored compomers compared with those receiving traditional composite.

**Methods:** A total of 30 children aged 5 to 12 years with occlusal caries in the deciduous or permanent posteriors were selected and randomly allocated based on their choice of restorative material into 3 groups of (a) those receiving Conventional Composites (b) those receiving Blue Compomers and (c) those receiving Pink Compomers. The dental behavior was assessed using the Frankl behavior rating scale for all the groups. Dental anxiety was measured for all participants using the Venham Picture Test before and after the treatment procedure. The results obtained were then subjected to statistical analysis.

**Results:** The children who chose multicolored compomers showed a higher reduction in anxiety levels when compared to those who chose conventional composite. Blue compomer was much preferred in males whereas majority of the female children opted for the pink compomer. The children who preferred conventional composite over the multicolored compomers were significantly lesser.

**Conclusions:** Clinicians could use multicoloured compomers in the pediatric population which could provide a potential advantage to aid in enhancing their positive behavior in the dental operatory.

## 1757 | Pre-emptive analgesia to reduce post-operative pain in primary tooth extraction

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**Background:** This prospective, placebo-controlled, randomized, double-blind trial was planned to compare the efficacy of the pre-emptive administration of ibuprofen, paracetamol, ibuprofen paracetamol combination and placebo in reducing post-extraction pain in children.

**Methods:** Seventy two children, aged between 6–12 years, who needed primary molar tooth extractions were treated in paediatric dental clinics, with treatment preceded by local anaesthesia and analgesic drugs given during the preoperative period. A five-face scale was used to evaluate pain reaction during injection, extraction, and postoperative period. Self-report scores were recorded when local anaesthesia was administered in soft tissues, and before and after the primary tooth extraction was completed. Statistical analysis was done using SPSS (Statistical package for social science) Inc 21. Normality was assessed using Shapiro Wilk test. Depending on which all variables followed normal distribution, bivariate analysis was

done using parametric and nonparametric tests like ANOVA, Kruskal–Wallis, chi-square and Mann-Whitney tests

**Results:** The use of pre-emptive analgesics showed lower scores of pain compared to the placebo. These findings were irrespective of age, weight, gender of the child, and the number of teeth extracted in the study groups. Additionally, ibuprofen paracetamol combination drug group exhibited lower pain scores ( $p$  0.05) compared to ibuprofen and paracetamol drug groups when used separately.

**Conclusions:** Preoperative use of ibuprofen and paracetamol combination and ibuprofen alone may provide a better pre-emptive analgesic effect as compared to paracetamol alone in paediatric patients for the primary tooth extraction.

### 619 | Reliability of different pain scales used for assessment of dental pain in children using mobile application: A pilot study

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**Background:** The study has been aimed to evaluate and compare the reliability of different pain assessment scales namely, Wong Baker Facial Pain Rating Scale, EMOJI Pain Scale and indigenously made GIF Pain Scale in children aged 4–6 years.

**Methods:** The pilot study included 13 children aged 4–6 years with a Frankl Behaviour Rating of score 3(positive) requiring dental treatment under local anesthesia. After infiltration local anesthesia, each child along with two independent observers were asked to mark the response of current pain on Wong Baker Facial Pain Rating Scale, EMOJI Pain Scale and GIF Pain Scale. Reliability of the pain scales was assessed based on similar responses given by all three individuals. Reliability analysis was done using Cronbach's Alpha value.

**Results:** GIF pain scale was most reliable followed by Wong Baker's Facial Pain Rating Scale and Emoji Pain Scale, respectively.

**Conclusions:** GIF pain scale can be successfully used in regular clinical practice for the assessment of pain in children as they can easily relate to the emotions portrayed through animations. The study with a larger sample size is still going on.

### 1985 | Breastfeeding duration among babies under two years of age born at the University Hospital of Brasília, Brazil

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**Background:** The World Health Organization (WHO) recommends exclusive breastfeeding until 6 months of age and its maintenance for up to 24 months or more since it promotes numerous benefits. The aim of the study is to evaluate the duration of breastfeeding until 2-year-old of babies in Brasília, Brazil.

**Methods:** Data were collected from a cohort study of babies that was born from August 2017 to July 2018 at the University Hospital of Brasília. During the 2-year follow-up appointment, a questionnaire about breastfeeding information was applied to the parents. Data were tabulated, and a descriptive statistical analysis was performed.

**Results:** Of the 130 babies evaluated, the mean age ( $\pm$  SD) was 24.18 ( $\pm$  0.61) months and 50.8% were girls. The prevalence of exclusive breastfeeding for the first 6 months of age was 47.6%. The average of total breastfeeding duration ( $\pm$  SD) was 16.62 ( $\pm$  8.31) months. In 28.4% of the babies, the weaning happens before completing the first year of life and only 36.1% of the babies continue to be breastfed until 2-years-old. Reasons for winning reported by the mothers were lack of support and appropriate information (53.1%).

**Conclusion:** The prevalence and the average of breastfeeding were low; it is important to reinforce the role of the health professional in guiding and supporting breastfeeding.

### 1470 | Paradigm shift in behaviour guidance techniques: In autism spectrum disease

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**Background:** Behavior guidance techniques aim at alleviating anxiety, nurturing a positive dental attitude and performing oral health care efficiently. Innovations in behaviour guidance techniques facilitate a personalized treatment approach for patients with autism spectrum disease.

**Literature review:** Behavior guidance of patients requires a thorough knowledge of the individual's behaviour profile. Many newer behaviour guidance techniques have been

introduced, such as sensory adapted dental environment, animal assisted therapy, picture exchange communication systems, applied behaviour analysis, memory restructuring, non-verbal communication, desensitizing to dental settings, analytical behavior treatment, and many others that are more apt for patients with limited verbal communication skills.

**Conclusions:** This review highlights the newer behaviour guidance techniques in order to acquaint health care providers with these techniques and aid them in clinical decision making.

### 365 | Effectiveness of child-centered distraction in the management of a child's dental anxiety during invasive dental procedures

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**Background:** The study evaluated the efficacy of child-centered distraction (CCD) in alleviating dental anxiety in children using three techniques during invasive dental procedures.

**Methods:** After obtaining Institutional Ethical Committee approval, sixty children (40 boys and 20 girls), aged 7 to 11 years, were randomly allocated into three groups: Group 1- Mobile video games (VG), Group 2- Virtual reality (VR), and Group 3- Mobile cartoons (MC), respectively, during the treatment sessions. The anxiety of the children was assessed using physiologic measure (heart rate) at three different time points, i.e., before, during, and after the procedure, whereas RMS pictorial scale was employed as a subjective measure before and after the procedure. Kruskal-Wallis ANOVA and Wilcoxon Sign Rank test were used to analyze the RMS Scores, and repeated measures of ANOVA were used to test the mean difference of pulse rates.

**Results:** On intergroup comparison, there was no statistical difference among the three groups before commencing the treatment ( $p$ -value  $\leq 0.001$ ). But, a statistical difference in all the groups ( $p$ -value  $\leq 0.001$ ) was evident after instituting the distraction techniques. Amongst all the three groups, a significant reduction in anxiety scores was elicited by the children in group 1.

**Conclusion:** This study has attempted to enhance the salience of distraction techniques in tumbuling a child's dental anxiety. Involving the child in decision-making while using distraction techniques has a foremost impetus in most children, instilling a new positive attitude towards the dental procedures.

### 354 | Impact of parental presence at chairside on children's behaviour during dental visits

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**Background:** This study examined the impact of parental presence at the chairside on children's behaviour during dental visits.

**Methods:** This quasi-experimental study involved an age-matched sample of children assigned to dental care with parent present chairside (test group) or without parent present chairside (control group) during the first dental visit. Children's behaviour was rated by a masked trained assessor via the Sarnat Behaviour Scale (SBS) on a 5-point Likert scale and the FLACC Behavioural Discomfort/Pain Scale (possible range of score 0-10). Furthermore, children pulse rate was monitored, and children rated their dental anxiety by the Vernham Picture Test (VPT). The age and gender of the child were recorded, as was the type of dental treatment.

**Results:** Assessments were conducted at 260 dental visits (130 test and 130 control appointments). The mean SBS scores were 1.5 (SD 0.8), and the mean FLACC scores were 2.3 (SD 1.9). There was a strong correlation between SBS scores and FLACC scores ( $r$  0.8,  $p$ 0.001). Bivariate analyses identified that the chairside's parental presence was associated with SBS scores ( $p = 0.002$ ) and FLACC scores ( $p = 0.001$ ). Controlling for child's age and gender, type of dental treatment, pulse rate changes and changes in child's rating of dental anxiety (VPT), parental presence at chairside remained significantly associated with SBS scores ( $\beta$  0.2, 96%CI 0.1-0.4,  $p = 0.003$ ) and with FLACC scores ( $\beta$  0.7, 96%CI 0.3-1.2.4,  $p$ 0.001).

**Conclusions:** Disturbance in child behaviour during dental visit varied but was generally positive. Parental presence chair side was associated with improved behaviour.

## 352 | Effect of audiovisual distraction on children's anxiety during dental treatment in a Nigerian setting

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**Background:** Dental anxiety in children is associated with avoidance of dental treatment and delayed presentations which can result in oral health complications. Therefore, audiovisual distraction video eyeglasses were developed to address this problem. The aim of this study is to evaluate the effect of audiovisual distraction using video eyeglasses on children's anxiety during dental treatment.

**Methods:** An interventional randomised controlled study was conducted among 100 children aged 6 to 11 years requiring routine exodontia. The sample was equally randomised into the audiovisual distraction group and the 'no distraction' group. Anxiety was assessed in both groups using the Facial Image Scale, Venham's clinical anxiety rating scale and pulse rate. Acceptance of audiovisual distraction by children and their parents was assessed using a questionnaire. Data were analysed using Chi-square test and student *t*-test.

**Results:** The audiovisual distraction group showed lower anxiety scores using Facial Image Scale than the 'no distraction' group ( $p$  0.001). Also, using the Venham's clinical anxiety rating scale, lower anxiety scores were observed in the children in the audiovisual distraction group in comparison to the 'no distraction' group ( $p$  = 0.001). Furthermore, the pulse rate was lower in the audiovisual distraction group as compared to the 'no distraction' group ( $p$  0.001). The acceptability of audiovisual distraction technique by the children and their parents was 98% and 100%, respectively.

**Conclusion:** The audiovisual distraction technique using video eyeglasses was more effective in reducing children's anxiety during dental treatment in comparison to the 'no distraction' method. Audiovisual distraction had high acceptance by the children and their parents.

## 1746 | Reframing the less voyaged path in paediatric dentistry: A review of literature

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**Background:** Managing the child's behavior and anxiety are very important to render successful and high-quality dental treatment by the pediatric dentist. Stimuli such as strange

environment, loud noise, bright light etc; can easily arose anxiety in a child during dental visits. Hence, it is important to mold the child's attitude towards dental outcomes and dentistry during the child's visit to the dentist. Behavior guidance techniques that deal psychologically can be used for alleviating dental fear and anxiety. One such technique is the 'Reframing' which can be used effectively in dental office.

**Literature review:** Reframing is a communication technique that helps in strengthening the relationship between dentist and child patient. It is a part of a neuro-linguistic programming which is used to convert unpleasant notions to acceptable notions to the patients. It works on the principle that the content of an event which one perceives is dependent on the frame in which one sees. When there is transformation in the frame, it changes the behavior and response of the person. In pediatric dentistry, reframing is proven and considered as one of the behavior guidance techniques. There have been studies using reframing to successfully treat habit cessation in children.

**Conclusions:** Although reframing is used commonly in medical literature as a means of coping stressful situation both by the patient and the care giver. The dental literature is very scanty with its application. Hence, more studies need to be done with this technique as a behavior guidance method for children in the dental office.

## 872 | HSPM in primary dentition: Protect, predict & prevent

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**Introduction:** Hypomineralised second primary molar (HSPM) is a qualitative defect of enamel due to idiopathic hypo mineralization that affects 1 to 4 primary molars, with unclear etiology. Due to defective enamel and its increased porosity, it is more prone to comorbidities like caries, dentin hypersensitivity, and enamel breakdown. As per recent evidence, CariesCare International consensus is the most contemporary patient-centered, risk-based approach to caries management designed for the dental practice.

**Case Report:** This case report is an illustration of the management of HSPM in primary dentition in 3 year old with

unestablished etiology due to poor socio-economic background. Restorative rehabilitation as minimally invasive paediatric dentistry (SDF, SMART, Halls crown) in conjunction with Nitrous Oxide-Oxygen Inhalational Sedation was done chair-side which was further complemented by contemporary clinical caries consensus augmenting the preventive protocol.

**Discussion:** Prompt diagnosis and management of HSPM are often missed due to the progression to post-eruptive enamel breakdown and subsequent decay cycle leading to the increased burden of care. According to the recent systematic reviews, the presence of HSPM is predictive of MIH as they have a shared period of development and mineralization. In this case, with the CariesCare International Consensus approach, a care plan was co-created with the patient and delivered to obtain optimal health outcomes.

**Conclusion:** As per the latest evidence, the presence and recognition of HSPMs may serve as a vital and reliable risk predictor for future MIH emphasizing the need for its early recognition along with personalized interventions as preventive measures and structured management.

## 806 | Prevalence of musculoskeletal disorders among paediatric dentists

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**Background:** Work-related musculoskeletal pain had high prevalence and was the most common symptom of musculoskeletal disorders among dentists. Unnatural working posture could lead to the development of musculoskeletal disorders. Work that involves children requires the operator to flex their body on a regular basis during work. The aim of this study was to investigate the prevalence of musculoskeletal pain and risk factors, as well as protective factors during the work of specialists of preventive and paediatric dentistry.

**Methods:** Self-reporting questionnaire developed for the study which consisted of 78 questions that was distributed among 300 active working paediatric dentists from Serbia.

**Results:** The results of the study indicated that 81.4% of paediatric dentists have experienced work-related musculoskeletal

pain. The most common regions of the body affected by musculoskeletal pain were the neck and back. The main risk factors are working with kids, and being female as female dentists were at higher risk than male dentists. Other risk factors are working long hours, working with a high number of patients daily, usage of non-ergonomically designed equipment, and presence of general disorders.

**Conclusions:** Paediatric dentists are exposed to a wide variety of causative factors which are correlated with musculoskeletal pain in dentistry. Dentists should take preventive measures, such as doing physical activity and using ergonomically designed devices and equipment to reduce risk. The use of ergonomically designed dental equipment, such as ergonomically designed chairs with armrests and body supports, can significantly contribute to the reduction of musculoskeletal pain experienced by dentists.

## 405 | Comparative evaluation of administration of nitrous oxide, oxygen inhalation and intranasal midazolam as pre-anaesthetic medication in paediatric dental patients: A clinical trial

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**Background:** Behaviour management often poses a challenge to Pediatric dentists. Various techniques ranging from non-pharmacological to pharmacological have been tried over the years. The present study was undertaken to evaluate the effect of intranasal midazolam and conscious sedation as a behaviour management technique. The aim of this study was to compare the effect of nitrous oxide -oxygen inhalation and intranasal midazolam as pre-anaesthetic medication.

**Methods:** After approval from ethical committee, a split mouth design was planned. A total of 30 children aged 5-10 years with Frankl behaviour rating score 2 and ASA1 requiring class I restoration in at least two primary molars were included in the study. They were randomly divided into two groups of 15 children each. In the first visit, class I restoration with GIC was performed under Nitrous oxide-oxygen inhalation (Group-1) sedation in all the children. In the second visit, intranasal midazolam (Group-2) was used for sedation and class I restoration using GIC was performed in all children. At each visit, oxygen saturation, heart rate and behaviour parameters were recorded according to Houpt-behaviour scales. Post-operatively, patient's anxiety and parent's satisfaction were assessed by visual-analogue scale and questionnaires, respectively. Data analysis was done using Wilcoxon's signed rank test and Paired *t* tests with a *p* value set as 0.05.

**Results:** Average oxygen saturation levels and physiological parameters were within normal range in both the groups.

There was no significant difference in pre to post-operative anxiety scores between the groups in final sedation.

**Conclusion:** Nitrous oxide -oxygen inhalation and intranasal midazolam were found to be equally effective and provide adequate sedation for easy separation from the children during procedure.

## 816 | The first dental visit: A cross-sectional survey in Rabat-Morocco

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**Background:** The first dental visit is critically important in the prevention of oral diseases that represent a global health problem because of its prevalence and its impact on the overall health status of the child. The purpose of this survey was to determine the age and the most common reasons for first dental visit among children (between 0 - 6 years old) in the city of Rabat.

**Methods:** A cross-sectional survey conducted at the Children`s Hospital of Rabat. 100 children aged 0 to 6 years were sampled. A questionnaire was completed by the interviewer according to the parents` responses. The statistical analysis was done using the "IBM SPSS Statistics version 20" software.

**Results** Average age of our population was  $44 \pm 2$  months with a minimum age of 12 months and a maximum of 72 months, half of which was male between the ages of 0 and 6 years. 56% of children have already benefited from a 1st dental consultation.

The mean age of the first dental visit in the children studied was  $36 \pm 2$  months. The 1st consultation is considered late compared to international recommendations (6 months to 1 year).

Most common reason for consultation in the sample was urgency caused by pain with 85.7%, followed by aesthetic demands with 8.9% and lastly preventive consultations with 5.4%.

At the first consultation, 70.4% of children did not receive prevention advice.

32.1% made this first consultation with non-graduate practitioners, 44.7% in public health centers and 23.2% in private institutions.

**Conclusions:** The various results recorded in this survey highlight the interest of extending the program of prevention of oral diseases to the age of birth and preschool, the

establishment of a 1st consultation at the age of 1 year remains a necessity, special attention should be given to mothers during the pregnancy period and after birth, and prevention messages should be fairly simple and appropriate because of the low level of education of the parents.

## 881 | Advancements in local anaesthetic techniques: A review of literature

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**Background:** Pain and its successful management have been one of the keystones of dentistry worldwide. Knowledge of the local and topical anaesthetic agents and the ability of the clinicians to choose the best delivery methods has become a most important thing in today`s dentistry.

**Literature review:** Pain is like a double-edged sword to a dentist. The reason which brings the patient to dentist side is the same that takes away from receiving treatment due to fear and anxiety associated with various treatments. To eradicate the pain during the treatment procedures, usually anaesthesia have to be administered. Conventionally and even today in many areas, anaesthesia is administered by injections. This is the reason that children dislike dental treatment due to the fear and anxiety related to needles. This fear-related behaviour has been recognised as the most difficult aspect of patient management. It can be a barrier for delivering successful treatment. It remains as a negative experience and this will later on develops a negative attitude towards dental treatment. The agents and anesthetic delivery equipments available today provide the practitioner an array of options to effectively manage the pain associated with dental procedures.

**Conclusions:** This review widens up the scope of recent advances in local anaesthetic solutions, topical anaesthesia and the various delivery techniques which can be applied to pediatric as well as in adult patients.

## 1723 | Consequences in psychosocial development of the patient with severe early childhood caries: A case report

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**Introduction:** Severe early childhood caries (S-ECC) has a high prevalence in the Chilean children, causing a public health problem. There are different conditions that can cause

this situation, and it is also important to consider how S-ECC affects the psychosocial development of the patient and their behavior. The objective is to present the consequences of S-ECC in the psychosocial development of a preschool patient. **Case Report:** Patient 3 years 9 months old, Frankl 3, dmf 9, S-ECC, phonoarticulation in "T" / "D" / "S", lingual interposition, inter and intramaxillary alteration and bad habit of bottle using. The patient's tutor expressed that she had previous symptoms that prevent her from carrying out her daily activities. Communication problems were reported due to her altered phonoarticulation, affecting her interaction with the environment, difficulty in expressing herself, frustration and bad behaviour.

**Discussion:** This case of S-ECC was analyzed based on different parameters, such as dental history, hygiene, diet and habits. The patient presents low hygiene, cariogenic diet, delayed first dental visit and a bad habit of bottle using. Consequently, the dentist can become aware of alterations that the patient presents respect to her relationship with the environment, such as the way she speaks, how she expresses herself and her behavior in the social sphere.

**Conclusion:** S-ECC constitutes a problem in public health in Chile. S-ECC not only affects the dental level, but also affects the patient through their self-esteem, communication, behavior and social interaction, demonstrating possible alterations in their future psychosocial development.

## 1779 | 'Sense of coherence': Review on future directions

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**Background:** The concept of salutogenesis was advanced almost four decades ago and has been adopted in health promotion research and practice. Suggestions for improving the salutogenic model of health include addition of a positive health continuum and a path of positive health development linking resources to this new continuum.

**Literature Review:** This model posits that life experiences shape the Sense of Coherence (SOC) that helps to mobilize resources to cope with stressors and manage tension successfully (determining one's movement on the health Ease/Dis-ease continuum). It shows how diverse psychological, physical and biochemical stressors can be successfully managed by a range of cultural, psychosocial, genetic and constitutional general resistance resources (GRRs). A second application involves the use of the concept and measurement of SOC as the core element of the salutogenic model

of health that promotes the ability to mobilize GRRs and specific resistance resources (SRRs). A third application is the exploration of a salutogenic orientation focusing on resources leading to positive outcomes rather than focusing on disease and underlying risk factors. The three-dimensional SOC (i.e., comprehensibility, manageability, meaningfulness) is posited as the key answer to the question about the origin of health.

**Conclusion:** Suggestions for improving the salutogenic model of health include addition of a positive health continuum and a path of positive health development linking resources to this new continuum. Expansion of the theory and of the model will support health promotion researchers and practitioners in efforts to address the full spectrum of the human health experience.

## 612 | Content analysis of behaviour change taxonomies in smartphone-based toothbrushing apps

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**Background:** Smartphone mobile app is an innovative concept for health behaviour-based interventions. The present study aimed to analyse apps developed for smartphones that promote tooth brushing amongst children using the Coventry, Aberdeen, and London-Refined (CALO-RE) taxonomy for behaviour change.

**Methods:** Tooth brushing apps available in English and free to download that purported to assist with brushing were searched on the Apple app store using search terms based on Boolean logic and included AND combinations for keywords tooth brushing, children, toothbrush and motivation in the health and fitness category; six apps met the inclusion criteria and were downloaded. The behaviour change taxonomies were assessed individually for each app and scored as per coding and analyzed for presence or absence.

**Results:** Only three of the behaviour change taxonomies were present in all apps, i.e. information provision (general), goal setting (behaviour) and prompt practice. Setting graded tasks, self-monitoring of behavioural outcome, demonstration of behaviour, prompt use of imagery and time management were included in four out of six apps.

**Conclusions:** The present study explores a new arena for oral healthcare motivation and prevention in children through the use of mobile phone apps.

## 778 | Behaviour management in pedodontics

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**Background:** Humans, like other animal species, have a typical life course that consist of successive phases of growth, each of which is characterized by a distinct set of physical, physiological and behavioral features. These phases are pre-natal life, infancy, childhood, adolescence, and adulthood. A primary motivation of many investigators in the field has been to determine how the culminating mental abilities of adulthood were reached during the preceding phases. For treatment of biological development, see human development. For further treatment of particular facets of behaviour development, see emotion, learning theory, motivation, perception, personality, and sexual behaviour of human.

**Literature Review:** The systematic study of children is less than 200 years old, and the vast majority of its research has been published since the mid-1940s. Basic philosophical differences and their growth occupied psychologists during much of the 20th century. The most important of such controversies concerned the relative importance of genetic endowment and environment, or 'nature' and "nurture" in determining development during infancy and childhood. Most researchers came to recognize however, that it is the interaction of inborn biological factors with external factors, rather than the mutually exclusive action or predominance of one or the other force that guides and influence it.

**Conclusions:** Appropriate use of management techniques can improve the child's behaviour in subsequent dental visits. Finally, the most effective communication always reflects the personality of the dental professional themselves.

## 226 | Effect of personal protective equipment on anxiety of 5 to 10 year old children in dental operator: An experimental study

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**Background:** The purpose of this study was to evaluate the effect of personal protective equipment on anxiety of 5 to 10 year old children in dental surgery.

**Methods:** 60 children of 5 to 10 years were randomly allocated to three study groups; Group A – A Pediatric dentist wearing colorful cartoon printed scrub, head cap, N95 mask,

face shield and hand gloves, Group B - A Pediatric dentist wearing complete PPE (gown, shoe covers, head cap, N95 mask, goggles, hand gloves and face shield) and Group C - A Pediatric dentist wearing modified colorful PPE (Protective gown and face shield modified with cartoon pictures). Child's anxiety was assessed at baseline and after showing photograph of pediatric dentist in the particular attire using the Facial image scale. Preference for attires was later evaluated.

**Results:** Intergroup comparison of mean anxiety scores after showing photographs in the three groups showed statistically significant difference between group A and group C ( $p = 0.024$ ) and group B and group C ( $p = 0.0001$ ). A statistically significant increase in anxiety in group B and decrease in Group C was observed. 88.8% of the children preferred modified PPE.

**Conclusion:** PPE decreases the non-verbal communication affecting the rapport between a pediatric dentist and patients. But modifying it with colorful relatable content can allay children's anxiety.

## 1920 | Effectiveness of videos with and without binaural beat audio for anxiolysis in children undergoing dental treatment: A pilot study

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**Background:** Emotional and behavioural responses of children to dental treatment is a matter of serious concern to Pediatric Dentists. Audiovisual stimuli with specific frequency cause the brain to adapt to the same frequency, known as 'brain entrainment'. Research using audio beats has been conducted, identifying their positive effects on verbal memory, relaxation, dual cognitive tasks, working memory and pain reduction. This pilot study is aimed at evaluating the effect of delta audio beats on anxiety reduction in apprehensive children during dental procedures.

**Methods:** Ten children belonging to the age group of 5-8 years were shown cartoon videos with and without delta beat audio alternatively at 2 consequent visits. This was carried out over a span of 30 minutes using noise cancellation earphones. Since the findings of biofeedback could be correlated to decrease in anxiety, the pulse rate and oxygen saturation (SpO<sub>2</sub>) levels were noted at the baseline and after 30 minutes.

**Results:** The resultant pre-and-post values were used to calculate the mean and compared using paired and unpaired *t*-test. The decrease in the pulse rate was significantly higher 6.8 (mean) for the delta wave audio group, compared to 3.6 (mean) in the control group. The Oxygen saturation level also

showed a significant increase 6.8 (mean) in the experimental group, when compared to 2.9 (mean) in the control group.

**Conclusion:** Binaural audio beats utilise a non-invasive therapeutic method, targeting the centers of the brain dedicated for psychological and physiologic processes of the body, thus providing effective anxiolytic effects.

## 1582 | How to rebuild trust after a bad dental experience? Managing the fearful patient with the help of medical hypnosis

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**Introduction:** Dental fear is a common health care issue in the child population. There are many methods for coping with the issue e.g. tell-show-do, positive reinforcement, voice control and medical hypnosis.

**Case Report:** This report presents the behaviour management of a 5-year-old child who experienced pain and discomfort when seeking/receiving first aid in a dental office because of a fever and swelling of the first lower left molar. During a check-up a week later, he appeared afebrile and no swelling was seen. However, using the tell-show-do technique, only an examination was possible; when spotting the intention to use a drill, he closed his mouth and refused any intervention in the mouth. On the second appointment a week later, some elements of medical hypnosis were used and full cooperation was achieved.

**Discussion:** It is vital to establish security and confidence at the beginning of the treatment, especially with younger patients. However, in case of swelling and fever, a dental emergency is urgent. Re-establishing trust and cooperation after a previous bad experience can be challenging. In children, it may increase resistance to subsequent interventions. Medical hypnosis is an effective non-pharmacological approach to establish trust and encourage participation of children without the use of drugs and side effects. There is also no requirement for specialized equipment.

**Conclusions:** Besides professional medical knowledge, the practitioners should be equipped with additional patient-managing techniques. In children, hypnosis is a useful therapeutic method, as they tend to have an active imagination and are very susceptible to hypnotic suggestions.

## 298 | Preparing a child for the first dental visit: Parent's/guardian's knowledge, attitude and practice

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**Background:** The first dental visit is important to develop a good dentist-parent-child relationship.

The aim of this research was to assess parent's/guardian's knowledge, attitude and practice (KAP) in preparing a child for the first dental visit.

**Methods:** A cross-sectional study was carried out within 6 months on 150 participants who brought their children to the Kulliyah of Dentistry dental polyclinic, IIUM. Validated questionnaires consisting of parent's/guardian's K, A and P related to the development of the tooth, oral disease, caries prevention, habits, role model, the reason for dental visit, introduction to dental clinic and dentist were distributed. Pearson correlation was used to analyse the associations.

**Results:** The significance between K, A and P was P0.05 with rho between K and A, K and P, and A and P of +0.213, +0.246, +0.406, respectively. Early exposure was given to the children before their first dental treatment explaining the main purpose of going to the dentist and the impact of good oral hygiene towards quality of life, watching videos and pictures describing dental treatment in child-friendly clinic. Skilled dentists, painless, gradually and enjoyable dental treatment were participant's preferences. As role models for children, parents had taught dental home care, the right attitude of rewarding and not frightening children with dental treatment, as well as supporting school dental programmes.

**Conclusion:** The relationship between K, A and P was significant. However, the associations were fair.

## 517 | Level of knowledge and experience regarding child abuse: A survey study of dental practitioners in Morocco

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**Background:** The aims of the study were to investigate dentists' level of knowledge and experience regarding child

physical abuse in Rabat the capital of Morocco, to identify barriers that prevent the reporting of suspected cases by dental practitioners, and to assess need for training dentists in detecting child abuse.

**Methods:** A self-administered structured questionnaire was drawn up and delivered to 110 dental surgeons in the region of Rabat; Morocco. The questions were closed, with multiple choice, to allow to answer them in a limited time and, by this means, to obtain a greater participation of the doctors. The response time has been set at 1 week (7 days).

Responses were coded and processed using IBM.SPSS software. Statistics.v22.MacOSX. And analyzed using descriptive analyses for responses to each question.

**Results:** Of all dental practitioners invited to participate, only 77% have responded.

Almost half of the dentists encountered a suspicious child abuse case at least once in their career, but only 11% of those reported their suspicion.

The most common barriers that preclude the dentists from reporting child abuse cases were uncertainty about their diagnosis followed by the lack of knowledge regarding referral procedures.

However, the majority of participants were aware of their legal responsibilities toward protecting children from abuse and they expressed their need for further training in this area.

**Conclusions:** Based on the results of this study, it appears that the level of knowledge among the respondents regarding the recognition and reporting of child physical abuse was lacking. Therefore, specialized training in this area is highly recommended.

## 299 | Oral health seeking practices among University of Nairobi dental students

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**Background:** Oral health seeking practices is behavior that prompts individuals to seek preventive dental care. The study aims to study oral health seeking practices among students of University of Nairobi Dental School.

**Methods:** A total of 73 students who study at the University of Nairobi Dental School who gave informed consent and fit the inclusion criteria were interviewed using self-administered questionnaire (open and close ended).

**Results:** Most participants were aged between 21-23 37(50.7%). 30(41.1%) were male and 43(58.9%)female. 63(86.3%) participants had visited a dentist with 20(13.7%) having gone within the last three months, 14(22.2%) within the last six months, 10(15.9%) more than six months to a year, 8(12.7%) more than a year and 11(17.5%) more than two years. 22(30.1%) visit the dentist after 2 years while 7(11%) visit every six months, 19(30.2%) every six to twelve months, 10(15.9%) visit after every twelve months and 5(7.9%) every two years. The main reasons stated for visiting were 17(37%) pain and 27(58.7%) due to pending appointments.

Most common procedures done were 14(23.3%) simple fillings and 11(18.3%) scaling. Majority 32(50.8%) had missed appointments mostly due to lack of time 18(52.9%) and lack of pain as a symptom 6(17.6%). 42(57.5%) had an existing dental problem not sought treatment for.

**Conclusion:** Most students have existing dental problems not sought treatment for; with most reporting irregular dental visits and a significant number citing pain as the motivation to visit a dentist. This may suggest that dental treatment is only sought in the emergency stages of the disease.

## 944 | Application of various behavior management techniques by graduates and intern dentists to manage children in dental clinic

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**Background:** Application of various behavior management techniques (BMTs) need skills to manage children in dental clinic. The aim of this study is to assess the application of various behavior management techniques used by graduate students and intern dentists to manage children in the dental clinic.

**Methods:** A cross-sectional study was conducted among dental students from College of Dentistry, Jouf University. All fifth year BDS students and intern dentists studying in College of Dentistry were included as the study sample because they had already received didactic classes about BMT and involved in clinics treating child patients. A structured close-ended questionnaire comprising 12 questions related to the behavior management techniques and their application in dental clinics was given to the participants.

**Results:** The data were obtained, tabulated, and analyzed statistically using one-way ANOVA and Mann-Whitney tests. Tell-Show-Do is considered to be the most common BMT used by interns followed by positive reinforcement, parental presence and distraction. Positive reinforcement is the most common technique used by fifth year students followed by

parental presence, Tell-Show-Do, distraction and protective stabilization. The least common technique used by both interns and fifth year students was general anesthesia.

**Conclusions:** Tell-Show-Do and positive reinforcement are considered the most common BMTs used in the present study followed by parental presence. Hence, the present study helped graduates to analyse and apply various behavior management techniques to better manage children in dental clinic.

## 1788 | The use of hypnosis in pedodontic pain and anxiety control: A review of literature

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<sup>3</sup>Department of Pedodontics, Medipol University, Faculty of Dentistry, Istanbul, Turkey

**Background:** Hypnosis has a long tradition in medical procedures, being widely used in dentistry for moderate fears of dental procedures, excessive gag reflex, treatment of orofacial pain and managing procedural pain. One of the most challenging aspects in pediatric dentistry is to convince the patient to accept all treatment procedures promptly. Traumatic or painful previous experiences are the most significant etiological factors for pediatric patients' dental fear and anxiety. Using the hypnosis technique to prevent dental anxiety becomes even more attractive because children are more prone than adults to hypnosis as a consequence of their imaginary capacities.

**Literature Review:** The benefits of non-pharmacological interventions like hypnosis, relaxation, audio-visual distraction methods and cognitive behavioral approaches in reducing the mental suffering during dental care were researched, with the greatest effects demonstrated for hypnosis. Fear of the dentist is included under certain phobias according to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV and classification of Statistical Diseases and Related Health Problems (ICD)-10. Dental phobia is classified as a specific phobia in DSM-IV-TR. The frequency of dental anxiety in children and adolescents varies widely between 5% and 40%, and tends to decrease with age.

**Conclusion:** The purpose of this literature review was to compare the effectiveness of hypnosis and other behavior management techniques in reducing pain or anxiety before dental treatment in pediatric patients.

## 822 | Ethical issues in clinical paediatric dentistry

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**Introduction:** Paediatric dentists are faced with complex ethical issues in their practice. This is due to the normal doctor-autonomous-patient relationship being replaced by a more complicated one involving a not fully autonomous young patient, and their parents or guardians.

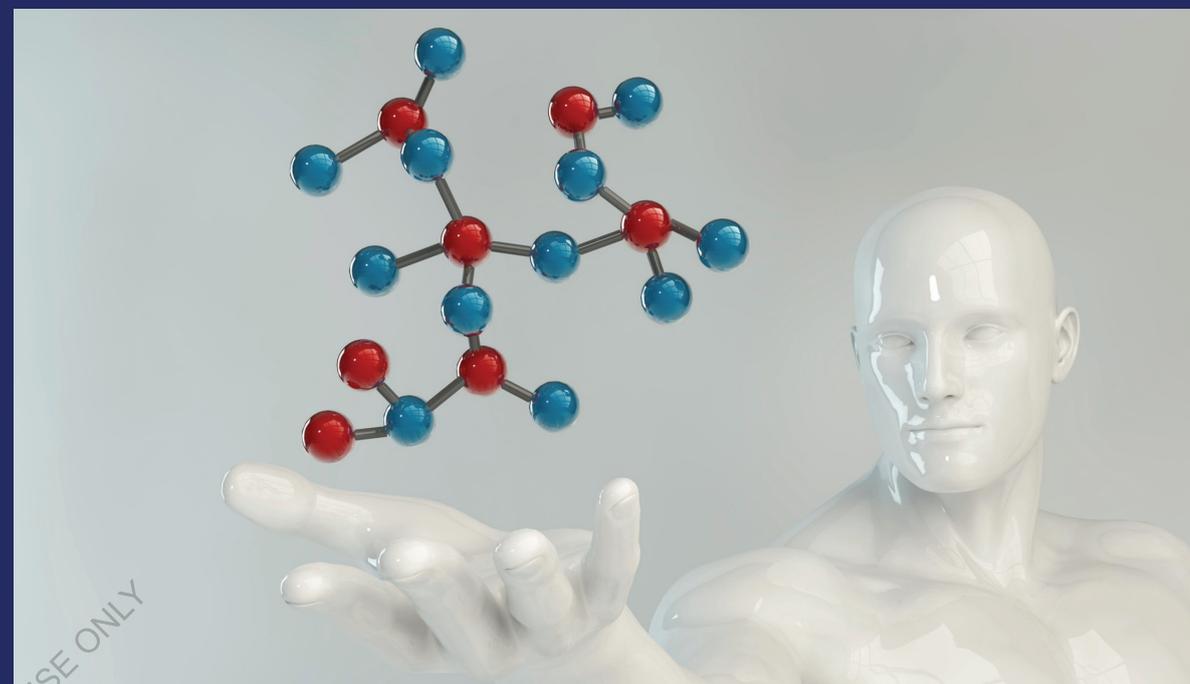
**Case Report:** First Case: A fifteen-year-old presented at the office for a recall exam with her mother. Before treatment, she requested to speak privately with the dentist. She revealed that she had a frenulum piercing which she herself had done and did not want her mother to know.

Second Case: A three-year-old with severe early childhood caries presented for the first time at the office with his parents. In the medical history form, the father noted that the child was not vaccinated.

**Discussion:** According to the fundamental ethical principles, the dentist must respect the patient's decisions (autonomy), only do what is right for the patient (beneficence), refrain from doing harm (non-maleficence), and offer equal treatment (justice). The dilemma arising from the first case is whether the dentist should respect patient autonomy given the perceived competence of adolescents or take a paternalistic approach, and reveal the patient's secret to the mother. In the second case, the dentist, taking into consideration justice, beneficence, and non-maleficence must decide whether to treat the unvaccinated patient but potentially put the health of others at risk.

**Conclusions:** Ethical issues make paediatric dental practice challenging, but it is vital that the dentist is able to assess each case individually and make appropriate decisions to maximize the benefit for the young patient.

Oral cavity acts as a niche for numerous microorganisms. Among them, some are pathogenic and cause infections. Hence to control and prevent such infections, a lot of researches are conducted on different materials using various advanced techniques. Nanotechnology and nanoscience have emerged in the recent years exploring the antimicrobial effects of metal nanoparticles. Distinct physical, biologic and chemical properties of metallic oxide nanoparticles make them efficient antimicrobial agents. Application of this nanotechnology in dentistry termed as Nanodentistry, has brought many effective changes in the dental materials.



Dr. Hema Kanathila, is currently working as Reader in KAHERs KLE VK Institute of Dental Sciences, Belagavi, India. She is a Prosthodontist. And her field of interest is Herbal and Laser dentistry.

HEMA KANATHILA  
ASHWIN PANGI  
RAHUL JAISWAL

# METALLIC OXIDE NANOPARTICLES AS ANTIMICROBIALS

APPLICATIONS IN DENTISTRY



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**METALLIC OXIDE NANOPARTICLES AS  
ANTIMICROBIALS AND THEIR  
APPLICATIONS IN DENTISTRY**

**CONTENTS**

<b>CHAPTER NO</b>	<b>CHAPTER</b>	<b>PAGE NUMBER</b>
1	<b>INTRODUCTION</b>	4
2	<b>HISTORY</b>	8
3	<b>SILVER AND SILVER OXIDE NANOPARTICLES</b>	10
4	<b>TITANIUM DIOXIDE(TiO<sub>2</sub>) NANOPARTICLES</b>	12
5	<b>ZINC OXIDE NANOPARTICLES</b>	15
6	<b>COPPER AND COPPER OXIDE NANOPARTICLES</b>	18
7	<b>NANOMETALS AS ANTIMICROBIALS IN DENTISTRY</b>	20

8	<b>NANOMETALS AS ANTIMICROBIALS IN DENTAL MATERIALS</b>	22
9	<b>NANOMETALS AS ANTIMICROBIALS IN IMPLANT DENTISTRY</b>	29
10	<b>NANOMETALS AS ANTIMICROBIALS IN MAXILLOFACIAL PROSTHETIC MATERIALS</b>	32
11	<b>A NOTE ON CYTOTOXICITY OF NANOPARTICLES</b>	34
12	<b>ADVANTAGES AND DISADVANTAGES OF NANODENTISTRY</b>	36
	<b>SUMMARY AND CONCLUSION</b>	38
	<b>BIBLIOGRAPHY</b>	40

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# CHAPTER -1

## INTRODUCTION

Nanotechnology is a rapidly growing entity in the modern science. The impact of nanotechnology has brought many changes in treatment aspects in healthcare sector. Nano sized materials show different properties. Colour, conductivity, strength etc change in case of nanosized materials. This nanotechnology in dental field, “Nanodentistry” is a multidisciplinary field of science and technology, that uses nanomaterials and devices in diagnosing, treating and preventing oral and dental diseases, relieving pain and improving dental health using nanosized material.

Bacterial infections remain as a gross reason for morbidity and mortality in this world. The main concern is about multi drug resistant bacterial strains and biofilm-associated infections. Despite the innumerable potent antibiotic drugs and other existing modern antibacterial means, bacterial infections remain as a challenge. Antimicrobials used in the clinical field at present have shortfalls like risk of microbial resistance, weak antimicrobial activities, difficulty in functioning in a dynamic environment etc. Long-term effective antibacterial and biofilm-preventing materials account for a prompt need in medicine and dentistry. Hence a gross change in the antimicrobial therapy was required and the attention was moved to nanotechnology. The new and emerging nanoparticle-based biomaterials in healthcare field brought a good change in various materials as well as therapies applied.

Nanotechnology has been applied widely in medical as well as dental field. This has brought immense changes in research as well as in the application field, bringing a lot of improvements in diagnosing, preventing and treating oral and dental pain and diseases. Metallic oxide nanoparticles have been applied in biomedical field such as drug delivery, anticancer, antifungal, antibacterial etc.

Due to the increase in the number of microorganisms and their resistance to antimicrobials, scientists have researched on materials that can be effective against microorganisms as well as cost effective. Decreasing the size of the particle has been found to be an efficient tool in improving the biocompatibility. Nanoparticles of metals have various applications in industry, agriculture and healthcare. Antimicrobials in the form of nanoparticles have been studied, and suggested their use as bactericidal materials. In various research works, metals and metallic oxides have proved to show antimicrobial activity at low concentrations.<sup>1,2,3</sup>

Nanotechnology has become an integral part in dental research. The antimicrobial activity of different metals like silver (Ag), gold (Au), titanium (Ti), copper (Cu) and zinc (Zn), which are considered to be safe for human beings, have been used in various areas since a long time<sup>4</sup>. As years passed, Metallic oxide nanoparticles such as silver oxide (Ag<sub>2</sub>O), titanium dioxide (TiO<sub>2</sub>), zinc oxide (ZnO), calcium oxide (CaO), copper oxide (CuO) and magnesium oxide (MgO) were identified to display antimicrobial activity.

Oral cavity has numerous microorganisms which can cause many infections. Dental and periodontal diseases have multiple etiological factors, but the common being bacteria. Oral infections can influence the progression and pathogenesis of many systemic diseases like cardiovascular disease, bacterial pneumonia etc. Hence, maintaining oral health is a major goal in dentistry. Nanomaterials along with nanotechnology in dentistry help in bringing down the microbial infections.

The accurate mechanism of action of nanometals is still being studied. The mechanism of action thought to be behind its antimicrobial activity is that they act by deactivating the cellular enzyme and DNA by engaging the electron donating groups such as carboxylates, Amides, Thiols, Indoles, Hydroxyles, etc. They cause pores in bacterial cell walls, thus leading to increased permeability leading to cell death. Certain possibilities which have been put forward

include free metal ion toxicity due to the dissolution of metals from the surface of nanoparticles or oxidative stress caused by generating reactive oxygen species (ROS) on the surfaces of nanoparticles.<sup>5</sup>

Antimicrobial effectiveness depends on the kind of the materials used for preparing the nanoparticles and its particle size.<sup>6,7</sup> Reducing the particle size of the materials is considered to be an efficient tool for improving biocompatibility.<sup>5</sup> Nanotechnology at present gives a good platform for changing the physical and chemical properties of various metals to transform them into effective antimicrobials. Hence antimicrobial efficacy of various nanometals are dedicated to their morphology and physicochemical properties.<sup>6,8</sup>

The antimicrobial efficacy of nanoparticles are found to be greatly influenced by its shape.<sup>9,10</sup> Nanoparticles when compared to their own larger particles show different characteristic features. This can be credited to the fact that the surface/volume ratio of the nanoparticles increase with the decrease in the particle size.<sup>11,12</sup> Because of this small particle size, nanoparticles have a better penetration into cells and tissues, showing strong bactericidal effect.<sup>13,14,15</sup> It is believed that, the positively charged surface of the metallic nanoparticles help in their attachment to the negatively charged surface of the bacteria thus resulting in a higher bactericidal effect.<sup>6</sup>

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# **CHAPTER 2**

# **HISTORY**

A few researchers think nanotechnology as a newer form of science that did not develop until the late 1980s or early 1990s. But some others have traced it back to the 1950s.

**1867** - In 1867 by James Clerk Maxwell proposed that a tiny entity known as Maxwell's Demon shall be able to handle individual molecules in the time ahead.

**1914** - During the first decade of the 20th century, the first observations and size measurements of nano-particles was made. Richard Adolf Zsigmondy did a research of gold sols and other nanomaterials with sizes down to 10 nm or less. He was the first person who used the term "nanometer" for specifying the size of a particle.

**1959** - The Nobel prize winning physicist Prof. Richard Feynman described atomic scale fabrication of nanomaterials. Prof Feynman suggested that nanomachines, nanorobots and nanodevices could be utilized to develop a wide variety of precise microscopic instruments and tools.

**1974** - Norio Taniguchi, coined the term "nanotechnology" in his article and the name gained popularity.

**1977** - Many researchers accept to the fact that the term "Nanotechnology" was coined by Prof. Kerie E. Drexler, researcher at Massachuehettes Institute of Technology. Researchers claim that that Prof. Drexler also introduced molecular nanotechnology concepts in the late 1970's.

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# **CHAPTER 3**

**SILVER(Ag) AND SILVER OXIDE**

**NANOPARTICLES (Ag<sub>2</sub>O)**

Of all the metal nanoparticles, silver nanoparticles have been effectively used as antimicrobial agent against bacteria, fungi, and viruses. Applications of Silver and its compounds have been used for disinfection of various medical devices and in water purification. Among nanometals, with antimicrobial properties, silver is being used against microbial infections since many years. Silver compounds are commonly used to treat wounds and a number of infectious diseases. Silver was reported to be an efficient antibacterial agent against different pathogens in various studies.

Silver nanoparticles are the most popular inorganic nanoparticles employed as antimicrobial agents in numerous products and has vast biomedical applications. The antibacterial activity of silver nanoparticles reduces patient infection, antibiotic dependence as well as associated costs. Besinis et al. in their study concluded that the antibacterial effectiveness of Ag nanoparticles against *S. mutans* was high-up than that of chlorhexidine.<sup>16</sup>

Hernández-Sierra et al, in their comparative study on the antimicrobial activity of Ag nanoparticles, ZnO, and Au against *Streptococcus mutans* (*S. mutans*) showed that Ag exhibited the highest activity against *S. mutans*. They also suggested that as *S. mutans* being responsible for dental caries, Ag nanoparticles may be considered helpful.<sup>17</sup>

Properties based on the shape of nanoparticles have also been investigated by various researchers. Bera et al stated that the size as well as the shape of the fluorescent Ag nanoparticles (1–5 nm) controlled its antimicrobial activity against *Staphylococcus epidermidis* and *Bacillus megaterium* and *Pseudomonas aeruginosa*.<sup>18</sup>

Ag<sub>2</sub>O nanoparticles were found to have good antimicrobial activity. Sondi and Salopek-Sondi in their study suggested the antimicrobial efficacy of Ag<sub>2</sub>O nanoparticles against *E. coli*.<sup>19</sup>

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# **CHAPTER 4**

## **TITANIUM DIOXIDE(TiO<sub>2</sub>)**

### **NANOPARTICLES**

TiO<sub>2</sub> nanoparticles are considered as advanced materials because of their impressive optical, photo-catalytic and dielectric, properties. Titanium dioxide (TiO<sub>2</sub>) is used as a disinfecting and cleansing material. It is used for environmental purification which can be attributed to its photo induced super-hydrophobicity as well as antifogging results.<sup>20</sup> These properties are very well utilized in eliminating bacteria and harmful agents from air and water.<sup>21</sup> These nanoparticles are also used for sterilizing surfaces in healthcare centres.

Antimicrobial property of TiO<sub>2</sub> is attributed to its crystal structure, shape and size .<sup>22</sup> The oxidative stress via the generation of reactive oxygen species (ROS) may be an important mechanism for TiO<sub>2</sub> nanoparticles. The ROS causes site specific DNA damage.<sup>23,24</sup> Haghghi et al. in their research on the antifungal effect of TiO<sub>2</sub> nanoparticles against fluconazole resistant standard strains of *Candida albicans*, showed that the synthesized TiO<sub>2</sub> nanoparticles had improved antifungal effect on the fluconazole resistant strain of *C. albicans* biofilms. Therefore, it was suggested that TiO<sub>2</sub> nanoparticles could be used effectively to inhibit the fungal biofilms especially those formed on the surface of medical devices.<sup>22</sup>

TiO<sub>2</sub> nanoparticles have the potential to produce ROS under UV light. Photocatalytic properties of the TiO<sub>2</sub> nanoparticles make them efficient in eradicating bacteria. But, the use of TiO<sub>2</sub> nanoparticles under UV light can cause genetic damage in human cells and tissues, hence restricted. It has been found that, doping of TiO<sub>2</sub> nanoparticles with metal ions can be a good idea to solve this problem. <sup>25</sup>Carré et al. noted that the antibacterial activity was accompanied by lipid peroxidation that causes the disruption of the cell integrity.<sup>26</sup>

*Main characteristics as antimicrobial agent-*

- Photocatalytic activity
- High stability
- Bactericidal effects on both Gram-positive and Gram-negative bacteria
- High stability
- Effective antifungal for fluconazole resistant strains.

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# **CHAPTER 5**

## **ZINC OXIDE NANOPARTICLES(ZnO)**

Zinc oxide is a bio safe material which exhibit antibacterial properties. The white color, UV-blocking, and ability to prevent biofilm formation makes them suitable for fabric and glass industries as coating materials for medical and other equipment. ZnO nanoparticles were shown to have broad range of antimicrobial activity against various microorganisms, and it was dependent on the concentration and particle size. Emami-Karvani et al.<sup>27</sup> studied the antimicrobial activity of ZnO nanoparticles against *E. coli* and *S. aureus* bacteria, by using different concentrations and reducing the particle size. They concluded that the antibacterial activity of ZnO nanoparticles increased by changing the concentrations and by reducing the particle size. This improved antibacterial activity of ZnO nanoparticles compared to its microparticles was mainly attributed to the surface area enhancement.

ZnO nanoparticles are of low cost. They are effective size- dependent antimicrobial against *Klebsiella pneumonia*, *Listeria monocytogenes*, *Salmonella enteritidis*, *Streptococcus mutans*, *Lactobacillus* and *E. coli* and with low toxicity to human cells. ZnO nanoparticles exhibit high photocatalytic properties which enhance their antimicrobial efficiency. These nanoparticles generate ROS under UV light as well.

#### ***Proposed mechanism of antimicrobial action-***

By ROS generation on the surface of the particles and zinc ion release leading to membrane dysfunction and internalization of nanoparticles into cell.

Azam et al. in their comparative investigation of antimicrobial activity of ZnO, CuO, and Fe<sub>2</sub>O<sub>3</sub> nanoparticles against Gram negative and Gram-positive bacteria reported ZnO as the most bactericidal.<sup>28</sup> Some studies have demonstrated that metal ion doped nanoparticles can increase antimicrobial properties of metallic nanoparticles. Sun et al. from their studies

suggested that the titanium doped ZnO powders showed antimicrobial action against E. coli and S. Aureus.<sup>29</sup>

The treatment using zinc was approved by the FDA and an added point is nowadays Zn is available as a food additive.

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# **CHAPTER 6**

## **COPPER (Cu) AND COPPER OXIDE (CuO)**

### **NANOPARTICLES**

Copper nanoparticles have unique biological, chemical and physical properties, antimicrobial activities as well as the low cost of preparation. Eventhough copper oxide (CuO) nanoparticles are found to be effective against various bacterial pathogens, their antibacterial efficacy has been inferior to that of Ag or ZnO. Hence, a higher concentration of nanoparticles is required to achieve the same good results. Cu is much less expensive than other nanosized metal particles, it can be utilized for efficacy enhancement like the other metallic nanoparticles, to express their antibacterial activity by membrane disruption and ROS production.

Mahapatra et al.investigated the antibacterial activity of CuO nanoparticles and reported that copper oxide nanoparticles showed good antibacterial activity against the tested bacteria.<sup>30</sup>

Azam et al investigated the antibacterial activities of CuO nanoparticles against *S. aureus* and *B. subtilis* and *Pseudomonas aeruginosa* and *E. coli*. According to their study, nanoparticles exhibited size dependent -inhibitory effects against both groups of the mentioned bacteria. These nanoparticles prevent bacterial growth by entering the nano- pores existing on the cellular membranes of most of the bacteria.<sup>31</sup>

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# **CHAPTER 7**

## **NANOMETALS AS ANTIMICROBIALS IN DENTISTRY**

Nanomaterials have been considered as materials in which the shape as well as the molecular composition can be controlled at nanometre scale. Hence, they have extraordinary properties which are useful for the development of new and improved applications in dentistry. In dentistry, several research efforts are being carried out, for the improvement of the properties of materials used in dentistry.

Various studies done on the different nanoparticles were applied into different aspects of dentistry starting from the biomaterial aspect to the treatment level considerations. Silver, titanium dioxide and zinc oxide nanoparticles have been extensively studied and applied in various dental materials.

Nanomaterials are used in various dental applications –

- **Tissue regeneration**
- **Reinforcement of polymeric composites**
- **Endodontics application**
- **Implants as coatings.**

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# **CHAPTER 8**

**NANOMETALS AS ANTIMICROBIALS IN**

**DENTAL MATERIALS**

## **MATERIAL ASPECTS**

Dental health care standards has been enhanced due to the development of newer nano-biomaterials and also by changing the properties of the existing materials.

These promising materials will find wider dental applications with improved therapeutic application.

### **Impression Materials-**

Dental impressions form vital part of all specialities of dentistry. The most commonly used impression material in dentistry is the hydrocolloid alginate impression material. Impressions get contaminated with saliva as well as blood during clinical procedures and there are chances of cross infection. The incorporation of different antimicrobial agents into impression materials could be effective in decreasing cross-infection.

Alginate powder can be incorporated into water containing silver hydrosol to provide an antimicrobial effect, which will prevent the contamination of stone cast from the infected impression.<sup>32,33</sup> Wangchuk et al, in their study, evaluated the *in vitro* antimicrobial efficacy of silver nanoparticles incorporated to alginate against *Staphylococcus aureus*. According to this study, silver nanoparticles (AgZrPO<sub>4</sub>) at different concentrations added to the powder of impression material showed inhibitory effect against pathogenic bacteria.<sup>34</sup>

**Dental cements-**

Dental cements play a key role in restorations as well as cementation of crowns and bridges. So antimicrobial activity of dental cements has become an important criteria, to prevent the pathogenic microorganisms from gaining access to the cavity or the prepared tooth after cementation. The antibacterial activity of the dental luting cements is important considering the microleakage after cementation. Considering this, studies were carried on the efficacy of nanometals in inhibiting microorganisms. Silver nanoparticles show good antimicrobial activity, which is mainly due to the release rate of silver ions. These reactive ions act on the bacterial cell wall and results in the structural changes by binding to the tissue protein and causing cell death. Magalhaes et al in their study,<sup>35</sup> incorporated silver nanoparticles into glass ionomer cement, endodontic cement and resin cement and the antimicrobial activity against *S. mutans* was studied. These cements doped with silver nanoparticles presented significant antimicrobial properties compared to cements without nanoparticles.

Glass ionomer-containing TiO<sub>2</sub> nanoparticles possessed antibacterial activity against *S. mutans* in contrast to the unmodified glass ionomer.<sup>36</sup> A study evaluating the antibacterial activity of zinc oxide nanoparticles incorporated self cured GIC and light cured resin reinforced GIC on *S. mutans* biofilms, concluded that ZnO nanoparticles incorporated into GIC, at concentrations of 1% and 2% by weight did not help in their antibacterial action.<sup>37</sup>

## Dental Composites-

The resin based dental composites are commonly used in dental restorations due to their aesthetic superiority and strong bonding ability and strength. Plaque accumulations on these materials can cause recurrent caries and ultimately failure of restorations. Silver and titanium particles were incorporated into dental composites to provide antimicrobial properties as well as to improve the biocompatibility. To reduce the biofilm accumulation over composite, antimicrobial restorative materials have been developed by the incorporation of silver nanoparticles to composite resins. Cheng et al reported that silver nanoparticles incorporation into composite resins enabled good mechanical properties along with notable antimicrobial effect, at lower concentrations.<sup>38</sup> Reham et al evaluated antimicrobial efficacy of ZnO nanoparticles incorporated into resin composites against organisms causing caries and the results show 85% reduction in growth of different kinds of bacteria which tested under study.<sup>39</sup> In a study conducted by Shahin Kasraei et al, antibacterial properties of composite resins with zinc oxide and silver nanoparticles concluded that it can inhibit the growth of *S.mutans* and *Lactobacillus*.<sup>40</sup>

Light cured flowable composite resin material can function as an effective antimicrobial by adding silver hydrosol. This silver hydrosol that gets leached from the composite resin matrix can help to decrease the incidence of dental caries.<sup>41</sup> Such studies showing antimicrobial properties of silver nanoparticles-containing composite resin might reduce the development of secondary or recurrent caries by reducing the bacterial biofilm formation on the teeth and thereby increasing the longevity of the restorations.

**Endodontic materials-****Guttapercha-**

Success of endodontic care is connected to the bacterial elimination, to a large extent. Many materials have been used as root canal fillings, among which gutta-percha being the most widely used. The zinc oxide component present in gutta-percha makes it have its own antimicrobial property. Iranian researchers, Dianat and Ataie had introduced nanosilver-gutta-percha, to enhance the antibacterial effectiveness of gutta-percha. The new material demonstrated significant antimicrobial effect against *Enterococcus faecalis*, *Staphylococcus aureus*, *Candida albicans*, and *Escherichia coli*.<sup>42</sup>

**Mineral trioxide aggregate (MTA)-**

Mineral trioxide aggregate is a well-known dental root repair material. MTA is used for an apical plug formation during apexification, in case of any root perforations during root canal treatment and in cases of internal root resorption. Also used as root-end filling material and pulp capping material. Samiei et al modified MTA by incorporating silver nanoparticles and it was found to act against oral bacteria and fungi species. They concluded that a group-containing MTA possesses higher antimicrobial action compared to unmodified MTA.<sup>43</sup> Eventhough AgNP is a potent antimicrobial, there are only a few studies incorporating it in endodontic materials.

**Dental adhesives-**

Dental adhesives are materials which help in the adhesion and cohesion of two different materials or between material and natural teeth. Li et al, in their study incorporated silver nanoparticles (AgNPs) to an adhesive system in order to evaluate the bacterial inhibition. According to their results, AgNPs reduced Colony forming units (CFU) number and lactic acid production on biofilms suggesting their antibacterial potential.<sup>44</sup>

Melo et al in their study evaluated antimicrobial efficacy by incorporating silver nanoparticles to an adhesive system and results showed a reduced metabolic activity on biofilm, compared to control group without AgNPs.<sup>45</sup> Mahshid S et al, studied the effect of adding zinc oxide nanoparticles to dental adhesives on their antimicrobial activity and bond strength. According to their results, adding zinc oxide nanoparticles to dental adhesives inhibited the formation of *Streptococcus mutans* colonies, without compromising the bond strength.<sup>46</sup>

**Acrylic resins-**

Dentures are fabricated by poly (methyl methacrylate) (PMMA) acrylic resin. Various factors can contribute to the roughness of their inner surface which can act as a niche for microbial (*Candida* species) colonization, which can cause denture stomatitis in denture wearers.<sup>47</sup> Due to the smaller size, silver nanoparticles possess greater dispersion in PMMA matrix and produce larger area for oxidation. The release of silver ions act by rupturing the cell wall and denaturing the protein and ultimately leading to microbial death, thus explaining the antimicrobial action and effectiveness of silver nanoparticles.

Acosta-Torres et al in their research observed that PMMA- AgNPs specimens showed less *Candida albicans* adherence compared to unmodified PMMA, thus reporting the antifungal potential of AgNPs incorporated to acrylic resin.<sup>48</sup>

**Tissue conditioners or Soft liners-**

Tissue conditioners are used in denture patients who present inflamed or abused mucosa and getting them back to normal health. It is mainly used to aid in the treatment of chronic soreness caused by dentures. Tissue conditioners are susceptible to microbial colonization. Many studies were conducted by addition of metallic and metallic oxides in tissue conditioners to study its antimicrobial activity. Nam in his study, incorporated AgNPs into a commercial tissue conditioner, in the following concentrations: 0.1%, 0.5%, 1.0%, 2.0%, and 3.0%. Their inhibitory effect was evaluated against *Staphylococcus aureus*, *Streptococcus mutans*, and *Candida albicans*. He reported that the modified tissue conditioner presented antimicrobial properties even at lower concentrations, that is, 0.1% (for *S. mutans* and *S. aureus*) and 0.5% (for *C. albicans*).<sup>49</sup>

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# **CHAPTER 9**

## **NANOMETALS AS ANTIMICROBIALS**

### **IN IMPLANT DENTISTRY**

Dental implants have become an integral part of reconstructive dentistry. Bacterial invasion can occur during surgery or post operatively. Infection being one of the most important complications in Implantology, various measures have been considered in order to avoid bacterial contamination. Nanotechnology is increasingly used for the surface modifications of dental implants.

It has been reported in various literatures that titanium dioxide nanoparticles coating on titanium implants can increase antimicrobial efficacy of implants. Singaravel et al in their study, evaluated the antifungal effect of titanium, zirconium and aluminium nanoparticles coated titanium oxide plates. Titanium oxide nanoparticles coated titanium plates showed greater antifungal effect against *Candida albicans*, compared to zirconium oxide and aluminium oxide.<sup>50</sup>

Flores et al suggested that incorporation of silver nanoparticles on titanium implants as a method to guard implant surface against the pathogen. And they also reported that silver nanoparticles showed bactericidal action at lesser concentration which does not interfere with the osseointegration process.<sup>51</sup>

Zhao et al in their study, incorporated silver nanoparticles into titania nanotubes (TiO<sub>2</sub>-NTs) on Ti implants. The antibacterial effect against *Staphylococcus aureus* was evaluated. According to this study, Ti implants incorporated with silver nanoparticles showed its ability to prevent bacterial adhesion for a time period of 1 month.<sup>52</sup>

Zhang et al, in their study coated TiO<sub>2</sub> implants by silver nanoparticles using Micro Arc Oxidation (MAO) and their results showed enhanced antimicrobial activity which was attributed to the interaction between silver nanocrystals and bacterial cell membrane.<sup>53</sup> A study conducted by Xiaojing He et al suggested that the Micro Arc Oxidation (MAO) technique effectively introduces inorganic antibacterial metals (eg: Ag, Cu, Zn) into biomedical implants, thus successfully solving the issue of periimplant infection. Flores et al studied the antibacterial

activity of silver nanoparticles (AgNPs) against *Pseudomonas aeruginosa* and suggested that the incorporation of AgNPs on Ti implants as an effective approach to guard the surface of implants against microbial colonization.<sup>54</sup>

Miguel A et al, studied antimicrobial activity of metal oxide nanoparticles against pathogens causing periimplantitis. In their study they considered six metal (Ag) and metal oxides [cuprous oxide (Cu<sub>2</sub>O), cupric oxide (CuO), zinc oxide (ZnO), titanium dioxide (TiO<sub>2</sub>), tungsten oxide (WO<sub>3</sub>)] and two of their composites[(Ag+CuO), (Ag+ZnO)] against bacterial pathogens. The antimicrobial activity of the nanoparticles tested showed silver showing the most and tungsten oxide the least antimicrobial effect. And they suggested that composites of nanoparticles should also be considered as antimicrobial agents. In this study, bacteriostatic activity showed by the composites were greater than that of nanoparticles alone.<sup>55</sup>

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# **CHAPTER 10**

## **NANOMETALS AS ANTIMICROBIALS IN MAXILLOFACIAL PROSTHETIC MATERIALS**

## **MAXILLOFACIAL PROSTHESIS**

Maxillofacial deformities negatively affect patient's physical and mental health affecting their family and social life. Maxillofacial prostheses repairs and replaces artificially the lost or missing parts in the maxillofacial region. Maxillofacial prosthesis has a crucial role on the patient's self-confidence and quality of life, as it's an instant corrective way that can help the patient get back to his normal social life.

Maxillofacial reconstruction involves using artificial substitutes for intraoral as well as extraoral parts like eyes, ears, nose, cranial bones, jaw bones etc. A variety of materials, procedures and clinical approaches are used in maxillofacial prosthetic reconstruction. Maxillofacial prostheses are basically fabricated of acrylic resin or silicone based on the facial structure of the patient in need. These prostheses are retained by various types of retentive mechanism like anatomic, mechanical and chemical.

Maxillofacial prosthesis can be classified as restorative or complementary. In these, restorative prostheses substitute for repair deformities of facial contour or for bone loss. They can be either internal within the tissue or external like oral, ocular or facial prostheses. Whereas, the complementary prostheses help with plastic surgery, during pre, trans or post operative time frame or in radiotherapy sessions. Maxillofacial prostheses are more prone for contamination and thereby can cause infections.

Maxillofacial prostheses fabricated from silicone material are more prone to fungal infection caused by *Candida albicans*. Coating silicone materials with silver nanoparticles could be advantageous to the patients using maxillofacial prostheses, to prevent or reduce fungal infection. Silver nanoparticles have been incorporated in maxillofacial prosthesis and it showed reduced adherence of *Candida albicans* to maxillofacial prosthesis surface.<sup>56</sup>

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# CHAPTER 11

## A NOTE ON CYTOTOXICITY

## A NOTE ON CYTOTOXICITY OF METAL AND METALLIC OXIDE NANOPARTICLES

Mechanism behind the toxicology of nanomaterials and their hazardness extent are still unknown. The toxic effects they pose can be attributed to various factors. The generation of ROS is considered the main determinant for both their *in vitro* and *in vivo* cytotoxicity.<sup>57</sup> Many cellular events are driven by low levels of ROS. An increase beyond certain limits lead to oxidative stress causing cell death via oxidation.<sup>57</sup>

Nanoparticles of Ag, ZnO, and TiO<sub>2</sub>, show moderate to high levels of cytotoxicity against a variety of animal cells. In addition, some nanoparticles like SiO<sub>2</sub>, Au, Fe<sub>2</sub>O<sub>3</sub>, and TiO<sub>2</sub> have shown good biocompatible properties. This cytotoxic nature of nanoparticles has been converted into biocompatible materials by introducing slight changes in their surface structural features. Nanoparticles have a wider level of biological properties that are dependent upon their structure, size, quantity and receptor cell type.

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# **CHAPTER 12**

## **ADVANTAGES AND DISADVANTAGES OF NANODENTISTRY**

## **ADVANTAGES**

Advantages of nano-dentistry include

- Superior flexural strength, hardness, translucency, modulus of elasticity and durability of nano-dental materials.
- Faster and apt diagnosis of many oral diseases with small diagnostic machineries.
- Less treatment time and faster healing
- Better aesthetics
- Better treatment outcome
- Reduced number of visits for the patient
- More economical

## **DISADVANTAGES**

Disadvantages of nano-dentistry include

- Toxicity associated with nanomaterials can affect the humans
- Ethical issues /social acceptance

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## **SUMMARY AND CONCLUSION**

Many microorganisms and antimicrobial resistant microorganisms pose a real threat to human life. Certain bacterial strains are resistant to the antibiotics now in use and pose a serious public health concern. This demands newer materials against such strains, in order to overcome such issues. Nanotechnology has been successful in creating many novel bactericidal antimicrobial materials and strategies. Advances in the field of nano-structures and nanomaterials with suitable properties led to an increase in the making of stable nanoparticles that are capable of biomedical applications. Nanoparticles of metals have shown great potential as fungicidal and bactericidal agents in treating many medical issues. Applications of metal and metallic oxide nanoparticles, and their surface modifications, with good antimicrobial activity in lesser concentration locally destroy pathogens, without being toxic. The efficacy of these nanoparticles varies with their size, shape, and concentration. As the size of the particle reduces, the percentage of atoms on the surface increases, thus enhancing the effectiveness of action.

Different nano- metals and metallic oxides show good biocompatibility as well as antimicrobial pathogenic activity against different viral and bacterial species in small measures. These nanoparticles of metallic oxides offer extended antimicrobial activity with minimal toxicity. Hence metallic oxide nanoparticles might be considered as a new alternative to most of the antibiotics and if applied in drug delivery systems in medical and dental field can be a boon to the human race, where antibiotic resistant pathogens have aroused to be alarming. More researches and application in this field will bring many newer results and advances in different fields.

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## ABSTRACT

## Cariology and Preventive Dentistry

### 717 | Oral health-related quality of life (OHRQoL) following clinical interventions of odontogenic infection in 3–8-year-old children: A randomised controlled trial

Emma Marlisa Abdul Malek<sup>1</sup>; Tengku Nurfarhana Nadirah Tengku Hamzah<sup>1</sup>; Zamros Yuzadi Mohd Yusof<sup>2</sup>; Lily Azura Shoaib<sup>1</sup>

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**Background:** This study investigated the changes in oral health-related quality of life (OHRQoL) in children aged between three to eight years presented with localised odontogenic infection before and five days after receiving treatment with Odontopaste, calcium hydroxide or oral Amoxicillin.

**Methods:** A single centre randomised control trial of three-arms was conducted at the Faculty of Dentistry, University of Malaya on 71 children who fulfilled all inclusion criteria. The dentition status and severity of dental caries were recorded using ICDAS II and PUFA/pufa index. A self-administered questionnaire comprising the Malay-ECOHIS was given to parents at the baseline and follow-up visit on day 5. Children with parents who completed both sets of questionnaires were included in the final analysis.

**Results:** The recruitment rate of this study was 65.7% with a high completion rate of 98.6%. Majority of the parents reported a negative impact on their child's QoL before receiving treatment. Only 21.4% of parents reported good QoL for Malay-ECOHIS, with the majority of parents reporting low negative impact after their children received the treatment. The decrease in the mean score of the Malay-ECOHIS in the Odontopaste group had an effect size of 0.6, with the study's power being 0.8.

**Conclusions:** The result showed there was no significant difference in the decrement between treatment groups over time ( $P = 0.05$ ). There was no significant difference in OHRQoL with different treatment modes. Future multi-centred studies including rural areas are recommended for better representation of the paediatric population.

**Funding:** University of Malaya Research Grant (Grant No.: RP053C-17HTM)

### 1334 | Remineralization ability of self-assembling peptide (P11-4) on early enamel carious lesions: A review of the literature

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**Background:** Dental caries, which is a serious public health problem, is one of the most common chronic diseases in childhood. Prevention begins with appropriate nutrition and brushing habits and is maintained with the aid of remineralizing agents. In order to find better solutions for caries prevention, the necessity to develop new materials that are safe and effective has gained importance. In this review, we aimed to summarize the ability of self-assembling peptides as a remineralization agent by evaluating previous in vitro studies.

**Literature Review:** Self-assembling peptide (P11-4) mimics the enamel matrix proteins and accumulates in the enamel lesions by forming a biomimetic matrix to form hydroxyapatite within the sub-surface body of the initial enamel lesion. Unlike traditional remineralization agents, it creates a 3-dimensional scaffold that allows ions to precipitate within the subsurface carious lesion. Through this formed scaffold, it acts as a mineral deposition core for hydroxyapatite, which promotes tissue regeneration. In the vast majority of in vitro studies, the remineralization potential of self-assembling peptide (P11-4) was found to be better when compared with other remineralization agents such as CPP-ACP, CPP-ACFP, TCP, fluoride, bioactive glass and silver diamine fluoride. Furthermore, the combined use of P11-4 with other agents increases the remineralization efficacy. Today, P11-4 is marketed under the trade name Curodont (Credentis AG, Windisch, Switzerland).

**Conclusion:** P11-4 can be accepted as an effective, biocompatible and preferable agent in the remineralization of early enamel caries lesions. With its non-invasive regeneration potential, it provides more benefits from long-term remineralization regimens.

## 1199 | Early childhood caries in infants and the relation with feeding practices and milk formula cariogenicity

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**Background:** Early Childhood Caries (ECC) is related to feeding practices. Our objective was to report ECC prevalence and risk factors, and measure associations between feeding habits and cariogenicity of different milk formulas with ECC.

**Methods:** Children younger than 48 months-old from Jordan were included. A questionnaire was applied to the parents and a clinical examination was performed; dental caries (dmft/dmfs) was recorded, and saliva-pH was measured before and 10-minutes after milk-formula consumption using Saliva-Check BUFFER (GC America®). Laboratory analysis of sugar, calcium, phosphate, casein, and fluoride content of 7 different milk-formula brands was conducted using High-Performance-Liquid-Chromatography. Data was analyzed using SPSS. Significance was set at  $P$  0.05.

**Results:** Two hundred one (201) children (mean age  $24.4 \pm 9.9$  months) were included. Most consumed Bebelac® (40%) and Nido® (37%). Mean dmft and dmfs scores were  $0.4 \pm 1.1$  and  $0.4 \pm 1.4$ , respectively. Saliva pH significantly dropped after milk-formula consumption. The highest fructose, glucose, sucrose and maltose levels were in Similac®3, Bebelac®3, Similac®2 and Nido®2, respectively. Meanwhile, the highest levels of calcium, phosphate, casein and fluoride were in Nido®, Similac®3, Bebelac®3, and Nido®. ECC was significantly associated with older age, lower maternal education and nursing habits. Subjects who were fed Nido®2 had higher probability of having ECC compared with other milk formulas. Correlation between dmft and dmfs scores with drop in saliva pH and milk formulas was not significant.

**Conclusions:** ECC was associated with older age, lower maternal education and nursing habits. Higher sugar content in milk formulas did not have a significant correlation with dmft and dmfs scores. These results can be used to increase awareness, prevention, and management efforts against ECC.

## 651 | The association of early childhood caries with salivary antimicrobial peptide (LL37) and mutans streptococci bacteria

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**Background:** Salivary LL37 is an essential innate immunity component that plays an important role in maintaining oral health. This study aimed to determine if salivary LL37 level and mutans streptococci levels were related to early childhood caries (ECC).

**Methods:** A case-control study was carried out on children aged  $\leq 71$  months old. Unstimulated whole saliva were collected. Salivary LL37 level was measured by enzyme linked immunosorbent assay kit. Mutans streptococci oral bacteria were isolated and identified using a modified SB-20 culture medium (SB-20M). Data were analyzed with descriptive statistics, bivariate and Spearman's rank correlation analysis.

**Results:** Salivary LL37 level showed a great variability among children. Its level was significantly associated with children's age and races. The median (IQR) value of salivary LL37 of caries free (CF) children was significantly higher 393.50 (580.55) ng/mL compared to 172.50 (234.65) ng/mL in ECC group. ECC children exhibited significantly higher count of *S. mutans* and *S. sobrinus* compared to CF children, with an inverse weak correlation between salivary LL37 and dmft.

**Conclusions:** ECC children exhibited lower salivary LL37 level and higher count of *S. mutans* and *S. sobrinus* compared to CF children. These findings supported the protective role of salivary LL37 against dental caries. Further studies are required to explore the definite relation between salivary LL37 levels and dental caries.

## 688 | Smart Burs: A Review of Literature

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**Background:** Dental caries is a multifactorial, infectious disease that contributes to the burden of oral disease globally. Over the last few decades, the management of dental caries has evolved from the paradigm of "extension for prevention" to "prevention of extension" following extensive research in cariology and material sciences. In this ultraconservative era of dentistry, caries removal by smart burs has been a new leaf for caries excavation.

**Literature review:** Smart burs also described as (dentin safe) are paddled-shaped polymer rotary burs, made up of polyether-ketone-ketone. The hardness of Smart Bur (50 KHN) is higher than infected dentin (15–20 KHN) and less than healthy dentin (68 KHN), which allows it to selectively cut the infected dentin, leaving behind affected dentin intact due to which fewer chances of odontoblasts are exposed thereby minimizing pain and sensitivity. It rotates at the speed of 500–800 rpm. It is developed on the basis of the differential hardness of carious and sound dentin. Smart bur dulls and vibrates when in contact with healthy calcified tooth structure. The burs being indicated for single-use also helps in minimizing cross-infection. Few drawbacks of these burs are the clinician's belief in newer techniques, cost, and time factor.

**Conclusion:** Smart burs are found to be effective as compared to carbide burs in the removal of carious teeth. Hence should be employed in day-to-day practice based on advanced research. Further long-term clinical studies are recommended comparing smart burs with high-speed drills.

## 1945 | Anticariogenic and remineralising potential of plant extracts in white spot lesion: A review of literature

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**Background:** Enamel is the outermost covering of the tooth which lacks the functional capacity to regenerate and predisposed to numerous challenges in the oral cavity. Any drop in pH below the critical value results in enamel demineralization. This denotes the caries initiation with subsurface mineral

loss and relatively intact superficial layer appearing as white spots. Fluoride is a proven agent for caries prevention but excessive use may cause dental fluorosis. So, there is a need for alternative options that are safe, effective and economical. Also, there is an increase in interest among both the general people and researchers, to explore the possibility of using the traditional systems of medicine which depends on the use of plants and herbal extracts for its therapeutic measures.

**Literature review:** Extracts of cocoa bean (*Theobroma coca*), galla chinensis (*Rhus chinensis*), ginger rhizome (*Zingiber officinale* Roscoe, Zingiberaceae), rosemary (*Rosmarinus officinalis* L., Lamiaceae), Grape seed, Moringa species, have been used for medicinal purpose for centuries. Moreover, they are natural materials, showing no toxicity, and are considered 'generally recognized as safe' (GRAS) by the US Food and Drug Administration (FDA). In particular, their pungent oil components arbor a series of polyphenolic ketones with many pharmacological activities. Their antimicrobial effects on cariogenic pathogens and remineralization potential have been reported in many studies

**Conclusion:** The plant-based phytochemicals and bioflavonoids could find greater acceptability among the general public compared to the fluoride-based systems for prevention and remineralization of white spot lesion.

## 1041 | ECC Risk Factors Assessment in Belarus

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**Background:** ECC is a risk-specific disease, depend on exposure to causative factors: prolonged breastfeeding, early introduction of free sugars, high-frequency intake of free sugars and fluoridated toothpaste use.

**Methods:** 393 children (1–6 years) were examined according to a new protocol for ECC Diagnosis and Risk Assessment (2018) by four calibrated dentists ( $\kappa = 0.95$ ) in Minsk, Minsk and Brest regions. Children were divided in 5 groups: 12–23 months ( $n = 55$ ), 24–35 months ( $n = 77$ ), 36–47 months ( $n = 93$ ), 48–59 months ( $n = 77$ ), 60–71 months ( $n = 91$ ). Parents answered the questions from Protocol. Regional Ethics Committee approval and parental informed consents were obtained. The results were analyzed statistically.

**Results:** The mean ECC1-3mft was noted for children that were breastfed beyond 12 months, was 4.98 (3.72), which is almost one unit more (4.00 (4.33)) than in children whose parents stopped it before one year. The ECC1 (initial lesions) of children under 12 months exposed to free sugars was 2 times more (1.29 (3.43)) than mean level of its indicator in those who were not exposed to it - 0.67 (1.50). The highest level of

mean ECC1-3mft and ECC1-3mfs have children with high-frequency intake of free sugars – 5.15 (4.46) and 8.56 (10.22) accordingly. The mean ECC1 of children whose parents used F-toothpaste was almost 30% less (1.00 (1.69)) than those, who use F-free toothpaste (1.40 (2.04)).

**Conclusions:** Critical ECC1 factors were early exposure and high-frequency intake to free sugars and usage of F-toothpaste. Dentists should promote hygienic oral care using fluoride-containing toothpaste as well as the regimen of free sugars consumption.

## 1294 | Effect of a dual nanocarrier of chlorhexidine and fluconazole on salivary microcosm biofilms

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**Background:** The resistance of acidogenic microorganisms associated with dental caries has led to the use of nanocarriers as an alternative therapy. The study evaluated the effect of a dual nanocarrier of chlorhexidine (CHX) and fluconazole (FLZ) on the lactic acid (LAc) production and number of *Streptococcus mutans* and *Lactobacillus* spp. in salivary microcosm biofilms.

**Methods:** Iron oxide nanoparticles (IONPs) coated with chitosan (CS) were loaded with different concentrations of CHX (39, 78 and 156 µg/mL) and FLZ (156, 312 and 624 µg/mL). The inoculum for biofilm formation was pooled saliva from two healthy volunteers. Biofilms were formed for 72 h on the Amsterdam Active Attachment model and treated for 24 h with the nanocarrier IONPS-CS-CHX-FLZ. IONPs (218.4 µg/mL), CS (218.4 µg/mL) and CHX-FLZ (156–624 µg/mL) were tested as controls, while the untreated biofilm was the negative control (NC). The antibiofilm effect was assessed by enumeration of colony-forming units (CFUs) and enzymatic analysis of LAc production. Data were analyzed by one-way ANOVA and Fisher LSD's test ( $\alpha = 0.05$ ).

**Results:** IONPs-CS-CHX156-FLZ624 was the most effective treatment in reducing CFUs, overcoming the effect promoted by all other compounds, regardless of the microbial species evaluated. All compounds tested also significantly reduced the production of LAc compared to NC, and the

nanocarrier did not differ statistically from the compound CHX-FLZ.

**Conclusion:** The nanocarrier IONPs-CS-CHX-FLZ can be a promising alternative in the control of cariogenic biofilms.

**Funding:** This research was funded by, São Paulo Research Foundation (FAPESP, Grant number 2017/24416-2), and CAPES, Finance Code 001.

## 1001 | Egg-cartons as simulated teeth models for teaching tooth brushing to pre-school children: A randomised control trial

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**Background:** Tooth brushing should be taught to pre-school children based on their cognitive and psychomotor skills focusing on imparting knowledge along with developing skills. Enabling pre-school children into efficient oral hygiene not only protects them from ECC but also builds fundamental attitude of maintaining oral health for life.

**Methods:** A randomized controlled trial was conducted to teach tooth brushing to pre-school children based on a novel method using egg cartons. Tooth brushing technique was taught to a total of sixty pre-school children (Age - 4 to 6 years) using either of the methods: (i) demonstrated by using study model [Conventional method, n = 30] (ii) involvement of a group of children in hands on activity on egg-cartons as simulated teeth models [Novel method, n = 30]. The technique of teaching tooth brushing was randomized. Measurement of plaque index was done as per Silness and Loe Plaque – index, before and after 3 weeks of the teaching session by assessors who were blinded to the type of teaching method.

**Results:** Dependent t-test was used to compare plaque scores which showed there is a significant reduction in plaque score in both groups after the teaching sessions (P.01 for both methods). However, when comparing improvement between these two teaching methods by independent t-test, the result showed an insignificant difference (P.01).

**Conclusions:** The novel method based on 'activity-based learning' using egg-cartons as simulated teeth models is as effective as the conventional approach in teaching tooth brushing to the pre-school children.

### 333 | Multidisciplinary and early approach to RT1 gingival recession in a 13-year-old young patient: A clinical case report

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**Introduction:** The period between childhood and late adolescence reserves a series of physiological events that can influence the periodontium. Gingival recession is a multifactorial and a common mucogingival defect with advancing adulthood, however, its presence and forms of treatment during childhood and adolescence is not widely discussed in the literature

**Case report:** This case report describes a 13-year-old adolescent medically fit and well child with no previous history of orthodontic treatment. The intraoral exam revealed class RT1 gingival recessions on the two upper canines associated with muscle fibers inserted close to the gingival margins of the defects and a large enamel projection on the cemento-enamel junction region of tooth 13. The treatment was carried out in a multidisciplinary approach, combining surgical removal of muscle fibers close to the recession area, adjustments of canine guides and periodic plaque control through basic periodontal therapy. An improvement in the depth of recession in both affected areas was observed after 8 months of follow-up

**Discussion:** Gingivitis together with anatomical factors such as muscle fiber insertions close to the gingival margin, thin scalloped periodontal phenotype and enamel projection in the cemento-enamel junction may have provided a condition for the development of recession with a strong association with the period of complete eruption of canines.

**Conclusion:** The early diagnosis of gingival recessions as well as the treatment directed to the associated local factors allowed an improvement, even if a root covering intervention may become necessary in the future.

### 1472 | Hormonal fingerprint – A potential anatomic biomarker for predicting caries susceptibility: A review of literature

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**Background:** Hormonal fingerprint (2D:4D ratio) is the ratio between second and fourth digit length. It is being used as a biological marker for prediction and diagnosis of many metabolic disorders like coronary heart disease and autism. In dentistry, it is being used as a potential screening tool for the early diagnosis of dental caries.

**Literature Review:** The ratio of lengths of second to fourth digits is a sexually dimorphic trait. Researchers have noticed that men's ring finger was relatively longer than the index finger, i.e., low digit ratio, while in females it was more likely to show the opposite pattern. Sexual dimorphism concerning the 2D:4D digit ratio is thought to be influenced by prenatal sex hormones. High prenatal androgens may produce a low digit ratio. The sex and individual differences in the 2D:4D emerge in-utero at the beginning of the second trimester. The ratio once formed remains almost stable throughout life.

Studies show a strong correlation between low 2D:4D ratio, i.e., high prenatal androgen levels, and high caries index. It was concluded that hormones have an impact on taste perception and dietary preferences. The prevalence of individuals who like sweets was higher in the low digit ratio category, thereby indicating their increased caries susceptibility.

**Conclusions:** Since the hormonal fingerprint is formed early in intrauterine life, it can be used as a tool for predicting caries susceptibility through taste perceptions. This could be a breakthrough in neonatal and preventive dentistry to predict risk factors and implement new preventive measures.

### 567 | Revascularization treatment in permanent teeth: A case report

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**Introduction:** Regenerative endodontics aims to replace necrotic pulp tissues with regenerated pulp-like tissues to revitalize teeth. Revascularization therapy is indicated to induce apical barrier formation in teeth with open apex.

**Case Report:** A 9-year-old female patient was admitted to the clinic with the complaint of pain caused by biting in her left upper lateral tooth. It was learned that the tooth was traumatized one year ago. Revascularization treatment was

planned for the tooth with an open apex, which was clinically asymptomatic and no pathology was observed on radiographic examination. In the first session of the patient's tooth, the canal length was determined by opening the access cavity under local anesthesia. After irrigation with NaOCl, serum, CHX a double antibiotic paste was placed in the canal. When the patient arrived two weeks later, after making sure that he had no symptoms, the temporary filling was removed and irrigated with serum and EDTA. There was bleeding from the root tip, the canal was waited for filling with blood and clot formation. Then, the top filling was performed after MTA occlusion up to the coronal 1/3 of the root. First month, 6th month and 1 year controls of the patient were made.

**Discussion:** Especially, which has been used recently, is seen as a promising new approach this treatment method compared to traditional treatment methods.

**Conclusion:** Revascularization treatment seems to be effective for thickening of the canal walls and continuity of root development in young permanent teeth with an open apex with infected necrotic pulp tissue.

#### 749 | Regeneration with miracle peptide SAP P11-4

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**Background:** The initial carious lesions are the so-called "white spot" lesions (WSLs), which implies that there is a subsurface area with most of the mineral loss beneath a relatively intact enamel surface. Various agents are used to promote remineralization, newer concept suggests possibility of regeneration of these lesions via matrix forming peptides. The study compared the effectiveness of Resin Infiltration (RI) and Self Assembling Peptide (SAP) p11-4 (Curodont Repair, Credentis AG, Switzerland) on White spot lesions in primary teeth with 12 months follow up.

**Methods:** Following the ethical approval, this Randomized Clinical Trial was performed on 60 sites on primary teeth including all smooth surface lesions. Children between the age group of 4-10 years selected from Outpatient department of pediatric dentistry department. 60 sites were randomly divided into two groups and application of RI and SAP p11-4 was performed as per manufacture's recommendation. All the sites were followed up clinically and photographically for 6 and 12 months.

**Results:** At 6 months follow up clinically RI and SAP p11-4 were equally effective in regression of WSLs compared to baseline and photographically SAP p11-4 was more effective in regression of WSLs compared to baseline. Clinical and

photographic evaluation at 12 months found SAP p11-4 was more effective in regression of White spot lesions.

**Conclusions:** At 6 months RI and SAP p11-4 were equally effective. At 12 months follow up SAP p11-4 was more effective clinically as well as photographically.

#### 803 | Importance of remineralization of non-cavitated carious lesions

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**Background:** Dental caries is a continuous process which starts from the level of initial demineralization, progresses to non-cavitated white spot lesion and often can cause dental involvement eventually leading to cavitation. Various antibacterial and chemical methods can be used to facilitate remineralization and reduce demineralization if dental caries detected in early stages. Remineralization can be defined as the delivery and deposition into the caries lesion of the mineral elements, mostly calcium and phosphate, lost through demineralization of the tooth tissue. Thus, this study aims to analyze effective treatment strategies to facilitate non-operative care of initial caries lesions.

**Literature review:** Ideal remineralization material should diffuse or deliver calcium and phosphate into the lesion or boost the remineralization properties of saliva and oral reservoirs without increasing the risk of calculus formation. Fluoride is recognised as the main active ingredient in different fluoridated products for remineralization and prevention caries. New treatment strategies either facilitate fluoride action, enhance the effect of fluoride by adding other potentially active ingredients to the formulation, such as calcium, phosphate, stannous, xylitol, and arginine or work synergistically with fluoride or by creating remineralizing scaffolds within the lesions to provide a fuller remineralization of lesions.

**Conclusions:** Newer biomimetic remineralization products have the capability to create apatite crystals within completely demineralized collagen fibers. Preventive approach of non-restorative treatment of non cavitated lesion is the optimal way of regeneration of lost tooth, saves both dental manpower, expense and suffering for the patient.

## 853 | Impact of oral health promotion in early childhood on caries experience among adolescents

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**Background:** Dental caries is the most prevalent chronic disease among children. Oral health promotion in childhood may impact the development of healthy habits throughout life. This study evaluated the impact of preventive educational strategies implemented in early childhood on the oral health of adolescents.

**Methods:** In phase I of this study, 1,142 dental records of children (0–6 years old) enrolled in a public preventive oral health program between 1995–2016 were analyzed. Sociodemographic data, medical history, dietary and oral hygiene habits, dmft, and patient adherence to the program were recorded. Then, the patients were divided into 2 groups: children who completed the program, and children who dropped out the program. In phase II, the dental records of the patients from groups 1 and 2 were searched in the public health service database in 2018 and dmft and DMFT collected from the odontograms.

**Results:** 604 patients (mean age of 13.5 years) remained enrolled in the public health service database. 432 patients completed the preventive program protocol. Low maternal education was associated with high levels of program dropout ( $P = 0.001$ ) as well as low tooth brushing frequency ( $P = 0.04$ ). The child's non-collaborative behavior during dental treatment was associated with program dropout ( $P = 0.000$ ). Children who dropped out of the program presented significantly more caries lesions than those who completed the program.

**Conclusions:** The completion of the preventive oral health program in early childhood positively impacted the oral health of the patients over the years.

## 1443 | Effect of vitamin D, copper, selenium on the prevention of dental caries in children

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**Background:** This study highlights the relationship that could exist between the intakes in immuno-elements and the risk of caries disease in children.

**Methods:** A 24-hour dietary survey was carried out in 232 children examined in the dentistry department. The results were processed using NUTRILOG\_260 software.

**Results:** The evaluation of the weight status of the children showed a significant difference of the body mass index (BMI) between the subjects with caries ( $16.85 \pm 0.22$ ) and without caries ( $17.87 \pm 0.43$ ). It also showed a significant decrease of Vitamin D, copper and selenium intakes in the children with caries compared to the subjects without caries (for all comparisons,  $p < 0.01$ ).

**Conclusions:** Dental caries could be prevented in children by adequate intake of vitamin D, copper and selenium, elements that play a key role in immune defenses against infection.

## 1453 | Vitamin D, copper and selenium induce a high preventive action against dental caries risk in children

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**Conclusions:** Dental caries could be reduced in children by adequate intake of vitamin D, copper and selenium, elements that play a key role in immune defenses against infection.

**Funding:** Laboratory of Applied Molecular Biology and Immunology, Tlemcen University

### 366 | Detection of proximal caries in children: A clinical study

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**Background:** The study aimed to determine the prevalence of infra-clinical proximal caries in children and to define the sensitivity and the specificity of the used diagnostic methods.

**Methods:** the sample consisted of children who were recruited from a private pediatric dentistry practice in Casablanca, over a 5 month period. The proximal surfaces of the primary molars were examined using an initial clinical examination, periapical radiography, direct visual and tactical examination after separation with orthodontic elastics. In addition, the sensitivity and specificity of the methods were assessed. Statistical analysis was performed using SPSS software.

**Results:** The average patient age was  $7.87 \pm 1.75$  years. Of the 391 proximal surfaces found to be healthy at initial clinical examination, 22.8% showed enamel radiance and 5.4% had radiolucency beyond the enamel/dentin junction. Of the 286 surfaces with no visible radiographic transparency, 10% showed an initial lesion on direct visual examination. Of the 391 proximal surfaces judged to be healthy at initial clinical examination, 25.11% had a carious lesion beginning with direct visual examination and 6.6% exhibited cavitation.

**Conclusion:** The main findings showed a clear underestimation of the prevalence of proximal carious lesions when only the basic clinical examination is performed. This detection of caries will allow us to apply the most appropriate therapy. Dentistry tends to become less invasive with the evolution of techniques and biomaterials. This minimal dentistry can be conceived only after a very early detection of proximal lesions.

### 1266 | Remineralizing agents in pediatric dentistry: A review of literature

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**Background:** The purpose of this review is to have an in-depth knowledge of the natural phenomenon of enamel demineralization and remineralization while discussing the clinical relevance of various remineralizing agents aiming to treat early carious lesions.

**Literature Review:** Remineralization is the process where demineralized enamel is repaired through the recrystallization of tooth enamel mineral salts. Remineralization of early carious lesions may be possible with a variety of remineralizing agents, fluoride being the cornerstone in caries prevention. The goal is to manage non cavitated lesions non-invasively through remineralization in an attempt to prevent disease progression and improve aesthetics, strength, and function.

**Conclusions:** Understanding the remineralization process allows dentist to treat the carious lesion before cavitation. With a clearer understanding of the implementation of remineralizing agents and new technologies accessible to dentists, we can create a more favorable relationship in which equilibrium is positively influenced when fluoride, calcium and phosphate ions are added favoring remineralization.

### 377 | Correlation of caries assessment spectrum and treatment (CAST) index with ora test to evaluate caries activity in children

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**Background:** Dental caries is one of the most commonly seen chronic diseases in children. Caries Assessment Spectrum and Treatment (CAST) index and Ora test are some of the new innovative assessment tools used to estimate caries activity. The aim of this study was to evaluate and correlate caries activity using CAST and Ora test in 5 to 8 year old children.

**Methods:** Thirty children aged 5 to 8 years were included in the study. Fifteen children in Group A (n = 30) had DMFT/deft score less than 5 whereas 15 in Group B (n = 30) had DMFT/deft score more than 5. All children were initially subjected to CAST scoring, which were assessed by one examiner followed by Ora test performed by another examiner. CAST severity scores and time taken for color change in Ora test were statistically analysed using Pearson correlation test.

**Results:** In Ora test, mean time taken for color change was 118.53 minutes in Group A and 53.33 minutes in Group B, whereas CAST severity scores were 3.67 and 15.7 for Group A and Group B respectively. Statistically significant negative linear relation was observed between time taken for color change in Ora test and CAST scores. ( $P = 0.039$ )

**Conclusion:** A direct correlation exists between CAST scores and Ora test, proving that microbial activity correlates well with lesion activity.

## 1007 | Revascularization treatment of permanent molar tooth with open apex: A case report

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**Introduction:** Revascularization is a treatment method that aims to provide a vascularization in the root canals of permanent young teeth whose pulp has lost its vitality, and thus, to continue root development.

**Case Report:** A 9-year-old girl presented to the clinic with the complaint of vertical percussion pain in the right lower first molar tooth. Secondary decay was detected in the tooth. Revascularization treatment was planned in the mouth, since the apex hadn't yet closed. In the first session, the canal length was determined by opening the access cavity under local anesthesia. After make irrigation with NaOCl, serum, CHX without extirpating the pulp, a double antibiotic paste was placed in the canal. When the patient arrived two weeks later, after making sure that he had no symptoms, the temporary filling was removed and make irrigation with NaOCl, serum and EDTA. Bleeding was noted from the apex. Then the coronal 1/3 of the root was occluded with MTA. The patient was given an appointment 1 day later for permanent filling. First month, 3rd month, 6th month and 1 year recall of the patient were made.

**Discussion:** The patient, whose follow-up continues, no symptoms and apex closure continues.

**Conclusion:** Revascularization treatment seems to be effective for thickening of the canal walls and continuity of root development in young permanent teeth with an open apex with infected necrotic pulp tissue. However, more studies are needed to evaluate its long-term effectiveness and new approaches.

## 1009 | Prevalence of dental caries in premature and term children

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**Background:** This study evaluated the prevalence of dental caries and their risk factors on primary dentitions of prematurely-born children (37 weeks) and term children.

**Methods:** Two hundred children were examined, 50 born prematurely and 150 born term, in the age group between 0 and 6 years. The demographic variables, medical history, feeding habits and oral health behaviors were recorded on a questionnaire. The caries were registered, focusing on decayed, missing, filled primary teeth (dmft).

**Results:** 55% of the participants were female. While 61.5% of them do not brush their teeth regularly; only 15% of them brush their teeth twice a day. There was no significant relationship between gender ( $P = 0.42$ ) and dmft scores. The dmft scores of children with premature ( $P = 0.033$ ) and low birth weight ( $P = 0.017$ ) were significantly higher than the term group. A significant relationship was found between socioeconomic level ( $P = 0.04$ ), feeding bottle use ( $P = 0.037$ ), brushing teeth ( $P = 0.043$ ) and dmft ( $p = 0.05$ ).

**Conclusions:** It was concluded that prematurity and low birth weight may be predisposing factors in the formation of dental caries. More comprehensive studies are needed on this subject. Early oral hygiene training should be given to families of premature and low birth weight children.

## 463 | Relationship between the salivary concentration of matrix metalloproteinase 8, 20 and severe early childhood caries

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**Background:** Dental caries is initiated by mineral dissolution resulted from bacterial acids and collagen degradation by endogenous proteolytic enzymes, mainly collagenolytic matrix metalloproteinases (MMPs). This research aimed to evaluate the relationship between severe early childhood caries (S-ECC) and salivary MMP-8 and MMP-20 concentrations.

**Methods:** Fifty children aged 36–60 months were assigned into two groups: caries-free (control) and S-ECC. Standard clinical examinations were performed, and approximately one milliliter of unstimulated whole expectorated saliva was collected from all participants. In the S-ECC group, sampling was repeated three months after restorative treatments. All samples were analyzed for salivary concentrations of MMP-8 and MMP-20 using an ELISA assay. T-test, Mann-Whitney test, Fisher's exact test, and Paired T-test were applied at  $P = 0.05$ .

**Results:** At baseline, subjects in the S-ECC group presented with significantly elevated levels of MMP-8 compared with the control group ( $P = 0.001$ ); however, salivary concentrations of MMP-20 did not exhibit significant differences between the two groups ( $P = 0.05$ ). A significant reduction occurred in levels of MMP-8 ( $P = 0.001$ ) and MMP-20 ( $P = 0.05$ ) after three months following restorative treatments in the S-ECC group.

**Conclusions:** Salivary levels of MMP-8, 20 were significantly affected by dental restorative treatments in children, implying their potential efficiency as non-invasive diagnostic and prognostic indicators.

## 501 | Comparison of antimicrobial effects of stevia rebaudiana extract and xylitol on dental biofilm: an in vitro study

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**Background:** This study aimed to assess the antibacterial effects of xylitol and *Stevia rebaudiana* (*S. rebaudiana*) ethanolic extract on oral biofilm.

**Methods:** A total of 96 acrylic discs were divided into two main groups for inoculation with *Streptococcus mutans* (*S. mutans*) and *Streptococcus sobrinus* (*S. sobrinus*). Each group consisted of 6 subgroups including a positive control subgroup and 5 subgroups of discs immersed in 1% or 3% xylitol solutions, 2 or 4 mg/mL *S. rebaudiana*, or a combination of 3% xylitol and 4 mg/mL *S. rebaudiana*. After incubation, the discs were rinsed and transferred to fluid universal medium. The solutions were cultured on specific culture media and incubated. The colony-forming units (CFUs) were counted for each disc. The structure of biofilm in each group was evaluated under a scanning electron microscope (SEM).

**Results:** ANOVA revealed significant differences between the subgroups in both *S. mutans* and *S. sobrinus* groups ( $P = 0.03$  and  $P = 0.01$ , respectively). In *S. mutans* group, the logarithmic mean of colony count in the positive control subgroup was 6.75 while this value was significantly lower in 2 mg/mL (5.81) and 4mg/mL (5.92) *S. rebaudiana* subgroups using the post hoc Dunnett's test ( $P = 0.01$  and  $P = 0.04$ , respectively). The three other subgroups did not show significant differences. In *S. sobrinus* group, all five experimental subgroups demonstrated significantly lower colony count than the positive control group ( $P = 0.05$ ).

**Conclusions:** *S. rebaudiana* extract appears to be more potent than xylitol against dental biofilm.

## 1040 | Caries risk assessment in preschool children using the "Bangkok Checklist"

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**Background:** There is no published information for the validity of the Bangkok checklist (BCL) for early childhood caries (ECC) prediction. The aim of the study is to validate the Bangkok checklist (BCL) in predicting early childhood caries against the actual caries development in a cohort of preschool children from low and moderate socioeconomic areas and to compare its performance with two established risk assessment tools.

**Methods:** One hundred and forty six children aged 2–5 yrs old, were followed for two years and caries was assessed using incipient and cavitated lesions. The 2-years caries increment was recorded by counting the number of surfaces that changed from sound to decay during follow ups. Caries risk assessment was performed at baseline with three checklists: i) BCL, ii) AAPD form (CRAF), and iii) CAMBRA, using data derived from questionnaires and clinical examinations. Kendall's tau, Poisson regression models and ROC analysis were used to assess the predictive ability ( $p \leq 0.05$ ).

**Results:** Over 50% of the children developed new caries. The BCL assigned most of the children (87%) into the high-risk category. Sensitivity was 88% but specificity was low (16%). The accuracy of the BCL was similar to CRAF, but inferior to the CAMBRA tool.

**Conclusions:** BCL had a limited performance in accurately predicting future early childhood caries in this population. Furthermore, the proportion of children assessed with BCL as having high caries risk was overestimated. Nevertheless, the checklist can be used to increase awareness and educate caregivers on good oral health behavior.

## 744 | Can topical silver nitrate arrest dental caries? A systematic review

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**Background:** The dental problems are initially painless but as time progresses; they become chronic and destroy the tooth. It therefore essential to make people aware of

preventive aspects of oral health so that quality of life can be improved. Silver nitrate has strong antibacterial action and sodium fluoride has good remineralising properties, therefore a combined application of silver nitrate solution with sodium fluoride varnish was introduced for managing dental caries. Until now, there has been no comprehensive systematic review to evaluate the evidence about clinical effectiveness of using Silver Nitrate for arresting dental caries among children. Thus this systematic review was conducted.

**Literature review:** Databases search was carried out from inception to the present for four electronic databases-PubMed, Medline, Research Gate, Google scholar, and The Cochrane library. 104 publications were found in the initial search which were in English language and they were completely reviewed with respect to their title, abstract, and full text. 85 of 104 publications were removed because they were either literature reviews, case reports, laboratory studies or clinical studies on SDF/NSF or other materials. 15 out of remaining 19 publication were excluded due to duplication. A total of 4 clinical studies were qualitatively analysed for caries-arrest.

**Conclusion:** Biannual application of 25% silver nitrate effective in arresting dentinal caries in primary teeth and prevent recurrence after treatment. It helps to reduce the negative impact of established disease (cavity) and also improve the quality of life for children with early childhood caries.

### 1289 | Association between eating behavior and caries in a population of children aged 3 to 9 in the province of Alicante

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**Background:** Caries is the most common chronic disease of childhood. Much has been studied about the effect of a healthy diet on oral health, but little attention has been paid to the importance of eating patterns. The objective of this research was to establish the relationship between dental caries and eating behavior pattern using the Child Eating Behavior questionnaire (CEBQ) in a sample of children.

**Methods:** A cross-sectional, descriptive study was carried out, selecting any boy or girl between 3 and 9 years old who attended a dental clinic in the province of Alicante. An oral examination to diagnose caries was performed in children whose parents signed an informed consent. These parents / caregivers were also given the CEBQ to fill out.

**Results:** Two hundred seventy-six (276) children were examined. The mean age of the participants was 86.5

months. A higher average score was observed in the "food-avoidant" dimension in: "demand for food" and in the "response to satiety". A statistically significant difference was obtained in the mean values of the variables "response to satiety" ( $P = 0.001$ ) and "slow eating" ( $P = 0.016$ ) of the groups with and without caries. A statistically significant relationship was also found between the "food-avoidant" variable and the caries and non-carries groups ( $P = 0.003$ ).

**Conclusions:** The eating behavior pattern in children is a factor that leads to an increase in infant caries.

### 1553 | Psychological implications and addressability of children in dental practices in Romania during the period COVID-19

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**Background:** The study examined the psychological implications and addressability of children in dental practices during the period COVID-19.

**Methods:** A questionnaire included questions related to the addressability of patients during the pandemic, the fear related to the spread of the infection, the influence of media.

**Results:** During the epidemic period the addressability of children has decrease most often postponing their visit. Most often this was due to fear and lack of information on the spread of coronavirus. Despite the avalanche of information regarding COVID-19, there is a lack of consolidated information to guide dentist handling clinical management. It is essential to work on remote communication, including mass-media and education aimed at maintaining the oral health of children. The dentist must take into account that parents lack the knowledge of basic behavioural management techniques needed to approach a paediatric patient.

**Conclusions:** The main objective is to limit the spread of epidemic and the onset of cross-infections but it is also essential to work on remote communication and education aimed at maintaining the oral health of children.

### 392 | Parental motives and attitude towards controlling sugary foods among children with early childhood caries: A case-control study

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**Background:** Parents can influence children's diet by making some foods more available than others. The study investigated the association of parental food choice motives, attitudes towards sugar consumption and dietary sugar exposures with the presence of early childhood caries.

**Methods:** This study with case control design involved 200 children, aged 3–5 years, with equal number of cases (with caries) and controls (without caries). They were divided into cases and controls after oral examination, using WHO-DMFT criteria for dental caries and matched for age, gender and socio-economic status. The data for parental food choice motives and attitudes towards sugar consumption were obtained using questionnaire answered by their parents and the sugar exposures in the diet were calculated using a twenty-four hour diet chart. Binary logistic regression was used to analyze data.

**Results:** For parents, the most important food choice motives were 'maintaining health and nutrition' (99.5%) followed by 'mood of the child', 'child likes and dislikes', 'sensory appeal of the food item', 'natural foods', 'quality of the food' and 'weight control' with no significant difference between cases and controls. About 61% of the cases considered it important to buy food based on convenience as compared to 47% controls and the difference was significant. Cases and controls did not differ in attitudes towards sugar consumption. The sugar exposure was significantly higher amongst the cases.

**Conclusion:** Children with early childhood caries have higher sugar exposures, irrespective of parental attitudes towards dietary sugar exposures and are likely to buy foods based on convenience and availability.

### 469 | Correlation between nutritional status, dental caries experience and salivary mutans streptococci and lactobacillus counts in a group of Transylvanian school children

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**Background:** The prevalence of dental caries and obesity is high as both raise significant health problems. The objective of this study is to analyse the relationship between dental caries, the number of salivary colonies forming units of Mutans Streptococci (MS) and Lactobacillus (LB), and the nutritional status in a group of children from Transylvania.

**Methods:** This cross sectional study used a sample of 154 school children, aged 9 to 12 years. The prevalence of caries was measured using the decayed, missing, and filled teeth index for deciduous teeth (dmft index) and for permanent teeth (DMFT index). Height and weight were assessed for each subject, and their body mass index (BMI) percentile was calculated. Salivary levels of Streptococcus Mutans (MS) and Lactobacillus (LB) were determined using the CRT Bacteria Test from Ivoclar Vivadent.

**Results:** In our study, we found a positive association between the BMI percentile, MS count, LB count and the incidence of dental caries in children aged 9 to 12 years. There was a strong correlation between high MS and LB and the high prevalence of dental caries. The results showed a significant association between the high presence of MS (high) ( $P = 0.0083$ ), increased LB (high) ( $P = 0.0002$ ) and the increased BMI percentile. Overweight patients have higher levels of MS and LB than normal or underweight patients

**Conclusions:** The presence of high bacteria counts can be confidently used to predict dental caries in young children in this population. The multifactorial etiology of both diseases require future research, on larger samples, with a longitudinal approach, rather than a cross-sectional one.

## 985 | Salivary flow and capital capacity of saliva in preventing caries in early childhood

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**Background:** The objective is to conduct a literature review on the correlation of salivary indices with the prevalence of caries associated with children's diet and oral hygiene and how to use these data in the clinical environment

**Literature Review:** Many studies have reported that salivary flow and saliva composition have a protective effect against tooth decay. There is a strong relationship between salivary flow, quality of saliva and early caries in early childhood. In this context, saliva analysis is an option for diagnosing and monitoring the evolution of certain pathologies. Tests of salivary flow, buffer capacity of saliva can be associated with the risk of caries. Patients with changes in the buffer capacity of saliva, decreased salivary flow, are at a greater risk of developing oral problems, especially greater tooth decay activity.

**Conclusions:** Salivary analysis may be associated with general and intraoral clinical examination and is considered an important factor in the early diagnosis of caries and risk of caries

## 848 | Influence of preventive programs for reduction of DMFT index in 12 years old children in RNM on dental arch space changes

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**Background:** The aim of this study was to evaluate the effect after implementation of a set of preventive measures through the "National Strategy for prevention of oral diseases of children aged 0–14 years in Republic of North Macedonia (RNM) from 2008–2028" and the resulting need for orthodontic treatment in 12 years old Macedonian children.

**Methods:** This research was made in all 8 regions in RNM, including examined representatives from urban and rural areas equally.

Using the WHO methodology for preparing Oral health studies, 7169 children, born in the year of 2007, were examined

(33.3% from all the children in that generation). 3117 of them were boys and 3050 were girls.

The examinations were made in dental offices, by calibrated dentists-pedodontists, all employed in the public health sector.

The decay-missing-filled (DMF) index was used as an appropriate measure for the detection of dental caries where 12-year-old children were considered as target group. Impressions were taken from 100 children (50 boys and 50 girls) with premature tooth loss to analyze the space condition and dental arch space changes.

**Results:** After 11 years of implementation of preventive measures, evaluation showed impressive results – significant decrease of DMF index (from 6.88 to 2.43). Orthodontic analysis in the examined group with premature tooth loss showed greater extend of space loss and an increase in orthodontic treatment need.

**Conclusions:** The implementation of the National strategy for prevention of oral diseases in RNM was an effective approach for preventing caries-related premature tooth loss in 12 years old children, preserving relevant dental arch length.

## 914 | Vitamin D levels and dental caries in 7-year-old children in Porto, Portugal

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**Background:** Vitamin D deficiency has been associated with significant changes in dental structures. In children, it can induce enamel and dentin defects, which have been identified as risk factors for caries. This study aimed to assess the association between low serum 25-hydroxyvitamin D (25(OH) D) levels (75nmol/L) and the prevalence of caries in the permanent teeth and mixed dentition of 7-year-old children.

**Methods:** A sample of 335 children from the population-based birth cohort Generation XXI (Porto, Portugal) was included. Data on children's demographic and social conditions, health status, dental health behaviours, dental examination including erupted permanent first molars, and blood samples available for vitamin D analysis were collected. Dental outcomes included the presence of caries, including non-cavitated lesions (dA-6mft/DA-6MFT0), and advanced caries (d3-6mft/D3-6MF0). Serum 25(OH) D was measured using a competitive electrochemiluminescence immunoassay protein-binding assay. Bivariate analysis and multivariate logistic regression were used.

**Results:** Advanced caries in permanent teeth was significantly associated with children's vitamin D levels 75 nmol/L, gastrointestinal disorders, higher daily intake of cariogenic food, and having had a dental appointment at  $\leq 7$  years old.

**Conclusions:** Optimal childhood levels of vitamin D may be considered an additional preventive measure for dental caries in the permanent dentition.

**Funding:** Generation XXI was funded by Programa Operacional de Saúde (Regional Department of Ministry of Health). It has support from the Portuguese Foundation for Science and Technology (FCT) and from the Calouste Gulbenkian Foundation. Ana Cristina Santos holds a FCT Investigator contract IF/01060/2015. The authors received no specific funding for this work.

## 1462 | Caries risk assessment: A review of literature

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**Background:** Multifactorial caries disease causes damage to dental hard tissue and is dependent on patients' own unique make up of pathogenic risk and protective factors. Caries Risk Assessment (CRA) started with a pie chart in the early 90's. Over the last three decades, it has evolved to include multiple age-specific factors.

**Literature review:** Caries protective factors are biological or therapeutic factors that can collectively offset the pathologic challenge presented by the caries risk. A CRA is simply a way to formalize and expand upon the patient's caries balance /imbalance in the most predictable fashion to diagnose current caries disease, predict future disease and determine factors which are out of balance. CRA has great potential to enhance patient care, as it is the cornerstone of a minimally invasive care plan. The CRA model can improve the equity and efficiency of the oral health care system. CRA tools have

emerged as the main paradigm for managing and evaluating treatment and oral health interventions.

**Conclusions:** CRA has evolved from visual and tactile evaluation of the oral cavity and the use of microbiological testing to its current multifactorial model. This model includes: previous experience with caries, oral hygiene, diet, salivary factor, buffer capacity and patients' sociodemographic characteristics.

## 1307 | Comparative assessment of the association between salivary vitamin D levels and early childhood caries using enzyme linked immunosorbent assay

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**Background:** Vitamin D may have a role in the etiology of dental caries during childhood as it is essential for the maintenance of calcium homeostasis, which in turn promotes remineralization of enamel and reduces its demineralization. The study involved determination and comparison of the salivary levels of vitamin D in children with S-ECC and those who are caries-free (dmft = 0) using ELISA kit.

**Methods:** Thirty children aged 3–5 years were selected and divided into two groups. Group I (n = 15) - Children with severe early childhood caries [dmft score: 3years (4); 4years (5); 5years (6)] and Group II (n = 15) - caries-free children [dmft 0]. Unstimulated saliva samples were obtained by using spitting method and levels of 25-hydroxyvitamin D3 were measured using ELISA. Statistical analysis was performed using the Chi-square- and the Student's t tests.

**Results:** In Group I 66.67% of the children showed salivary vitamin D levels of 12ng/ml depicting deficiency compared to 33.33% in Group II. About 33.33% in Group I and 46.67% in Group II exhibited salivary vitamin D levels between 12–20ng/ml demonstrating insufficiency. About 20% in Group II exhibited sufficient values (20ng/ml) in comparison to 0% in Group I. The mean salivary vitamin D levels in Group I and Group II were 8.8+4.92ng/ml and 16.8+10.8ng/ml respectively, with a statistically significant difference ( $P = 0.05$ ).

**Conclusion:** An inverse correlation was observed between salivary vitamin D levels of children with S-ECC and those caries-free (dmft = 0). Saliva can thus be regarded as a non-invasive tool to determine vitamin D levels.

## 954 | Silver diamine fluoride: Clinical application in pediatric dentistry

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**Introduction:** Management of dental caries, a highly prevalent condition in children worldwide, may involve the use of agents capable of modifying the disease's activity and risk, including silver diamine fluoride.

**Case Report:** A 4-year-old boy presented with early childhood caries and a history of lack of cooperation in medical procedures. In order to overcome this difficulty, the initial approach was to apply silver diamine fluoride (38%) (RIVA STAR™, SDI) in the right maxillary primary lateral incisor which exhibited an active cavitated carious lesion with no clinical signs of pulp involvement. At the same appointment, a glass ionomer cement (3M™ Ketac™ Universal Aplicap™) restoration was carried out. All procedures were painless and performed relatively quickly and with the child's cooperation. The clinical follow-up is now about 12 months.

**Discussion:** Silver diamine fluoride is known for its cariostatic and desensitizing properties. Despite these potential advantages, the intense pigmentation of the lesions is pointed out as a disadvantage, along with some still controversial concerns regarding its safety.

**Conclusions:** Although it cannot be considered a complete solution in the management of early childhood caries, this alternative approach may comprise several advantages for some patients. Nonetheless, some issues still have to be addressed, namely its safety, action on soft tissues and aesthetic impact.

## 1130 | How to choose the best technique for treating caries lesions in primary teeth: A literature review

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**Background:** Restorative treatment is the therapy commonly used to treat carious lesions in primary teeth. However, the high rates of failure of this treatment remain a challenge for the clinician. With the current knowledge about the dynamics of dental caries and Minimal Intervention Dentistry, the management of lesions is no longer based on the removal of bacteria and tissues, but on the control of causal factors.

**Literature Review:** The subjectivity of dental care for pediatric patients does not allow the definition of a protocol for the indication of techniques, to be used in a generalized way, based only on the type, extent and depth of caries lesions. It is necessary to consider the patient's particularities, such as behavior and level of fear, of those responsible as their aesthetic preferences, the environment in which the child is inserted and the place where care will be performed. In addition, when operative procedures are performed in isolation, without a preventive program to monitor the patient, the caries disease will remain active. It is important that effective control of food and plaque from brushing with fluoride toothpaste and flossing in interproximal spaces is carried out.

**Conclusions:** The dentist must choose the technique that best suits his patient and his working reality, based on his scientific knowledge and technical skills. In addition, the professional should not only act in the execution of clinical procedures, but also as a mediator in the adoption of healthy habits by the family in caring for their children.

## 221 | Orthodontic appliance debonding changes physicochemical properties of saliva and favors remineralization of active caries: A 13 week follow-up study

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**Background:** This prospective cohort study aimed to investigate if the removal of orthodontic appliances (ROA) changes physicochemical properties of saliva, the activity of carbonic anhydrase VI (CA VIact), and  $\alpha$ -amylase ( $\alpha$ -AMLact), and favors remineralization of active caries lesions (ACL).

**Methods:** Twenty-two individuals aging 13 to 24 years old, were assessed regarding the presence of visible biofilm, daily sugar exposure, caries activity, salivary flow rate (SFR), pH and buffering capacity (BC), CA VIact and  $\alpha$ -AMLact at baseline, and 1, 5 and 13 weeks after ROA. Analysis of variance for repeated measures, Cochran's Q test followed by McNemar test, and Pearson's correlation analyses were used.

**Results:** The percentage of visible biofilm and sugar exposure decreased at 5 and 13 weeks after ROA. A significant decrease in the number of ACL was noticed at 5 (29% reduction) and at 13 (58% reduction) weeks after ROA. Saliva pH and  $\alpha$ -AMLact significantly increased at 5 and at 13 weeks after ROA. BC and CA VIact remained unchanged during the follow-up.

**Conclusion:** ROA favored remineralization of active caries lesions and increased saliva pH and  $\alpha$ -AMLact whereas buffering capacity and CA VIact remained stable.

## 1980 | Influence of sociodemographic conditions and early childhood caries on parental guilt concerning their child's dental problems

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**Background:** Unfavorable oral health conditions in children can be associated with the feeling of guilt of their parents. This perception can be related to the preventable nature of dental caries disease. Under this perspective, sociodemographic conditions may influence this perception. Thus, this study sought to investigate the influence of sociodemographic conditions and early childhood caries on parental guilt concerning their child's dental problems.

**Methods:** A cross-sectional study carried out with 261 children from two locations in small cities of Brazil northeastern. Dental caries status was evaluated according to the World Health Organization's diagnostic criteria (dmft) answered two questionnaires. Sociodemographic conditions and the parents' feeling of guilt were assessed by questionnaires. Statistical analysis considered the multivariate logistic regression model with a significance level of 5%.

**Results:** The feeling of guilty was associated with low paternal education (OR = 3.53; 95% CI 1.28–9.68;  $P = 0.014$ ), with low maternal education (OR = 2.7; 95% CI 1.16–6.42;  $P = 0.021$ ), the absence of filled or extracted teeth (OR = 2.00; 95% CI 1.10–3.62;  $P = 0.014$ ) and the presence of untreated caries lesions (OR = 3.37; 95% CI 1.54–7.34;  $P = 0.001$ ).

**Conclusion:** Low educational status of parents and untreated caries lesions influence parental guilt.

## 862 | Treatment of immature permanent first molar with MTA amputation: A case report

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**Introduction:** Permanent first molar teeth erupt earlier than other permanent teeth, so they are more exposed to cariogenic factors. In children with high risk of caries, deep dentin caries is frequently encountered in these teeth that have not yet completed their development. It is an important responsibility of pediatric dentists to know and apply current treatment approaches in immature permanent first molars. Vital amputation is one of these treatments. Mineral trioxide aggregate (MTA) is a material that provides successful results in amputation.

**Case Report:** A 9-year-old female patient applied clinic with complains of dental caries. In the radiographic examination, deep caries was detected in the lower left permanent first molar tooth. There were no clinical symptoms except for cold sensitivity of the patient. There was no pathology on radiograph. A pulp perforated 3mm occurred during the procedure. Coronal pulp tissue was removed was applied after bleeding control. Temporary restoration was done with glass ionomer. Permanent restoration was performed after one month later. Teeth were evaluated clinically and radiographically for 3,6,12 months. At the end of the 1-year follow-up, no radiographic pathology or clinical symptom was observed.

**Discussion:** When the pulp is exposed, it is important to apply minimal invasive treatment approaches that allow the vital pulp to be preserved in immature permanent teeth. Amputation therapy with MTA is quite successful compared to traditional treatments in ensuring root development and protecting the periapical tissues and alveolar bone in healthy way.

**Conclusions:** In this case, a successful result was obtained by performing amputation with MTA. Pediatric dentists should know and practice new treatments alternative to traditional treatments.

**Keywords:** Mineral Trioxide Aggregate, Amputation, Immature Permanent Teeth, Pediatric Dentist

## 867 | Total pulpotomy with CEM in young permanent molar with deep caries: A case report

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**Introduction:** Pediatric dentists frequently encounter young permanent molars exposed with deep caries. Alternative

treatments such as pulpotomy and revascularization replace traditional treatments. Root development can be achieved with total pulpotomy in young permanent molars and a stronger tooth structure can be formed. Mineral trioxide aggregate (MTA) is a successful but expensive material frequently used in total pulpotomy. Calcium enriched material (CEM) is a cheaper material that can achieve similar success with MTA.

**Case Report:** A 9-year-old male patient applied to clinic with the complaint of caries. Deep caries was detected in the right lower permanent first molar in clinical and radiographic examination. There was no pathology in the periapical area. A pulp perforation of more than 2 mm occurred during the procedure. Coronal pulp tissue was removed. After the bleeding control, CEM was applied and temporary restoration was made with glass ionomer. Permanent restoration was performed with composite resin after 1 month. No pathology or clinical symptom was observed radiographically in the controls of 3,6,12 months and root development was observed to continue.

**Discussion:** It is important was continued root development in young permanent teeth. Pediatric dentists should know and apply vital pulp treatments and materials used. CEM is a material that can be an alternative to MTA, which is accepted as the gold standard today, and it is successfully applied in vital pulp treatments. In addition, it is cheaper than MTA and can be applied instead of MTA with this property.

**Conclusions:** In this case, a successful result was obtained by performing total pulpotomy with CEM. Total pulpotomy with CEM is a preferable approach in the treatment of young permanent teeth.

**Keywords:** Calcium enriched material, young permanent teeth, pediatric dentist, total pulpotomy

### 1330 | Effect of holy basil (Tulsi) leaves on pH of saliva: An in vivo study

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**Background:** The study was to evaluate the effect of holy basil (tulsi) leaves on pH of saliva

**Methods:** A double blind, randomized controlled clinical trial was conducted in 15 caries free patients. All the children fell into both the control- and tulsi group. These children were assigned for two appointments. In first appointment, baseline pH was recorded, and then asked to drink juice. Changes in pH were recorded every 2 minutes up to 10 minutes, then after every 10 minutes up to 40 minutes. In the

second appointment, the baseline pH was recorded and they were asked again to drink fruit juice. The child was then asked to chew 4–5 fresh tulsi leaves and the pH was recorded with the pH meter in same manner as in first visit. Data was analyzed statistically.

**Results:** Mean salivary pH drops immediately after drinking fruit juices. A significant difference was observed between control and tulsi group after chewing tulsi. In the present study, the salivary pH of the tulsi group remained alkaline even after consumption of fruit juice.

**Conclusions:** Stimulating salivary flow through chewing tulsi has been shown to reduce the salivary pH and thereby helps in reducing the incidence for dental caries.

### 297 | Post-COVID SOPs in paediatric dental GA services: Utilisation of general anaesthetic slots

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**Background:** Paediatric dental services were hugely affected by the COVID-19 pandemic, including general anaesthetic (GA) treatments being cancelled. As services resumed, new standard operating procedures (SOPs) were established. In this 2 cycle audit, we assessed GA post-Covid SOPs and evaluated theatre utilisation.

**Methods:** Aims, objectives and standards were set. We recorded adherence to paediatric dental GA SOPs in July 2020, including swabbing and isolation requirements. The number of available GA slots, and un-filled cancellation slots were used to assess theatre utilisation. Following modification of SOPs, data collection was repeated for October 2020. SOP effectiveness was highlighted and changes made.

**Results:** In July 2020, there were 45 GA slots available and 91% of these were utilised. 100% of patients were swab-negative for Covid. Problems with re-filling cancellation slots were linked to SOP requirements of 2 week isolation for families prior to the procedure. SOPs were updated following new government guidance and identification of issues. In October 2020, reductions in fallow time and improvements in carrying out SOPs meant there were 95 GA slots available and utilisation was 98%.

**Conclusions:** Factors affecting theatre utilisation can be grouped into patient, clinical and administrative categories, and it is essential to improve controllable factors in each category. Thus far we have focused on cancellations prior to the procedure date, so cycle 3 will focus on reduction of on-the-day cancellations to further improve utilisation. It is essential to continue to follow guidance related to dental GA's in order to stay up-to-date and keep everyone safe.

## 894 | Co-relation of PUFA and oral health related quality of life in children

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**Background:** Dental caries although decreased world-wide, continues to remain prevalent in developing countries where it has become a prominent childhood problem. Owing to their poor socio-economic status and lack of access to dental treatment, majority of dental caries remain untreated. The present study aimed to co-relate the consequences of untreated dental caries and quality of life in children, using the Polyunsaturated fatty acids (PUFA) index and Child Oral Health Impact profile (COHIP) questionnaire.

**Methods:** The study was undertaken amongst 640 school children in the age group of 12–15 years. The oral health of the children was assessed with the help of PUFA index. The impact of untreated dental caries was evaluated using the COHIP questionnaire. Pearson's correlations co-efficient was used to determine the relationship between the PUFA and COHIP scores. To compare the PUFA and COHIP scores amongst gender, Mann Whitney U test was used.

**Results:** The mean PUFA score was found to be 0.98 and the mean COHIP score was found to be 15.31. The study showed a negative co-relation between the two scores (-0.80) which determines that as the PUFA scores goes on increasing the COHIP scores goes on decreasing. It also shows that males are more affected by females when it comes to the impact of oral health on the quality of life.

**Conclusions:** The consequences of untreated dental caries have a negative impact of the self-perceived Oral Health Related Quality of Life in 12–15 year old children.

## 645 | Antibacterial activity of cranberry-derived proanthocyanidin against oral pathogens: An in-silico approach

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**Background:** Proanthocyanidin rich cranberry extract has been reported to possess antimicrobial, antioxidant, anti-inflammatory and remineralizing properties. In view of the above research findings, an in-Silico study was conducted to

identify the specific Proanthocyanidin protein targets against oral pathogens which causes dental caries.

**Methods:** Molecular protein targets such as Glucan Binding Protein C (PDB: 5UQZ), cysteine protease (PDB: 3BBA), 4,6-alpha-glucanotransferase (PDB: 5JBD) and Calcineurin A (PDB: 6TZ6) causing dental caries were retrieved from RCSB protein databank. Molecular docking study was carried out through Autodock 4.2 tool and visualized through Maestro viewer tool. Molecular dynamic study was carried out for the potent target complex by Desmond package of Schrodinger suite.

**Results:** Proanthocyanidin showed potent binding affinity towards all the four targeted proteins. It showed score of -9.0 kcal/mol against cysteine protease, -10.3 kcal/mol against 4,6-alpha-glucanotransferase, -9.3 kcal/mol against Glucan Binding Protein C and -9.7 kcal/mol against Calcineurin A. Proanthocyanidin binds covalently with SER906, GLN908, ASN974, ARG1434 and TYR1521 of 4,6-alpha-glucanotransferase. Molecular dynamic result showed that the Proanthocyanidin with 4,6-alpha-glucanotransferase complex was stable during the 50ns. The Root Mean Square Deviation & Root Mean Square Fluctuation was found to be stable and showed a stable interaction with GLN908, ASN974 and ARG1434.

**Conclusions:** Proanthocyanidin had maximum binding affinity with 4,6-alpha-glucanotransferase compared to other targets. The result revealed the drug moiety is a promising candidate in the treatment of oral infection. Further the drug can be added into a suitable formulation for the prevention of dental caries.

**Funding:** This research project is a self-funded project

## 320 | Breastfeeding and child oral health: An umbrella review

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**Background:** Despite the unquestionable benefits of breastfeeding for children's systemic health, it has been recently reported as a risk factor for dental caries and malocclusions. The present umbrella review was conducted with the purpose to search, organise and assess the existing evidence from multiple systematic reviews on the relationship between oral health outcomes in children and breastfeeding.

**Methods:** The review followed the PRISMA guidelines, and was registered in PROSPERO (CRD42020207255). Searches were performed in PubMed, Scopus, Web of Science, Lilacs, Open Grey, Google Scholar, and other specific databases. Systematic reviews assessing the association of oral health outcomes and breastfeeding, in participants up to 18 years of age were included. The quality of systematic reviews and primary studies was assessed using the AMSTAR-2 Tool GRADE, respectively. The Mantel-Haenszel method was used for calculating the odds ratios (OR), considering 95% confidence intervals (CI) and a random effects model.

**Results:** Fifteen reviews were selected. Breastfeeding was shown to be a protective factor for dental caries (OR 0.52, CI 0.27–0.98), without a significant influence of breastfeeding duration. Furthermore, breastfeeding was not shown to increase the risk of open bite (OR 0.67, CI 0.57–0.79) and posterior crossbite (OR 0.68, CI 0.54–0.85), and duration  $\geq$  6 months was shown to be a protective factor for overjet (OR 0.70, CI 0.59–0.84) and crowding (OR 0.59, CI 0.45–0.77). However, breastfeeding was shown to increase the risk of overbite (OR 1.95, CI 1.47–2.59).

**Conclusion:** This review confirms the positive impact of breastfeeding on several oral health outcomes in children.

**Funding:** The study was supported by Coordination for the Improvement of Higher Education (CAPES, Finance code 001)

### 1327 | Role of stingless bee propolis from Coorg against *Streptococcus mutans*

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**Background:** Propolis is a natural product derived from honey bees. It has long been used in medicine and dentistry for its beneficial properties, including antimicrobial, anti-inflammatory, hypersensitivity and local anaesthetic effects. Bee propolis beneficial properties depends on its composition which varies depending on geographical origin and botanical sources the bee feeds on. Stingless bee propolis from Coorg has been claimed for its beneficial use in health. The aim of the study was to assess the antimicrobial efficacy of indigenous propolis extract from stingless bee against *Streptococcus mutans*.

**Methods:** Indigenous propolis was procured and aqueous extract was prepared. Aqueous extract of propolis was compared with a standard drug (Amikacin-100mg/2ml) to evaluate the antimicrobial property against *Streptococcus mutans*. Antibacterial activity was evaluated by using the Himedia zone reader at different dilutions. The extract's time-kill

curve was examined using micro broth dilution assay at a concentration of 1 MIC, 4 MIC, and 8 MIC.

**Results:** Indigenous stingless bee propolis from Coorg has shown antibacterial activity at concentrations of 2000  $\mu\text{g}/\text{mL}$  inhibition and bactericidal at 1000  $\mu\text{g}/\text{mL}$ . In time kill assay, the bactericidal effect of the Indigenous propolis extract was apparent from 2h.

**Conclusions:** The extract of indigenous propolis from Coorg may represent a new option showing long-term beneficial effects against *Streptococcus mutans*.

### 1684 | Early childhood caries and iron deficiency anaemia: A systematic review and meta-analysis

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**Background:** Discernment of the association between Early Childhood Caries (ECC) and Iron Deficiency Anaemia (IDA) will aid paediatricians and paediatric dentists to enhance health promotion measures to reduce the related morbidity in children. This systematic review aims to determine an evidence based association between ECC and IDA.

**Methods:** A systematic search was carried out from MEDLINE via PubMed, EMBASE, LILACS, Cochrane Oral Health Group's Specialised Register, CINAHL via EBSCO, Web of Science and Scopus up to May 2020. Hand searching and grey literature screening were also conducted. Cross-sectional, case-control and cohort studies in English language which assessed the association was included. Two reviewers independently assessed the study quality and extracted the outcome data.

**Results:** A total of 1426 studies were identified. Fourteen studies qualified for qualitative review and eight of them for a meta-analysis. The meta-analysis revealed that children with ECC are at a greater risk for IDA. The GRADE approach exhibited the quality of evidence as high. Blood parameters (Hb, MCV and, serum ferritin) also showed a statistically significant difference between ECC and non-ECC groups.

**Conclusions:** The evidence suggests a strong association between Early Childhood Caries and Iron Deficiency Anaemia.

## 965 | Evaluation of caries progression and clinical performance of different agents on non-cavitated fissure areas: Randomized controlled clinical trial

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**Background:** The aim of this study is to compare the clinical and radiographic success of materials used in the treatment of non-cavitated pit-fissure lesions and the effects on the caries-lesions.

**Methods:** This study performed in vivo conditions with a randomized, controlled, double-blind, splint-mouth design. 180 patients and 360 teeth were treated and followed-up for 18-months. At the same time, oral hygiene instructions was given to these patients at the initial and control appointments. The distribution according to the control/study groups are; control group-resin based fissure sealant (Teethmate™-F1), sodium-fluoride and CPP-ACP containing varnish group (MI-Varnish™), fluoride and chlorhexidine containing varnish group (Cervitec®-F) and resin-infiltrant group (ICON®). The evaluations included visual-tactile (ICDAS-II), radiographic-evaluation, evaluation with laser-fluorescence and quantitative-light-induced-fluorescence device (QLF). The data obtained from the patients who were followed-up every 6-months for a total of 18 months was analyzed statistically ( $\alpha = 0.05$ ).

**Results:** Considering the findings-of visual-tactile evaluations, the changes in the scores of MI Varnish™, ICON® and their control groups (Teethmate™-F1), indicating the healing of the lesions were found to be statistically significant ( $P = 0.05$ ). In radiographic evaluations; Cervitec®-F, its control-group and the ICON®-control-group (Teethmate™-F1), indicating the healing of the lesions were found to be statistically significant ( $P = 0.05$ ). The evaluations made with a laser-fluorescence and a QLF device show that a decrease in fluorescence values and reduction in lesion areas were detected for all material groups compared to the all follow-ups ( $P = 0.05$ ).

**Conclusion:** Varnishes in the pit and fissure areas with initial caries lesions indicate successful results as well as resin-based fissure sealants.

## 1750 | Maternal oral health influence on the occurrence of severe early childhood caries

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**Background:** Severe early childhood caries (S-ECC) is nowadays a major public health problem among preschool children whose quality of life is affected from a very young age. The origin of this chronic infectious disease that affects smooth surfaces of the primary teeth comes from prenatal period but also after birth, when the mother's oral health plays an important role in the onset of S-ECC. Although S-ECC has a multifactorial etiology, in the foreground is the microbial factor represented especially by Streptococcus mutans correlated with other factors such as bad feeding habits.

**Methods:** The study group consisting of 17 mother-child pairs diagnosed with S-ECC was compared with a control group consisting of 15 mother-child pairs, without specific signs of S-ECC. The oral health of mothers was assessed by calculating the DMFT index and determining the level of cariogenic microorganisms using the CRT® bacteria test.

**Results:** The data obtained showed a significant correlation between high DMFT score, increased level of Streptococcus mutans in saliva of mothers and the incidence of S-ECC in children.

**Conclusions:** Mother's oral health plays a major role in the onset and evolution of S-ECC therefore prenatal and natal periods are ideal to promote primary prevention of S-ECC in children by ensuring appropriate education regarding the importance of oral health and feeding behavioral practices.

## 1807 | Apoptosis in ameloblast cells due to fluoride induction: A review of literature

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**Background:** High fluoride doses intake during enamel formation may result in enamel fluorosis. The mechanism of fluorosis remains unknown and apoptosis is regarded to be involved in the process by an unclear mechanism. Apoptosis is a physiological process that a disorder in such programmed cell death processes leads to the development of pathological lesions. The initiation phase of apoptosis can proceed

through two different pathways: the intrinsic pathway – mitochondrial, or extrinsic pathway – initiated by death signal transducers. The purpose of this literature review is to give an update on how fluoride can induce apoptosis in ameloblast cells.

**Literature Review:** The molecular mechanisms underlying fluoride-induced apoptosis include the stimulation of G protein-dependent signaling systems, oxidative stress, activation of caspases, alterations in the ratio of anti-apoptotic-apoptotic Bcl-2 proteins, activating FasL/Fas signaling pathway, upregulation of p53 expression, expression of apoptosis-related genes, and endoplasmic reticulum stress. Fluoride was demonstrated to be a potent activator of G-proteins in virtually all studied cell. An involvement of increased ROS production and lipid peroxidation in the fluoride-induced apoptosis has been proven in vitro and in vivo. The fluoride-induced apoptosis was found to be associated with elevated expression of caspase-3, caspase-8, and caspase-9. Elevated expression of another proapoptotic member Bax and corresponding suppression of Bcl-2 expression have been shown to implicate in apoptosis in the NaF-treated cells. Apoptosis was also induced in cells by the enhanced expression levels of Fas and Fas-L. Exposure to fluoride can inhibit protein synthesis, and this may also occur by agents that cause endoplasmic reticulum (ER) stress and unfolded protein response (UPR) that end with apoptosis.

**Conclusion:** Fluoride could induce ameloblast apoptosis via both intrinsic and extrinsic pathways.

### 859 | Relationship between dental erosion and asthma medication in children: A systematic review

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**Background:** Dental erosion is a multifactorial disease defined as irreversible progressive loss of hard dental tissues by chemical dissolution without bacterial involvement. The relationship between asthma and dental erosion, it has been related to the decrease in the saliva flow modifying and reducing the protective effects of saliva produced by the use of asthma medications. This study aimed to evaluate the possible relationship between asthma and dental erosion in children.

**Methods:** A systematic review of the last 18 years was conducted on the topic of dental erosion and asthma. Spanish, Portuguese, and English were the languages chosen for the

papers research. Studies were searched in PubMed, Google Scholar, Medline, and SCOPUS.

**Results:** The investigation and analysis of the three papers revealed the presence of a little amount of information related to dental erosion associated with asthma medication in children. The pooled weighted average prevalence of dental erosion in asthmatic children was 53%, compared with 50.42% in healthy controls.

**Conclusions:** The results revealed that the majority of studies show dental erosion is not associated with asthma medication. Although the prevalence of dental erosion in asthmatic patients is between 35% and 65%, not significant differences have been found.

### 345 | Minimally invasive dental bleaching technique in a young patient with white spot lesion pre-existing before orthodontic treatment begin: Clinical case report

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**Introduction:** White spot lesions are clinically revealed as opaque white areas or small lines that can develop into large, decalcified areas, with or without cavitation.

**Case Report:** A female, 14 years old patient complained about the presence of several white spots and poor positioning of her anterior teeth. The lesions were not cavitated, were present in all teeth and had a diffuse appearance, without clear delimitation. Initially, the patient was referred for orthodontic treatment and after completing this treatment, the patient returned to the Pediatric Dentistry clinic and the white spot lesions were reassessed. The treatment consisted of home and office techniques. In the homemade technique, the patient used 4 carbamide peroxide syringes, 2 of 10%, 1 of 16% and 1 of 22% for night use; and a 7.5% hydrogen peroxide syringe and a 9.5% syringe for daytime use. And, in the second office sessions, hydrogen peroxide was used, with a concentration of 37.5% and 35%. The products used were SDI made. At the end of the treatment, the enamel surfaces were polished with discs and finishing tips and presented satisfactory results.

**Discussion:** When planning treatment many aspects should be considered, such as extension of lesion, tooth affected and the age of patient. The non-invasive treatment is the best indication for young patients.

**Conclusion:** The minimally invasive treatment protocol used in this study proved to be efficient in teeth whitening in a young patient with white spot lesions.

### 1014 | Preventive therapy of white spot lesions in children from 3 to 12 years old using different remineralizing agents

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**Background:** There are no scientific studies comparing the effectiveness of sodium fluoride (Duraphat®), fluorosilane (Fluor Protector®) and tiefenfluoride (Tiefenfluoride®). The aim of this study was to compare the efficacy of sodium fluoride, fluorosilane and tiefenfluoride in treatment of white spot lesions by clinical examination, photographic examination, and fluorescence.

**Methods:** A randomized clinical trial was carried out in children aged 3 to 12 years at the Pediatric Dentistry Department of the International University of Catalonia, Barcelona, Spain. Eight variables were studied: age, sex, clinical caries examination (ICDAS), tactile examination, color, size, depth of the white spot, and sensitivity. The sample was divided into three groups (15 children per group). Professional hygiene was performed on all subjects and subsequently different fluoride agents were applied: sodium fluoride, fluorosilane, and tiefenfluoride. At 3 months, effectiveness was evaluated using clinical examination (ICDAS), tactile and photographic examination, and fluorescence.

**Results:** A total of 45 children were included in the study. All the study groups had positive changes in color, size, depth of the white spots and decreased sensitivity after treatment with sodium fluoride, fluorosilane, and tiefenfluoride (Duraphat®, Fluor Protector®, Tiefenfluoride®). There

were no statistically significant differences regarding sex and age (P 0.05).

**Conclusions:** The fluoride agents used in the study are effective in treatment of white spot lesions. No differences were observed in the treatments regarding sex and age.

### 1020 | Development of oral health guidelines for parents for prevention of early childhood caries: An interventional study

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**Background:** Early Childhood caries (ECC) is still the most common infectious disease among children. The common consequence is pain that affects the daily activities; eating and sleep disturbances, delayed physical development and decreased cognitive abilities. Mother's education level, bottle feeding, brushing frequency, and child's dental hygiene are few of the multiple risk factors for ECC. Lack of awareness amongst parents on preventing and treating dental caries has resulted in a very high prevalence of caries among children. Thus the aim of the study is to test the effectiveness of the guideline document in preventing ECC.

**Methods:** A Pretest questionnaire survey was conducted on 100 mothers with children below 6 years of age, regarding the knowledge, attitude and perception on ECC. Later the developed guidelines on prevention of ECC were given to them followed by a post-test questionnaire. The data collected were analyzed using SPSS version 22, IBM. 2013.

**Results:** The post intervention period showed a mean knowledge score of  $10.95 \pm 2.66$ , which was significantly higher as compared to pre intervention period of  $7.63 \pm 2.25$  leading to 50.29 % of increase in the knowledge scores among the study participants. This difference in the mean knowledge scores between pre and post intervention period was statistically significant.

**Conclusions:** Thus the guideline document in preventing ECC was effective in creating awareness on how to prevent ECC.

### 273 | Evidence based dentistry: A salient adjunct to clinical practice

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**Background:** Evidence based dentistry aims to bridge the gap between dental practitioners, dental researchers and

dental patients. It enables scope for new research, promote the use of best available evidence for improved clinical decision making.

**Literature review:** The concept of evidence-based medicine was introduced in the 19th century and was incorporated in the field of dentistry within no time. ADA and AAPD were the first to adapt and propagate this concept having the main pillars of evidence dental care as: relevant scientific evidence, patient needs and preference, and dentists' clinical expertise. As these are subjective to every patient and practitioner scientific evidence is of critical importance and a clinician's best bet. The methods involved in evidence-based dentistry of creating, synthesizing and disseminating knowledge have evolved overtime from 'learning by doing' to 'development of systematic reviews'. This has greatly evolved the way treatment is planned and delivered in current times. Pediatric dentistry is no exception, when the scope of evidence-based dentistry is spoken about. All realms of pediatric dentistry are rapidly adapting to this new age of evidence-based dentistry. **Conclusion:** Evidence-based dentistry provides an amalgamation of science, clinical expertise, and patient needs to optimize patient care. Its contribution cannot be underestimated and therefore its acceptance into dental practice is the need of the hour.

### 1193 | Reducing biofilm streptococcus mutans production through inhibition gtfB by terpenoid of sarang semut (*Myrmecodia pendans*)

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**Background:** Terpenoids from Sarang semut (*Myrmecodia pendans*) are known to have anti-microbial properties that can be used to prevent dental caries. *Streptococcus mutans* produces glucosyltransferase which can produce insoluble glucan and form biofilms. The purpose of this study was to determine the effect of Sarang semut's terpenoid on gtfB expression as a gene that regulates glucosyltransferase.

**Methods:** The type of research is laboratory experimental namely the preparation of *S. mutans* bacteria, followed by ethyl acetate extract of *M. pendans* bulbs (terpenoid fraction). The next step was analyzing 16s and gtfB gene expression which consisted of RNA total isolation, cDNA synthesis, sequencing, bioinformatics analysis, and validation using the

PCR Reverse Transcriptase method. Chlorhexidine was used as a positive control. The effect of terpenoid fraction and chlorhexidine on genes involved in biofilm formation was analyzed using ANOVA with a significance level of 0.05.

**Results:** The results showed that there was an increase from 0.74 to 1.93 in gtfB expression for the induction of Sarang semut's terpenoid fraction that lasted for 1 and 30 minutes, while the induction of chlorhexidine showed a decrease from 0.76 to 0.65. ANOVA test showed that there was a significant difference in gtfB expression in the *Streptococcus mutans* biofilm between the induction of terpenoid fraction and chlorhexidine with *P*-value of 0.0114. Post hoc analysis showed that the difference in gene expression occurred at induction for 30 minutes with a *P*-value of 0.0212.

**Conclusion:** Terpenoid of Sarang semut increased the gtfB *Streptococcus mutans* production which resulted in no reduction of the biofilm.

### 979 | Silver diamine fluoride in management of early childhood caries: A review of literature

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**Background:** Silver Diamine Fluoride (SDF) is a fluoride based preventive agent which has both antibacterial and remineralizing effect. The first approved SDF product was introduced by Dr Nishino and Dr Yamaga in Japan. SDF helps in the management of early childhood caries, in a minimally invasive manner.

**Literature Review:** The search for an innovative preventive tool to combat dental caries led to SDF through numerous clinical trials on its efficacy. The clinical trials conducted on more than 3900 children proved that SDF is an effective caries arresting agent. SDF enables caries arrest through bacterial killing and inhibiting multi-species cariogenic biofilm formation. Bi-annual application of 38% SDF is found to be more effective in reducing the demineralization process. Acute side effects have not been reported in any reviews or clinical trials using topical SDF. The minor side effects include metallic taste, transient gingival irritation and black discoloration of arrested carious lesion following SDF application. This resulted in less acceptance of its use on anterior teeth. Conditioning with 38% SDF enhanced the resistance of GIC and Composite resin restorations to secondary caries. The clinical success of SDF can be attributed to its antimicrobial activity and reduced rate of enamel and dentin demineralization.

**Conclusion:** SDF has garnered much interest among practitioners because it is an effective, affordable and safe option which is accessible even to the most vulnerable populations. SDF can be recommended as part of a comprehensive caries management program.

## 1050 | Caries experience among 12-year-old children in northwest russia: A cross-sectional study

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**Background:** The prevalence of caries in Europe has been decreasing over the last decades. The data from Russia are scarce and contradictory. We estimated the prevalence and experience of dental caries among 12-year-olds in Northwest Russia.

**Methods:** Altogether, 1233 schoolchildren at the age of 12 (52.9% girls) were selected at random from 7 urban and 5 rural areas in the Arkhangelsk region participated in the regional part of the 3rd Russian national cross-sectional dental study. Caries experience was assessed at D3 level. Caries experience was estimated using decayed (DT), missing (MT) and Filled (FT) teeth index (DMFT) and its components. Dichotomous and numerical data were analyzed using chi-squared tests and Mann-Whitney tests, respectively.

**Results:** Girls were more likely to have caries than boys (77.8% vs. 72.6%,  $P = 0.034$ ). Similarly, the DMFT index was greater in girls than in boys (2.25 vs. 2.62,  $p = 0.001$ ). No differences between the genders were found in DT ( $P = 0.281$ ) while girls had more missing (0.06 vs. 0.03,  $P = 0.021$ ) and filled (1.61 vs. 1.35,  $P = 0.006$ ) teeth. No significant differences in the prevalence of caries between urban and rural areas were observed. Urban boys had greater DMFT scores (1.47 vs. 0.95,  $P = 0.034$ ) due to more filled teeth (1.47 vs. 0.95,  $P = 0.006$ ) than their rural counterparts. The corresponding data for girls were 2.37 vs. 1.85,  $P = 0.034$  and 1.70 vs. 1.20,  $P = 0.006$ .

**Conclusions:** Caries prevalence and experience among Russian 12-year-olds in Northwest Russia are greater than in most European countries. Significant gender and urban rural variations were observed.

## 1674 | Are parents really aware of the preventive effects of dental sealants? A review

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**Background:** Preventive dentistry is one of the most important parts of Pediatric dentistry. In particular, dental sealants are a useful strategy to prevent caries and to manage early carious lesions. Despite the widespread use of this technique, efficacy and beneficial effects are not well known among parents of young patients. The aim of this review was to evaluate the knowledge and attitudes of dental technique among parents.

**Literature review:** A search from the following databases was conducted: MEDLINE, PubMed, Web of Science and Cochrane. Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement to guide article selection and reporting were applied for this study. No restrictions were placed on language or date of publication. From the initial research 146 articles were obtained, of which 26 were included in the systematic review. It turns out that most parents are unaware of the preventive effects of dental sealants. Besides, parents with a higher socioeconomic status and education levels tend to have better oral health knowledge than parents with a lower socioeconomic status. Despite this, an even lower percentage of these parents don't practice the preventive measures although they know their effectiveness and benefits. Furthermore, it has emerged that the primary source of information on preventive techniques is the dentist but often he doesn't encourage parents to embrace preventive techniques for lack of time and academic deficiencies in the preventive field.

**Conclusions:** Parent's dental sealants knowledge is insufficient and dentists need to encourage and educate them on the preventive techniques.

## 426 | Evaluation of monitored tooth brushing effect on oral biofilm structure in children

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**Background:** Saliva microbiological composition plays a significant role in maintaining oral microbial homeostasis. We found compositional difference in oral microbiota between children and adults. Microbial biofilm composition change plays a major role in the development of dental caries in children.

**Methods:** Biological material from children's fissure surface was taken and studied. Children aged  $8.54 \pm 0.06$  took part in the research. All the children were taught to brush their teeth properly.

The biological material was taken twice, before and after tooth brushing. The latter was done under medical supervision. The biological material was taken from the first permanent molars' masticatory surface with the help of sterile paper pins and transported to the laboratory in sterile test tubes with an added preservative within 2 hours after the material collection. Total bacterial count (TBC) was estimated. The data were analyzed using descriptive statistics.

**Results:** After the first monitored tooth brushing the TBC in children decreased by 95.8% (from  $2.5 \times 10^8$  CFU/ml to  $1.06 \times 10^7$  CFU/ml). Almost all *Treponema denticola*, *Staphylococcus aureus* and *Veillonella parvula*, the most common acidogenic anaerobic bacteria in the oral biofilm structure, disappeared. A significant decrease of *Actinobacillus actinomycet* and *Lactobacillus ssp* occurred (94% and 92%, respectively). The latter are facultative anaerobes, and they can effect acidity in the oral cavity under certain condition.

**Conclusions:** Correct and effective tooth brushing allows for significant decrease of dental plaque TBC and, thus, maintaining health of soft and hard tissues of the oral cavity.

## 1415 | Salivary levels of iron and zinc in children under 3 years of age and their association with caries

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**Background:** The prevalence of ECC in children under 6 years of age is still high in Indonesia. Saliva as a diagnostic

tool consists of trace elements which are known to have a protective effect on the formation of caries. This study was aimed to determine the concentrations of salivary iron (Fe) and zinc (Zn), and to investigate their association with caries, increasing age, and the number of deciduous teeth.

**Methods:** We conducted a cross-sectional study with 48 children under 3 years of age divided into caries free and low caries groups. One milliliter of saliva was used with the absorbent method. Salivary Fe and Zn concentrations were measured using Atomic Absorption Spectrophotometer. Descriptive statistics and bivariate analysis were performed. Data with a *P*-value of  $\leq 0.05$  was considered as significant.

**Results:** The Fe and Zn concentrations were  $0.0097 \pm 0.0153$  and  $0.0087 \pm 0.0186$ , respectively. There were no significant differences between salivary Fe and Zn concentrations either with caries (*P* = 0.05), increasing age (*P* = 0.05), or the number of the deciduous teeth (*P* = 0.05). The mean value of salivary Fe and Zn concentrations were higher in females than males, but no significant difference was found (*P* = 0.05). Salivary Fe concentration in the caries free group was higher than in the low caries group without any significant difference (*P* = 0.05). In contrast, Zn showed the opposite result.

**Conclusion:** No association was found between salivary Fe and Zn with caries, increasing age, and the number of deciduous teeth.

## 313 | Comparison between neutralizing effect of tap water and filtered water rinse on salivary pH after 50% sucrose rinse solution

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**Background:** To compare the effect of mouth rinse using tap water and different stages of filtered water on salivary pH following rinsing with 50% sucrose solution.

**Method:** A school based comparative cross-over trial was conducted among 101 children in the age group of 6–10 years. A pre-screening visit was initially held, participants were divided into 2 groups according to DMFT, and pH was measured at baseline, after rinsing with 50% sucrose solution and after rinsing with tap water. The same protocol was followed for measuring pH after rinsing with filtered water on the second day. Randomization was followed in selecting the type of filtered water to be used. The results obtained were compared with the salivary pH after tap water and filtered water rinse using Kruskal-Wallis test and pairwise test in between the three types of filtered water.

**Result:** There was a significant difference in salivary pH after tap water and filtered water rinse, with a higher pH after filtered water rinse (*P* = 0.020). Also, there was significant

statistical difference between the three groups in pH only with reverse osmosis type of filter ( $P = 0.012$ ), however, no statistically significant difference was found on the PH level after rinsing among the other two groups of filtered water ( $P = 0.547, 0.238$  respectively).

**Conclusion:** Rinsing mouth with water (tap or filtered) can lead to neutralization of pH immediately, regardless its fluoride content, thereby preventing the caries process.

### 1049 | Silver diamine fluoride is the magical stick against caries in paediatric patients during COVID-19

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**Background:** Dental caries continues to be a prevalent and severe disease in children. The use of silver diamine fluoride (SDF) to treat cavities is not new. Reports of the use of silver as an antimicrobial date back to the 1800. SDF is a topical antimicrobial and remineralizing non-invasive treatment for caries lesion. SDF inhibits dentin demineralization and collagen breakdown which results into increased dentin hardness. This non-aerosol generating technique allowed delivering dental treatment during Coronavirus disease-2019 (COVID-19) much easier.

**Literature Review:** COVID-19 pandemic has affected the world in an aggressive manner and the healthcare fraternity has been at the forefront in this fight. Dental professionals are at a larger risk to get infected owing to the proximity to the oral cavity. Along with other dental categories, paediatric dentistry too has to adapt quickly to new protocols so as to limit the increase of the global pandemic and possible cross-infections. SDF is a minimally invasive non-aerosolizing option that prevented non-cavitated lesions and arrested early decay among community dentistry patients when applied independently or concurrently with restorative procedures. SDF is a clear, odourless liquid indicated for treatment of sensitive teeth. It is also useful for arresting carious lesions in adults and children who are high caries-risk and/or have difficult-to-control, progressing carious lesions, those who are unable to tolerate invasive treatment, elderly populations, and those who are medically compromised or have additional care and support needs. Alice Trieu et al (2019) concluded that SDF is more effective caries management agent than NaF. Branca et al (2019) found that in primary teeth, SDF compared to no treatment, placebo or fluoride varnish appears to effectively prevent dental caries.

**Conclusion:** SDF is a non-invasive treatment option for cavities, using a topical medicine that is painted on the tooth instead of a more invasive surgical (drill and fill) approaches.

The unique characteristics of SDF in this global epidemic is the non-aerosolizing approach. Most of the parent's concern is permanent black staining of cavity after application of SDF. In conclusion SDF is safe, effective, efficient, patient centered, affordable and easy to apply material in the management of dental caries.

### 673 | "Herbal"- The natural way to go for better oral health? A review of literature

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**Background:** Over the last few years, an increased use of natural and organic products has caught by storm. People gravitate towards herbal products as they view these being safer than those with chemical additives. Herbal products in the form of dentifrices, mouthrinses and medicaments have found their use in the field of Pediatric dentistry. The aim of this poster is to elaborate the use of herbal products as an alternative to their conventional counterparts.

**Literature Review:** Various studies have shown the remineralizing and antimicrobial properties of herbal dentifrices. *Streptococcus mutans*, *Streptococcus sanguis*, *Actinomyces viscosus* and *Candida albicans* are opportunistic microorganisms found in the oral cavity and are implicated in several oral diseases. A study by Bhat et al showed herbal dentifrices were found to be effective in creating a zone of inhibition against these microorganisms and thus demonstrating antimicrobial efficacy. A study by Hosadurga et al showed herbal dentifrices reduced plaque and gingival inflammation in patients. The goal of pediatric endodontics is to eliminate infection and retain the tooth in a functional state until normal exfoliation. Turmeric, a natural herbal ingredient has been used as an alternative to the commercial intracanal medicament in pulpotomy owing to its anti-inflammatory properties. It was shown to have good clinical and radiographic success in a study by Purohit et al.

**Conclusions:** In conclusion, herbal products can be used in dentistry as antiseptic, antioxidants, and analgesic. They aid in healing of oral infections and boost immunity.

## 705 | Interim therapeutic restorations (ITR): A boon to pediatric dental practice

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**Background:** Minimally invasive dentistry (MID) is gaining popularity in children for the treatment of dental caries because it is perceived to be relatively non-invasive and therefore more likely to be accepted by children compared to the conventional approach to decay removal. Interim therapeutic restoration (ITR) is one of the techniques included under MID.

**Literature Review:** ITR involves caries management in infants, children, adolescents and persons with special health-care needs where delivery of definitive restorations needs to be postponed for a variety of reasons (e.g., age, medical risk). This concept is essentially derived from atraumatic restorative treatment (ART) which involves the removal of soft, completely demineralized caries-affected dental tissues followed by restoration of the cavity with a fluoride-releasing restorative material. Unlike ART, rotary instruments for caries removal in ITR. The ultimate goal remains to replace the 'interim restoration' with a 'definitive restoration' when suitable, though the comparative survival rates of these restorations may be indeterminate. A systematic review concluded that the success rates of ITR and ART in terms of durability of the restoration are comparable to traditional treatment methods. Another study comparing ITR with treatment under general anaesthesia concluded that ITR could be a viable alternative to treatment under general anaesthesia in pediatric patients.

**Conclusions:** ITR can be a boon to paediatric dental practice if utilized in proper clinical situations. This technique is a viable option to control caries progression and instill compliant behaviour during dental treatment among young child patients.

## 264 | Study of the cariogenic diet in a group of Chilean preschool children with early childhood caries

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**Background:** Early childhood caries is a multifactorial disease, in which diet plays an important role in its etiology. Evidence has shown that dietary practices, particularly the consumption of cariogenic foods, are critically important in the development of caries, constituting a necessary cause for their appearance. The purpose of this study was to analyze the cariogenic diet in a group of Chilean preschool children with early childhood caries.

**Methods:** The sample consisted of 214 children from 2 to 5 years of age with early childhood caries attended at the Pediatric Dentistry Clinic of the University of Chile. The data were collected through an oral examination and a questionnaire on cariogenic foods that was applied to the parents. The variables analyzed were: sugary foods and beverages between meals and carbohydrate consumption. The data obtained were analyzed using the Pearson chi-square test. To determine which of the cariogenic foods was the most associated with Early Childhood Caries, the OR calculation was performed through multivariate logistic regression analysis.

**Results:** The data show a highly significant association between ECC and the consumption of sugary foods and drinks between meals. In relation to the carbohydrate consumption, no significant differences were observed. The multivariate logistic regression analysis showed that the only significant determinant in the model was the consumption of sugary drinks between meals with an OR: 3.048 (95% CI: 1.462–6.355).

**Conclusion:** The results of this study are important in reducing the risk of early childhood caries and focusing dietary counseling for children.

## 1926 | Impact of caries classification on caries prevalence and treatment needs in schoolchildren: A comparison of Nyvad and df-s/DF-S

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**Background:** The assessment of different stages and activity of dental caries are important when strategies to halt and reverse the disease are target. This study aimed to evaluate the caries prevalence and treatment needs of schoolchildren when using Nyvad caries detection system versus decayed, filled surfaces (df-s/DF-S).

**Methods:** This study is part of a randomized clinical trial with 4–9-year-old children (n = 214) in a public primary school in Petrópolis, Brazil. Children were clinically examined for caries by one calibrated examiner using Nyvad criteria after 2-years of the implementation of two different professional toothbrushing (PTB) regimen. The Nyvad scores were converted into df-s/DF-S. Chi-square-test, McNemar-test and logistic regression analyses were used to analyze the data ( $\alpha = 5\%$ ).

**Results:** 167 children, with a total of 6,232 tooth-surfaces in the primary, and 10,975 tooth-surfaces in the permanent dentition were evaluated. Caries prevalence was higher when Nyvad was compared to df-s/DF-S, for both primary and permanent dentition ( $P = 0.05$ ). For the primary dentition, df-s resulted in higher treatment needs compared to Nyvad (5.7% versus 3.5%;  $P = 0.001$ ), while for the permanent dentition the opposite was observed (1.2% versus 3.0%;  $P = 0.001$ ). Additionally, the treatment needs were overall low and no statistical differences between PTB groups were found ( $P = 0.05$ ).

**Conclusion:** In the primary dentition, the use of the Nyvad resulted in higher caries prevalence, while the df-s resulted in higher percentages of treatment needs. In the permanent dentition Nyvad resulted in higher caries prevalence and higher treatment needs compared to DF-S.

### 595 | Serum and saliva vitamin D levels in relation to dental caries in young children

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**Background:** Several studies have reported that low levels of vitamin D (25(OH)D) are associated with an increased risk of dental caries and that optimal levels may offer protection. This study aimed to assess the relationship between serum and saliva 25(OH)D levels and caries among young children. **Methods:** A total of 120 healthy children were recruited; 93 with caries and 27 caries-free. Dental caries status was evaluated using decayed, missing, and filled in primary teeth (dmft) index. Blood and unstimulated whole saliva samples were collected. Laboratory analysis was performed using Enzyme-Linked Immunosorbent Assay Kit. Data were analyzed with descriptive statistics, bivariate and Spearman's rank correlation analysis.

**Results:** There were no significant associations between serum and saliva 25(OH)D levels and caries status ( $P = 0.05$ ). Levels of 25(OH)D in serum were significantly higher than

levels found in saliva ( $P = 0.05$ ), and a correlation between serum and saliva 25(OH)D levels was observed ( $P = 0.05$ ).

**Conclusions:** The association between serum and saliva 25(OH)D and dental caries in young children was inconclusive. However, a positive and significant correlation was observed between serum and saliva 25(OH)D level. Further studies are warranted to investigate the definite relation between 25(OH)D levels and dental caries and using saliva 25(OH)D as a non-invasive alternative method over blood samples.

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### 826 | Antimicrobial efficacy of herbal toothpaste containing bamboo salt

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**Background:** In recent years, toothpastes containing herbal antimicrobial ingredients have gained popularity due to their reduced side effects. This study aimed to assess the antimicrobial efficacy of herbal toothpaste containing Bamboo salt on pathogens responsible for dental caries.

**Methods:** Sixty dental students aged 18–30 years old were randomly assigned to the case (Tiger Herb® toothpaste) and control (Crest® Complete toothpaste) groups. Participants were instructed to brush their teeth twice a day with the Bass technique for four weeks and use dental floss every night. Saliva sampling was performed at baseline and was repeated after four weeks of toothpaste use. Salivary Streptococcus mutans and lactobacillus counts were determined. Mann-Whitney Rank, Independent t-test, and Wilcoxon test were applied at  $P = 0.05$ .

**Results:** Both toothpaste types significantly decreased the salivary counts of streptococcus mutans and lactobacillus ( $P = 0.001$ ). No statistically significant difference was observed between the antibacterial efficacy of two toothpaste types on streptococcus mutans ( $P = 0.108$ ) and lactobacillus ( $P = 0.796$ ).

**Conclusions:** Considering the observed efficacy of herbal toothpaste in the present study, it potentially qualifies as a complementary agent for self-care oral hygiene procedures.

## 554 | Effectiveness of diagnodent in detecting the extent of remineralization in primary teeth after pH cycling: An in vitro study

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**Background:** The changes after remineralization of teeth are difficult to detect clinically. A chairside device with a digital scoring helps the clinician to control demineralization and evaluate remineralization. This study evaluates the effectiveness of DIAGNOdent in detecting the extent of remineralization in primary teeth.

**Methods:** Ten exfoliated primary teeth with no visible white spots or caries were sectioned at CEJ. The samples were mounted on resin blocks to expose buccal surface, which were then serially polished to get a flat surface. The samples were submitted to demineralization and remineralization using fluoride varnish and then subjected to PH cycling process to promote remineralization. The Surface Microhardness (SMH) and Laser Fluorescence analysis were performed at baseline, after demineralization and after remineralization & PH cycling.

**Results:** Paired t tests were performed to compare the LF readings and SMH values at baseline, after demineralization and remineralization. Baseline SMH values showed significant differences from after demineralization & remineralization. Baseline LF values showed significant difference from after demineralization and remineralization.

**Conclusions:** DIAGNOdent proves to be efficacious in detecting the remineralization in artificially demineralized primary teeth under in vitro conditions.

## 1155 | Qualitative analysis and effects of three topical fluoride agents on demineralized human primary enamel using SEM, XRD and FTIR

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**Background:** Topical fluoride therapy has proven benefits in the prevention of demineralization. A novel fluoride agent silver diamine fluoride (SDF) has emerged as a potent caries arresting as well as caries preventing agent. The present study was aimed at assessing primary tooth enamel resistance to demineralization after topical application of SDF, ApF and NaF.

**Methods:** Enamel specimens were prepared from 30 caries free primary molars. These were randomly allocated to three groups of 10 each and were treated by three topical fluorides- Gr -1 SDF, Gr-2 ApF, Gr-3 NaF. Three specimen from each group were placed on custom made acrylic blocks with 5x5 mm of exposed window for SEM evaluation and rest of the specimen were ground into fine powder for XRD and FTIR analysis. The tooth blocks and treated specimens were subjected to demineralization for 168 hrs.

**Results:** Morphologically, SEM images of all samples showed some grooves and micro porosities along with homogeneously arranged crystals with well coalesced enamel rods without any loss of structural characteristics. Enamel was covered with a CaF<sub>2</sub> layer which showed a granular morphology.

Chemically, the Ca/P molar ratios of all groups were similar with slight variations.

Structurally, the crystalline phases found in enamel by powder XRD were hydroxyapatite and carbonate apatite. The initial peaks were obtained at 2θ values of 36.13, 40.20° and 46.92° and there was a higher amount of incorporated type B carbonate than type A carbonate as evidenced by FTIR which was registered between 4000 and 400 cm<sup>-1</sup> in a FTIR Spectrometer.

**Conclusion:** The study concludes that topical application of 38% Sdf can inhibit demineralization of enamel.

## 834 | Values of DMFT components among children aged 12 from Skopje region-Republic of North Macedonia (RNM)

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**Background:** To determine the values of DMFT components among children aged 12 from Skopje region to assess the effectiveness of the National Strategy.

**Methods:** About 30% of the population of RNM lives in the Skopje region. 627 children (314 males and 313 females), from urban and rural areas were examined. The examinations were performed by calibrated dentists following the WHO criteria and recording the findings in Oral Health Assessment Form for Children as per WHO's recommendation. Because the examinations were performed within the framework of

regular systematic examinations, no approval from the parents and ethics committee was required. During analyzing the data, a standard formula for DMFT index was used.

**Results:** The analysis showed a value of DMFT 2.77 where the number of carious teeth is 734 (42.1% of the total number of carious, extracted and filled teeth), the number of extracted teeth is 19 (1.1%) and the number of filled teeth is 990 (56.8%).

**Conclusions:** Comparing the values of each component of the DMFT index with the values of nearby countries, such as Montenegro, Albania and Bosnia and Herzegovina, in which the health system and socio-economic conditions are similar, it is clear that component M is the lowest. Components C and F show increased awareness of oral health but still at an unsatisfactory level, which indicates the need for further active education for proper nutrition with control over sugar intake and brushing teeth with emphasis on proper technique.

### 543 | Antibacterial efficacy of various dentifrices on *Streptococcus mutans* count in children with ECC: A pilot study

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**Background:** The study has been planned to evaluate the antimicrobial efficacy of various commercially available dentifrices namely, active oxygen based, amine fluoride based, sodium monofluoro-fluoride based, herbal and non-fluoridated dentifrices on the *S. mutans* count in children with ECC.

**Methods:** 20 participants aged 3–6 years with  $\text{def} \geq 4$  were selected and randomly divided into 5 groups of 4 children each, based on the dentifrice used as, Group I: Non-fluoridated dentifrice, Group II: Sodium Monofluoro-fluoride dentifrice (458 ppm), Group III: Amine Fluoride dentifrice (500 ppm), Group IV: Active Oxygen dentifrice and Group V: Herbal dentifrice. A baseline saliva sample was taken and cultured for *mutans streptococci* and the colonies were counted. Children were demonstrated the horizontal scrub method and then asked to brush their teeth using dentifrice given twice daily for 2 weeks. The saliva sample was then collected after 2 weeks and *streptococcus mutans* was again estimated. Data was analysed using Wilcoxon t-test.

**Results:** Statistically significant results were found where Group II and Group IV showed significantly higher reduction in *S. mutans* count after 2 weeks of intervention than those of Group I, Group III and Group V.

**Conclusions:** The results showed that all the dentifrices used in the study were effective in reducing the microbial load, however

Active Oxygen dentifrice and Sodium Monofluoro-fluoride dentifrice showed maximum reduction in cariogenic bacteria. The pilot study is still going on with much larger sample size.

### 765 | 38% Silver diamine fluoride (SDF): Literature review

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**Background:** Dental caries is most prevalent disease. Complete removal of caries can sometimes be difficult especially in case of un-cooperating child patient. Recently, a new concept that is, non-invasive dentistry is being practiced for prevention and arrest of the caries. SDF is a new material which arrest progression of the dental carious lesion by non-invasive treatment.

**Literature Review:** SDF is a clear, alkaline solution containing Silver and fluoride, which forms a complex with ammonia. SDF is painless, easy to use and inexpensive material. SDF has anti-bacterial action, inhibits caries progression via inhibiting biofilm formation and facilitates remineralisation. It used as caries arresting and preventing agent, as desensitizing agent and as endodontic irrigant. SDF is an effective non-invasive treatment for children's tooth decay and well tolerated by children as a treatment technique and can be quickly applied to isolated tooth without any extensive excavation. 38% concentration of the SDF has been used for arresting the dental caries. Major side effect of SDF is back staining of the tooth. Use of Potassium iodide immediately after the SDF application reduces the black staining of the tooth.

**Conclusions:** SDF has proven effective in management of dental caries. SDF treatment is an efficient, simple, quick and safe method of dental treatment

### 423 | Isolation of *Candida albicans* from pre-school children and a study of its forms and acidogenic nature in early childhood caries

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**Background:** ECC, a rampant type of dental caries in children below 71 months of age; a chronic childhood disease with a severe sequelae affecting the child and family. Recent literature suggests a probable role of *Candida Albicans* in Early Childhood

Caries etiopathogenesis. Under particular predisposing physiological or pathological conditions, *Candida* is capable of provoking pathologies via endogenous infectious mechanism for caries process. The aim of this study is to determine the *Candida albicans* counts, forms of existence and acidogenic potential in children without caries and with ECC and S-ECC.

**Methods:** 30 healthy pre-school children below 4 years of age were divided into Caries free, ECC and S-ECC based on AAPD definition. Non-stimulated whole saliva samples were, cultured and *Candida* colonies were isolated using germ tube technique and its forms; yeast, hyphal and pseudo-hyphal were determined by gram staining technique under Light microscope. Further the cultured *Candida* plates were subject to maltose fermentation test to compare its acidogenic potential in ECC and S-ECC groups.

**Results:** A Prevalence of *Candida albicans* of (63.3%) was found; it was mostly in S-ECC group. Yeast was the predominant (68.4%) morphological form exhibited. The acidic potential of yeast was found to be greater than the other pathological forms and was directly proportional to severity of Early childhood caries.

**Conclusion:** The study findings suggest that *Candida albicans* was most highly prevalent in S-ECC group. This may be contributing for the rapid and widespread progression of ECC in the very young children with immature immune system and not fully established microflora.

## 614 | Applications of silver nanoparticles in pediatric dentistry: A review of literature

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**Background:** The transition metal, “Silver” a natural biocide, has been used in dentistry in the form of silver amalgam since ages because of superior compressive strength. Ever since the emergence of nanosized elemental Silver, the horizon of its dental applications widened extensively. Paediatric dentistry a versatile speciality, never ceases to incorporate the newer advancements into its technical armamentarium.

**Literature Review:** The evidence from reviewed literature suggests that, silver disrupts cell wall, cell cycle, respiratory process and proteins of bacteria and also causes free radical mediated damage, resulting in bacterial cell death which is further enhanced by the nano-size and resultant high surface energy. In virtue of its antimicrobial effect, nano-silver is successfully employed as intracanal irrigants and medications. In addition, silver nanoparticles can infiltrate into demineralized area and precipitate, resulting in an increase in the enamel hardness and the resistance to demineralization.

Nano-silver was effectively incorporated into Glass Ionomer Cement, bonding systems, pit and fissure sealants, dental composites, to improve concurrently the physical properties, antimicrobial and remineralizing effect of the restorative material while not compromising their existing properties. Novel remineralizing biomaterials like nano Silver-Calcium Glycerophosphate, Silver impregnated Sodium trimetaphosphate etc., were developed to aid in remineralization. Silver nanoparticles were incorporated into fluoride varnish and a novel nano-silver fluoride varnish was also developed to improve anticaries efficacy.

**Conclusions:** Silver Nanoparticle incorporation into various biomaterials used in pediatric dentistry improves the antimicrobial and remineralization potency and can act as an effective anticaries agent. Hence, Nano-silver is an irrefutable biomaterial in Pediatric Dentistry.

## 1644 | Maternal vitamin D status and early childhood caries in young children

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**Background:** A questionnaire study was conducted to evaluate the knowledge and practices of mothers in respect to intake of Vitamin D and clinically correlate their vitamin D status with the presence of early childhood caries in their (2–6 years) aged children in Faridabad, India

**Methods:** Ninety-five mothers were interviewed for their visit to gynaecologist and prenatal supplements intake, knowledge and their practices in prevention of vitamin D deficiency. Children aged 2–6 years were clinically examined and their caries status was recorded by deft index. Data were analysed using descriptive analysis and correlation of maternal vitamin D status with the caries status was calculated by Independent T test.

**Results:** There was a good understanding of importance of vitamin D deficiency amongst the mothers. About 93.7% had visited gynaecologist and taken iron and calcium as basic supplements. The source of knowledge was mainly by doctor in 65% of mothers. However, only 11.6% knew the normal levels of vitamin D in blood. Most of them identified sunlight as main source of vitamin D followed by milk and fish respectively. Most of them exposed to sun daily, with 32.3% exposing for at least 30 minutes. About 59% agreed to be vitamin D deficient and opted for consumption of milk (78%); increased sun exposure (64.2%); supplementation (24%) to increase Vitamin D levels. deft (Mean 4.8) was found to be significantly more in children with vitamin D deficient mothers (p 0.05).

**Conclusions:** The study highlighted the need of awareness of importance of vitamin D deficiency amongst mothers and their children to prevent early childhood caries.

## 1889 | Oral health practice of a group of children during the early stage of the COVID-19 pandemic in Istanbul

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**Background:** The aim of this study was to evaluate changes in children's oral dental health and diet and to learn about parents' attitudes towards dental treatment during the COVID-19 pandemic.

**Methods:** A questionnaire related to the general and oral dental health, eating patterns of children under quarantine and socio demographic characteristics of the family and parents' attitudes towards dental treatment during the COVID-19 pandemic was sent online using WhatsApp to a convenience sample of mothers with children between the ages of 8 and 18, who lives in Istanbul.

**Results:** "The consumption of fast food, packaged food and carbonated beverages decreased during the COVID-19 outbreak" stated respectively by the 94%, 81% and 86% of mothers. "Children drinking much more water than they did prior to the COVID-19 pandemic" stated by the 85% of the mothers. Mothers stated that their children did not change tooth-brushing frequency when they were no longer going to school. However, fewer brushed their teeth under supervision during COVID-19 outbreak. Mothers of children reported that they were anxious or fearful about their children visiting a dentist during the pandemic and most children missed routine dental visits.

**Conclusions:** The mothers who participated in this study recognized the importance of oral health to the well-being of the body.

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## 794 | Management of incipient carious lesion

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**Background:** Dental caries is the most common cause of tooth destruction in the children. The Incipient carious lesions are non cavitated lesions which occur at the initial phase of tooth decay. These lesions can be treated early; hence preventing further tooth destruction. So, early detection of dental caries can prevent loss of tooth structure.

**Literature Review:** Most commonly these lesions appear as whitish spots on the enamel surface. There are various methods for the management of the incipient lesions, most effective been, use of remineralizing agents in the form of toothpastes, gels and varnishes and other being use of anti-plaque agents and use of fluorides. Dietary advices also play a very important role in the prevention of caries.

**Conclusions:** Management of incipient lesions as early as possible can save the teeth and hence preventing the other issues that may arise from severe tooth destructions.

## 937 | Health status of first permanent molars in 6-year old children from Bosnia and Herzegovina

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**Background:** The purpose of this study was to assess caries prevalence and the use of preventive and therapeutic treatments of first permanent molars in 6-year-old children.

**Methods:** The sample consisted of 324 erupted first permanent molars in 133 6-year-old children (mean age 6.6) who visited Dental Clinic, University of Banja Luka, Bosnia and Herzegovina, in the past two years (February 2019 – February 2021). The Study was retrospective and the data on first permanent molars was extracted from electronic patient records. Preventive treatments implied professional application of high-concentrated fluoride varnish and fissure sealants. Therapeutic treatment included dental fillings, deep caries treatment and tooth extraction. Chi-square test was used for data analysis.

**Results:** In 324 observed first permanent molars caries prevalence was 27%. Mean DMFT was 0.65. Prevalence of

caries in maxillary molars was 20.24%, while in mandibular molars 27% ( $x_2 = 1.19$ ,  $P = 0.275$ ). In the past two years, 64.26% observed molars were protected by preventive measures, while 35.74% received caries treatment. 61.18% maxillary molars and 57.67% mandibular molars ( $x_2 = 1,884$ ,  $P = 0.169$ ) received preventive treatments, while 38.81% and 42.32% respectively ( $x_2 = 4.546$ ,  $P = 0.0329$ ) needed therapeutic treatment.

**Conclusion:** Health condition in observed first permanent molars of 6-year-old children was not satisfactory, since the prevalence of caries and applied therapeutic measures were rather high.

### 891 | Photoreactive effect using indocyanine green and near-infrared diode lasers on *Streptococcus mutans* biofilm

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**Background:** This study evaluated the effect of Indocyanine Green (ICG) and Near Infrared (NIR) diode lasers on *Streptococcus mutans* biofilm according to the concentration of ICG solution.

**Methods:** *S. mutans* biofilms were formed on the hydroxyapatite disk. An ICG solution (0.5, 1.0, 2.0, 3.0, 4.0, 5.0 mg/mL) dissolved in sterile distilled water and NIR diode laser (300 mW output, 808 nm wavelength) were applied to the disk. All specimens were observed using a confocal laser scanning microscopy (CLSM) to estimate the inhibitory effect of the indocyanine green and near-infrared diode lasers. In addition, the temperature change of the biofilm surface during light irradiation was measured using a 1-channel thermocouple thermometer.

**Results:** There was a statistically significant decrease of bacteria in the "ICG only" groups compared to the control group when the concentration was 3.0, 4.0, 5.0 mg/mL. In addition, all groups of "ICG with NIR" showed statistically significant decrease in bacterial count compared with the control group. The increase in temperature ranged 9.53°C to 13.63°C, and the higher the concentration of the ICG solution, the greater the increase in temperature.

**Conclusions:** An ICG solution of 3 mg/mL or more shows the inhibitory effect of *S. mutans*. When ICG and NIR are used together, *S. mutans* can be more effectively inhibited without damaging the surrounding tissues. Therefore, this study presents the possibility of clinical application of the photoreaction using ICG and NIR diode lasers as a novel method of the dental caries prevention.

### 598 | Impact of dental caries, dental fluorosis and molar incisor hypomineralization on oral health-related quality of life in adolescents

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**Background:** This study aimed to assess the impact of molar-incisor hypomineralization (MIH), dental fluorosis (DF), and dental caries (DC) on quality of life (QoL) in a population of Brazilian adolescents.

**Methods:** Participants aged 11 to 14, from Paranoá, Brasília, Brazil, were evaluated for DC, DF, and MIH. For this, the CAST (Caries Assessment Spectrum and Treatment), the Thylstrup and Fejerskov, and the MIH-SSS (MIH Severity Scoring System) were used, respectively. To assess the QoL, the Child Perception Questionnaire (CPQ11-14) was used. The data obtained were submitted to descriptive statistical analysis and the chi-square test. To assess QoL, Mann-Whitney test was used ( $P = 0.05$ ).

**Results:** Of the 400 adolescents examined, 52.25% were girls. Considering the oral health perception, there was no difference between adolescents with or without fluorosis and with or without MIH. Adolescents with dentin caries lesions judged their overall oral health to be worse than those without dentin lesions ( $P = 0.038$ ). Assessing the CPQ11-14, there was no difference in the groups with or without MIH or fluorosis for the total score ( $p 0.05$ ). However, adolescents with dentin lesions presented higher CPQ11-14 values when compared to adolescents without dentin lesions ( $p 0.05$ ). Considering three conditions separately and coexisting, groups with only dentin lesion, as well as dentin lesion and fluorosis were statistically different from the others ( $p 0.05$ ).

**Conclusions:** Only DC presented an impact on QoL of adolescents. The presence or not of MIH and DF did not show an impact on QoL.

## 1601 | Effect of nitrite on dental plaque in children with dental caries: An ex vivo study

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**Background:** Dental plaque is considered more important in initiation and progression of carious lesion than saliva. Children with high salivary nitrite suffers lower caries experience. The study evaluated the effect of nitrite on dental plaque acidogenicity in children with caries experience.

**Methods:** 20 µl plaque was collected from 40 children (age range 3 -12yrs). The initial pH (pH0) of each sample was measured using a portable pH meter. The samples were incubated for 10 min, the pH was measured again (pH1). Next 5% glucose was added to the sample and then incubated for further 10 min; the pH was assessed for a third time (pH 2) using the pH meter.

**Results:** In comparison to control group, the plaque pH was buffered in nitrite treated sample. Furthermore, an increase of the mean plaque pH of nitrite treated sample (pH 6.72) was observed compared to control group (pH 5.9) after glucose addition and incubation. The buffering effect of nitrite on dental plaque acidogenicity was not significantly correlated with caries experience.

**Conclusion:** The present study demonstrates that nitrite could buffer acid produced in dental plaque. Nitrite might contribute in maintaining pH homeostasis in dental plaque by countering excess acidification.

**Taken together, the present study revealed that nitrite holds potential effect against dental caries by inhibiting acid production in dental plaque and thus contribute in maintaining pH homeostasis.**

## 1908 | Evaluation of prophylactic use of IgY containing chewable tablets on salivary Streptococcus mutans in children

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**Background:** The study evaluated the efficacy of Immunoglobulin Y containing chewable tablets on the levels of Streptococcus mutans in children.

**Method:** The study group consisted of 30 children aged between 6–12 years with def score 3 or DMFT score 1 visiting

the department. Resting saliva was collected from each child, transferred to sterile Eppendorf tubes stored in icebox and transported to laboratory within 6 hours to assess the number of Streptococcus mutans colony forming units per 1 ml of saliva. Each child was given one 20 mg chewtab (orange) soon after breakfast and one 40 mg chewtab (white) after dinner and tooth brushing. Instructions were given to chew the tablet, ingest and to avoid eating or drinking for at least 1 hour after taking the tablets. The resting saliva was taken before intervention and 30 days post intervention.

**Results:** The mean colony count of Streptococcus mutans before intervention was 320.67 and for the corresponding log transformation was 2.49. At 30 days post intervention, there was significant decrease in Streptococcus mutans count which was 25.70 and 1.36 for log transformation. ( $P = 0.001^*$ )

**Conclusion:** The results suggested that Streptococcus mutans was significantly reduced in children who consumed no-decay tablets. Early childhood caries development could be reduced by administration of Immunoglobulin Y containing chewable tablets as adjunct to daily use of fluoride containing toothpaste in children.

## 1706 | Evaluation of effect of fixed and removable appliances on oral microbiological flora in children aged 5–12 years

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**Background:** Guidance of eruption and development of the primary, mixed and permanent dentition is an integral part of comprehensive oral health care for all paediatric dental patients. Preventive and interceptive orthodontic therapy using fixed and removable appliances is meant to render the dentition in a more functional, occlusally harmonious and esthetic form. However, various deleterious effects associated with orthodontic therapy render the dentist and the patient in a dilemma to the receipt of orthodontic therapy. The present study was done to evaluate the effect of fixed and removable appliances on oral microbiological flora in children aged 5 -12 years.

**Methods:** Unstimulated whole salivary samples were collected from patients wearing fixed (Group I) and removable (Group II) orthodontic appliances for estimation microbial

counts (*Streptococcus mutans*, *Lactobacillus* sp and *Candida* sp.). The values were obtained at baseline (at the time of appliance delivery), one month, two months and three months after placement of these appliances and compared.

**Results:** Statistically significant increase in the microbial concentration (*Streptococcus mutans* and *Lactobacillus* sp.) of saliva was found at the end of three months. An unusual finding was the isolation of *Candida* sp. in three subjects with removable appliances at follow up periods. Species identification revealed *C. glabrata* in two subjects and *C. albicans* in one subject.

**Conclusions:** In children, fixed and removable orthodontic appliances act as opportunistic plaque retentive areas and call for appropriate oral hygiene appraisal and its reinforcement. Failing to follow a strict oral hygiene regime may lead to significant enamel decalcification and plaque retention leading to alteration in oral micro flora which has detrimental effects. As preventive dentists, this study paves way for provision of incorporating practice guideline information for both dentists and children undergoing long term orthodontic therapy.

## 964 | Risk factors for early colonization of streptococci mutans in infants: A literature review

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**Background:** Early childhood caries (ECC) describes presence of one or more decayed, missing or filled tooth surfaces in any primary tooth in a child under the age of 6. Despite significant advances in dentistry, ECC remains a serious problem. Mutans streptococci (MS) is one of the factors that is closely related to development of ECC and are usually established in the oral cavity during early childhood. The aim of this review was to identify factors associated with early colonization of streptococcus mutans.

**Literature review:** Based on the PICO criteria, longitudinal and observational studies involving infants and children ranging from birth to 24 months of age (P) who were examined clinically and evaluation of various factors like - diet, oral hygiene, educational status of mother, etc. (I/E) with respect to their streptococcus counts were identified (O).

The following MeSh words were used (((("child"[MeSH Terms]) OR ("infant"[MeSH Terms])) ) OR ("infants"[Title/Abstract]) AND ("streptococcus mutans"[MeSH Terms])) OR ("streptococcus mutans/growth and development"[MeSH Terms])) OR ("colony count, microbial"[MeSH Terms]) AND ("dental caries"[MeSH Terms])) ) AND ("risk factors"[MeSH Terms])) and a total of 220 studies were identified and 51 remained after we restricted our search to only English language articles and age group of infants to

24 months of age group. Another 26 studies were removed after the retrieved studies were scanned based on their titles and abstracts because they did not meet the inclusion criteria. Manual search revealed 14 articles out of which only 6 articles were included based on the inclusion and exclusion criteria. 3 articles remained after duplicates were removed. So a total of 29 studies were included in the literature review. The role of MS in the etiology of dental caries in children is important and of great interest to researchers. MS colonization in young children could be divided into bacterial factors, host factors and environmental factors. Bacterial factors include biofilm, bacterial virulence and bacterial transmission. Bacterial transmission results from increased numbers of MS in mothers or close contacts. MS can also be seen in infants before the teeth erupt. While host factors include heredity, surfaces for microbial adherence, diet, oral hygiene and saliva. Thus, defects on tooth surface could be an initiating factor for colonization. Poor oral hygiene also leads to early colonization of MS. Environmental factors include demographic characteristics and socio-economic status of children. Complex interactions among these factors determined the timing of MS colonization in children.

**Conclusion:** The main factors for early colonization of MS included its early exposure due to contact with caregivers who were high on MS, oral hygiene habits, exposure to carbohydrates and the defects of tooth surface.

## 229 | Mother-infant microbiome, cariogenic bacteria and oral probiotics – Mothers' point of view

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**Background:** In recent decades, there has been a growing interest in the use of oral probiotics in preventing caries, and the results of clinical trials to date have been promising. The aim of the study was to assess the knowledge and attitudes of Macedonian's mothers regarding the maternal and infant microbiome, cariogenic bacteria and the use of oral probiotics for caries prevention.

**Methods:** The survey was conducted in December 2020, by sending a questionnaire in a form of Google document to Macedonian's mothers, members of social groups that cover topics of their interest. Only mothers older than 18 years, with one or more children, who understand Macedonian language, were included in the study.

**Results:** Total number of respondents was 520. 68.7% of them knew that beneficial bacteria are transferred from mother to child during birth, but only 24.2% knew that cariogenic bacteria can be transmitted on same way during first years of life and 80.6% didn't know that cariogenic bacteria are needed for caries to occur. Although only 6.2% of respondents heard for probiotics for caries prevention, 81.5% of mothers would use probiotics if they knew that in that way would prevent tooth decay.

**Conclusion:** Insufficient knowledge versus mother's positive attitude towards the use of novel preventive measures indicates the need of additional educational and preventive actions targeted at mothers as it is well known mother- infant oral microbiome connection.

### 443 | Is bitewing radiography used appropriately for paediatric patients in primary care?: A multi-centre observational study

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**Background:** In the UK, guidelines have been published to support clinicians regarding the indications for bitewing radiography and time intervals for repeating them based on caries risk. However, despite evidence for their diagnostic yield, previous surveys have reported underuse of bitewings for children in primary care. Therefore, the aim of this study was to evaluate the actual use of bitewing radiographs for paediatric patients across four primary care dental practices in England.

**Methods:** Data were collected from four primary care dental practices in England (West Sussex, Kent, and Suffolk). A list was collated of children aged 5 to 17 years that attended for initial examination appointments from January 2016 onwards and at least one subsequent recall appointment. Fifty eligible cases from each centre were randomly selected for inclusion in the study.

**Results:** Bitewing radiographs were taken at the initial examination appointment in only 21% (42/200) of cases. Dental caries was diagnosed in 54 patients; and of those, 35.2% (19/54) had bitewing radiographs taken as an adjunct for diagnosis/management, 5.5% (3/54) had other radiographs taken (e.g., periapical), and 59.3% (32/54) did not have any radiographs. At recall appointments, only in 31% (62/200) of cases were bitewing radiographs taken.

**Conclusions:** Bitewing radiographs were not frequently taken at examination or recall appointments for children in

the four centres surveyed, which demonstrates their under-utilisation as adjuncts to dental caries diagnosis and management. More research is required to identify the barriers to behavioural change and best methods to improve current practice.

### 454 | A prospective audit on paediatric diet advice delivered by undergraduate dental students

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**Background:** Diet advice is an integral part of caries prevention, especially in high caries-risk children. This is often not delivered consistently by undergraduates. The aim was to evaluate diet advice provided by undergraduate dental students to paediatric patients.

**Methods:** Prospective audit of high caries-risk paediatric patients receiving treatment from undergraduates at the Sir Ludwig Guttmann Dental Centre between January and February 2020. Patients aged 3–16 years and deemed high caries risk according to the Scottish Dental Clinical Effectiveness Programme (SDCEP) guidelines were included. Using standards based on the SDCEP 'Dietary Advice' guidelines, the outcomes assessed were 24-hour diet history taken, 4-day diet sheet given, diet sheets returned, diet advice given, diet reviewed within 3 months, and compliance with advice recorded, expressed as positive or negative. Primary analysis was performed comprising all students as a collective and secondary analysis compared across student cohorts.

**Results:** 52 high caries-risk patients were included. 23.1% had 24-hour diet history taken, 61.5% were given a 4-day diet sheet, with 59.1% diet sheets returned. 40.4% were given diet advice and 5.8% had diet reviewed within 3 months. None recorded compliance with advice (0%). A general trend of improvement from third to fifth year was seen in all outcomes except giving 4-day diet sheets.

**Conclusions:** Further improvement in the delivery of diet analysis, advice, and monitoring by students is required to adhere to SDCEP standards. This will ensure all high caries-risk patients receive specific diet advice and improve the quality of undergraduate paediatric preventative care.

## 1274 | Perspective of dental students and surgeons regarding the management of deep carious lesions in deciduous teeth

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**Background:** The partial removal of decayed tissue, aiming to favor pulp vitality, has been the elective treatment in the management of deep caries lesions. The present study evaluated the knowledge of dental students and dentists regarding the management of deep caries lesions in deciduous teeth and their critical perspective on the concept of minimally invasive dentistry.

**Methods:** This is a quantitative descriptive study. The sample consisted of 105 scholars and 20 dental surgeons. In order to obtain the data, a semi-structured questionnaire with 10 objective questions was applied, which were later tabulated for statistical analysis and presented by means of graphs and tables.

**Results:** Considering the questionnaire answers, it was possible to verify that 49% (n = 49) of the scholars and 40% (n = 12) of the dental surgeons know the scientific evidence that justifies the partial removal of the carious tissue. As for the removal of carious dentin, 20% (n = 11) of the scholars remove all the softened darkened dentin, 15% (n = 3) of the professionals perform this conduct. 37% (n = 39) of the scholars say they remove the decayed tissue until it comes out in chips or flakes. 14% (n = 15) of the scholars and 5% (n = 1) of the professionals said they do not perform conservative management.

**Conclusion:** Although both scholars and dentists report adopting a conservative conduct during the removal of decayed tissue, they do not perform practices that justify this statement.

## 1191 | Caries prevalence and its association with sickle cell disease in children and adolescents

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**Background:** Sickle cell disease is a common hereditary disease worldwide. It can impair the dental structures,

facilitating the onset of dental caries. The objective of this study was to investigate the prevalence of caries and its association with sickle cell disease in children and adolescents.

**Methods:** This was a comparative cross-sectional study. The sample comprised 160 children and adolescents of both sexes, aged 6 to 18 years, 80 of them with the sickle cell disease (case group), and 80 without it (control group), matched for sex and age. Data was collected with the DMFT/deft indexes and interviews with the parents/guardians. The data were analyzed with the chi-squared, Mann-Whitney, and Kruskal-Wallis tests, aided by the SPSS program, version 23, using the 5% significance level.

**Results:** The prevalence of caries in the case group was 55.2%. In comparison with in the healthy group, the DMFT was greater in the sickle cell disease group (2.71 vs. 0.81) and in the group aged between 12 and 18-years-old (4.71 vs. 1.51). In the disease group, the mean “decayed teeth” condition was higher, and they were more likely to have dental caries (OR: 2.52), and a high caries experience (OR: 4.95). The deft index had a significant association in the “filled teeth” condition.

**Conclusions:** The prevalence and experience of caries were higher in the sickle cell disease group.

## 1126 | OXIS contacts as a risk factor for proximal caries: A retrospective cohort study

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**Background:** The aim of the present study was to evaluate the individual susceptibility of OXIS contact areas to proximal caries using electronic databases of children.

**Methods:** A retrospective cohort study was planned using clinical photographs of children which were available from Jan 1st 2014 till 31st Aug 2019 with the presence of at least one caries free contact area between primary molars. Further, only those contacts with a minimum of one year follow up period were selected. A single calibrated examiner scored 1102 selected contacts using OXIS criteria from occlusal view and subsequently evaluated the same contacts for the presence of proximal caries. The outcome was expressed as odd's ratio with 95 percent Confidence Intervals (CIs).

**Results:** Out of the 1102 contacts, number of contacts found to be carious or restored due to proximal caries were 259 (23.5%). The multivariate logistic regression analysis showed only the type of contact played a significant role in the caries prevalence ( $P = 0.05$ ). The odd's ratio of the OXIS contacts for development of proximal caries were S contact, 147.39 (19.719–1101.654)  $P$  value-0.000; I contact, 24.544 (3.386–177.897)  $P$  value-0.002; X contact, (1.109 (0.99–12.452)  $P$  value-0.933 and O contact, 1.00.

**Conclusions:** Among them, S type was the most susceptible to develop proximal caries owing to its complex morphology. The broad contact areas namely I and S types are at a greater risk for proximal caries than the O and X contacts.

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### 361 | Parental acceptance of silver diamine fluoride staining in Latvia

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**Background:** Recent research has shown the effectiveness of Silver Diamine Fluoride (SDF) in arresting carious lesions in preschool Children. The silver present in SDF stains the carious lesion. Our aim is to assess the Latvian parents' acceptance of primary teeth staining due to silver diamine fluoride (SDF) treatment and to identify factors that explain this acceptance.

**Methods:** Cross-sectional study; parents of preschool children were invited to fill a translated and validated online questionnaire (Crystal et al. 2017) during August-December 2020. Minimum sample size for national representativeness is 369, and this allows the detection of 7 multilevel factors. Data were analysed by descriptive statistics and logistic regression-model.

**Results:** We received 870 completed forms (97% mothers, 91% urban, 29% Master-PhD, 54% attended in public service).

Acceptance of SDF staining for anterior/posterior teeth is 49%/84%. Factors significantly associated with higher acceptance were: for anterior teeth, parents with Master-PhD degree (OR = 1.51, 95%CI[1.03,2.27]) or with 4 children (OR = 2.48,95%CI[1.09,6.44]), and for posterior teeth, parents of children who had been treated under general anaesthesia (OR = 8.60,95%CI[1.58,161]. For both anterior-posterior teeth, parents choosing private dentistry (anterior OR = 1.46, 95%CI [1.03, 2.07]; posterior 1.80, 95%CI [1.03, 3.22]. Less acceptance was evident in parents whose children were cooperative during restorative treatment (anterior OR = 0.53, 95%CI [0.30, 0.94]; posterior (OR = 0.28, 95%CI [0.14, 0.62]).

**Conclusions:** Latvian parents report moderate-to-high acceptance of SDF staining and the reasons associated with this acceptance vary according to tooth type.

**Funding:** Post-doctoral-Research-Aid-Programme (1.1.1.2./VIAA/3/19/540, Contract No. 9.-14.5/27).

### 1868 | Preservation of early cavitated lesion in primary tooth using resin infiltration technique: A review

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**Background:** Recent trends focus on conservative approaches for the preservation of primary teeth using a newer modality, Resin infiltration technique has been used for conservative management of cavitated smooth surface lesions in primary teeth, with the potential for improved behavioral management.

**Literature Review:** Resin infiltration technique is a micro invasive technology that reinforces, fills and stabilizes demineralized enamel without drilling or sacrificing healthy tooth structure. The minimal invasive technique can be used to treat proximal and smooth surface lesions. The principle of resin infiltration is that it acts upon the porous enamel structure with low viscosity resin, thereby sealing the early carious lesion by blocking the cariogenic pathway. In the conventional drilling method, there are more chances of dislodgement during the placement of proximal restorations in primary molars, where isolation is required. However, when treated with the resin infiltration technique, there is little chance of dislodgement.

**Conclusion:** Minimal invasive dentistry, such as the resin infiltration technique, seems to provide a good solution for dealing with early enamel lesions. Resin infiltration technique can be used for the management of early proximal lesions of primary molars using material such as ICON, a commercially available resin infiltration kit.

## 1364 | A literature review of the utilisation of school-based prevention and screening methods

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**Background:** Across the globe, children from lower socio-economic backgrounds are faced with barriers in accessing general dental services. These may present as financial, social, geographical, structural, or cultural in nature. The presence of dental screening and prevention services in schools, may help to improve oral health disparities amongst children, as schools should theoretically be accessible to all children. This literature review will highlight in what ways school-based dental programmes have affected their participants over the past ten years.

**Literature Review:** In some US states, dental hygienists can provide preventative services in schools unsupervised, including fluoride varnish, sealants and dental referrals. In Kerala, primary school teachers were trained in oral health education and an improvement in dental caries and oral health status of the children in the study group was found. A school-based oral health programme in Kuwait which involved children and their mothers found a positive effect on the child's dental health, but no significant impact to the mother's knowledge. An oral health education programme ran in Nigeria found that schools wanted to incorporate the programme into their curriculum.

**Conclusion:** Oral health programmes in schools range from the delivery of oral health instruction in assemblies, to screening and preventative interventions. Assemblies have shown to be implemented at low cost. Although the clinical effectiveness of this is unclear, there are still implications on developing countries and deprived areas, where introducing these low-cost programmes may have maximum impact by reaching all children, including the most disadvantaged.

## 1376 | Effects of dental biofilm and CO<sub>2</sub> laser irradiation on the inhibition of bovine enamel demineralization: An in vitro study

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**Background:** To evaluate if biofilm covering the enamel surface reduces the effect of CO<sub>2</sub> laser ( $\lambda = 10.6 \mu\text{m}$ ) irradiation in inhibiting lesion progression of the bovine dental enamel surface.

**Methods:** For in situ biofilm formation, 10 volunteers wore palatal appliances containing 08 specimens of bovine enamel each, during three-days to provide biofilm accumulation. On the 3rd day, the specimens were removed from the palatal appliances and irradiated with CO<sub>2</sub> laser ( $\lambda 10.6 \mu\text{m}$ ) and fluency of 11.3 J/cm<sup>2</sup> according to the following groups (n = 20): 1) pH cycling (Negative Control), 2) Biofilm + pH cycling, 3) Removed biofilm + CO<sub>2</sub> laser irradiation + pH cycling, 4) Biofilm + CO<sub>2</sub> laser irradiation + pH cycling. After pH cycling, 15 enamel specimens of each group were subjected to microhardness analysis and 5 specimens were evaluated using scanning electron microscopy (SEM) analysis. Data of the enamel mineral loss was analyzed by analysis of variance followed by the Tukey test.

**Results:** Microhardness results showed a statistically significant difference between control and laser groups ( $P = 0.05$ ). However, there was no difference between the laser-irradiated groups ( $P = 0.05$ ). The SEM observations showed evidence of melting and fusion in non-removed biofilm groups; however, in the removed biofilm group, it was possible to observe less surface alteration.

**Conclusions:** Biofilm covering the enamel surface did not reduce the effect of CO<sub>2</sub> laser irradiation in inhibiting lesion progression of the bovine dental enamel surface. Besides, it is suggested that dental biofilm exhibited a protective effect of the irradiated enamel surface.

## 1694 | Ultraconservative treatment on primary central incisors with 36 months of follow-up: A case report

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**Introduction:** The minimum invasive concept has been increasingly gaining notoriety in dentistry. This case report aimed to evaluate the clinical and radiographic results of dentine caries lesions treated with an ultraconservative protocol in a pediatric patient.

**Case report:** A 4-year-old male patient was referred to the School of Dentistry of University of São Paulo presenting dentin active caries lesions in teeth 51 and 61. The patient presented a good oral hygiene, absence of symptoms or aesthetic complaint. An ultraconservative protocol has been proposed. Firstly, the mesial surfaces were regularized using abrasive strips to avoid retentive areas and biofilm accumulation, thus facilitating access for toothbrushing with fluoride toothpaste (1,100 ppm). Secondly, a four-time fluoride varnish (22,600 ppm) application was also performed with an interval of one week between them. The patient's mother received instructions of oral hygiene and diet care. The patient was followed-up clinically and radiographically for 36 months.

**Discussion:** The fluoride therapy has an important role in the preventive approach of caries lesions. The association of its effects with a satisfactory oral hygiene allows an ultraconservative treatment which can inactivate caries progression. In this clinical case, the fluoride varnish sessions were associated with a surface regularization which concedes a better access to oral hygiene. The ultraconservative concept can be a valid alternative due to its simplicity, low cost, and good acceptance by young children and their parents.

**Conclusion:** Dental caries surfaces regularization associated with fluoride therapy showed a long-term success in controlling dental caries progression.

## 1186 | Relationship between dental caries and adherence to Mediterranean diet in a population of children aged 3 to 9

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**Background:** Dental caries is a multifactorial infectious disease which represents an important health problem

worldwide. The aim of the present study was to establish the relationship between dental caries and adherence to the Mediterranean diet through the KIDMED questionnaire in a population of 3–9 year old children.

**Methods:** A cross-sectional study was conducted in a population of 268 Valencian children aged 3 to 9. First of all, questionnaire KIDMED was filled out by every patient/caregiver to determine the adherence of every patient to the Mediterranean diet. Afterwards, a clinical exploration of the temporary teeth was carried out using dmf and dmfs indexes. Descriptive and inferential statistical analysis were performed using Kruskal-Wallis test.

**Results:** 63.4% of the studied population presented caries. The dmf and dmfs indexes obtained were 0.234 and 0.098 respectively. The mean value of the KIDMED index was 7,116 showing values from -1 to 11. Patients were classified as follows: High adherence to Mediterranean diet (47.4%), medium adherence (47%) and low adherence (5.6%). A statistically significant relationship was also found between dmf and dmfs indexes and a low adherence to the Mediterranean diet ( $P = 0.000$ ).

**Conclusions:** A direct association was observed between dental caries in children and a low adherence to the Mediterranean diet.

## 1403 | Early childhood caries and its relationship with the labial frenulum in children from 3 to 5 years of the city of Zacatecas

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**Background:** Early Childhood Caries continues to be a priority Oral Health problem, proof of this is the last epidemiological survey in Brazil in 2010, whose prevalence was 53.4% in children under 5 years of age. During the dental examination in preschool children, it was observed that the Maxillary Frenulum, which can influence the appearance of Early Childhood Caries, in the anterosuperior sector, in addition to the diastema caused by the low insertion of the frenulum, causes periodontal problems and malocclusions in permanent dentition.

**Methods:** Type of study: bivariate, relational analytical study, the sample size was 193 children. The direct visual method and buccal retractors were used in order to lift the upper lip, the morphology of the labial frenulum was classified according to the Sewerin typology and its fixation according to Placek et al. The ICDAS criteria were used in order to categorize Early Childhood Caries. The data were processed in the SPSS program. V.24. and Excel. 2016.

Pearson's correlation analysis was carried out, in order to correlate variables such as: Presence of Early Childhood Caries in the anterosuperior segment and maxillary frenulum, (type of insertion, shape and size of the Frenulum).

**Results:** The prevalence of White Spots. (ICDAS). It was 8.8% in the Anterosuperior sector (teeth 51, 52, 53, 61, 62, 63). The most prevalent morphological type of maxillary labial frenulum was the simple type that increased significantly with age followed by the persistent tectolabial frenulum that decreased significantly with age (P 0.001). The most common location of the frenulum junction was the alveolar mucosa followed by the gingiva and the papillary penetrating incisal papilla. The level of attachment tends to move apically and, therefore, the prevalence of attachment in the alveolar mucosa increased significantly with age. (5 years). There was no significant correlation at the 0.05 level (Bilateral), between Early Childhood Caries and persistent tectolabial frenulum.

**Conclusions:** The type of frenulum insertion contributes to early childhood caries or demineralizations (white spot), due to lack of proper tooth brushing and limited self-cleaning. It is necessary to expand the sample and perform another type of statistical analysis such as Student's T, or Chi square.

### 1885 | Caries risk prediction using salivary SIgA concentration in stunting children

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**Background:** Stunting in children is an effect of nutritional deficiencies during the first thousand days of life, which lead to irreversible disruption in a child's physical development, causing a decrease in cognitive and motoric abilities, along with the decrease in activity performance. The prevalence of stunting children in Indonesia in 2019 was 27.67%, placing it as the third-highest in the Southeast Asia region. Stunting children have atrophied salivary glands that decrease saliva production causing salivary functional degradation as a buffer, cleansing, antibacterial agent, and a decrease in sIgA expected to have an impact in greater caries risk. This literature review aims to analyze the possibilities of salivary sIgA concentration in predicting caries risk in stunting children.

**Literature Review:** In stunting, Protein Energy Malnutrition occurs, that is an imbalance between protein intake and energy alongside a decrease in the body's ability to function optimally. It affects the child in physical and cognitive growth disruption as well as vulnerability towards infections. Effects of stunting include impairment in helper T cells population decrease in mucosal plasma cells that produce immunoglobulin A and mucosal

epithelial atopy leading to decreasing sIgA concentration forming the defensive immunity of oral mucosa. These conditions lead to an increase in *S. mutans* ability to bind with a salivary pellicle, producing glucosyltransferase, facilitating Glucan Binding Proteins for bacterial colonization, increasing the ability of *S. mutans* to withstand critical pH causing pathogenic biofilms which contribute in demineralization which in turn leads to caries.

**Conclusion:** sIgA in saliva has potency in predicting caries risk in stunting children.

### 1247 | Antibacterial activity of *Plectranthus amboinicus* against oral pathogens: An in-silico approach

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**Background:** *Plectranthus amboinicus* is a medicinal plant, also known as Indian borage has antifungal, antiviral, anti-tumorigenic, antibacterial, anti-inflammatory, and anti-mutagenic properties. It is found that  $\beta$ -caryophyllene an active ingredient present in *Plectranthus amboinicus* was essential for these properties. In the present study an in-Silico study was conducted to identify the specific protein targets against *Streptococcus mutans* which is unexplored.

**Methods:** Molecular protein target of *Streptococcus mutans* - glucansucrase (PDB No: 3AIE) were retrieved from RCSB protein databank. Molecular docking study was carried out through Autodock 4.2 tool and visualized through Maestro viewer tool. Molecular dynamic study was carried out for the potent target complex by Desmond package of Schrodinger suite.

**Results:** Among the test molecules  $\beta$ -caryophyllene an active ingredient of *Plectranthus amboinicus* showed potent binding affinity towards targeted protein. It showed binding score of -7.7 kcal/mol protein targets respectively.  $\beta$ -caryophyllene binds covalently with TYR916, HIS587, ALA478, LEU433, TYR610, LEU382 and PHE907 amino acid residues of glucansucrase protein. Molecular dynamic result showed that the  $\beta$ -caryophyllene with 4 glucansucrase complex was stable during the 50ns and the Root Mean Square Deviation & Root Mean Square Fluctuation was found to be stable and showed a stable interaction.

**Conclusions:** Among the test phytochemical molecule,  $\beta$ -caryophyllene present in *Plectranthus amboinicus* was found

to be potent. The result revealed the drug moiety is a promising candidate in the treatment of bacterial oral infection. Further the drug can be formulated in a suitable formulation for the treatment of dental caries.

## 882 | Influencing caries through television advertising among indian children

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**Background:** Marketing directed towards children should be an issue of concern of the present day society. This practice has gained momentum with increasing globalization, children are recognized as easy targets in this process and their choice of can easily be influenced by advertisements. Increasing middle income strata, extent of technology and thorough market research strategies are all boosting the threat in developing economies like India. Thus, there arises a major concern for identifying current food marketing strategies.

**Methods:** The desired channels were recorded for selected weekend hours during which a large number of where maximum children intend to view the desired programmes. The advertisement was recorded for the time duration and product of sale. Two investigators cross verified the durations made on the recordings in order to avoid bias. The time durations were calculated and mean and SD were intended for easy comparison.

**Results:** The advertisement from the selected four channels were categorised as follows: first broadly candy, sweets and lollypop with maximum time of advertising, second were bakery products such as cookies and cakes followed by chips wafers and lastly morning packaged cereals were found to be advertised on television among food category.

**Conclusions:** There is an urgent need for the government to draft and implement laws that deal with advertisement targeting young children products. Strict regulations need to be laid towards potential cariogenic food items. Morally companies must ban/limit on advertising products with potential cariogenic influence. Warnings on packaging pertaining its cariogenic potential effects must be made mandatory to sensitise the parents towards its ill effects.

## 1809 | Comparative evaluation of the effect of immunoglobulin y and probiotic in reduction of S. mutans counts in caries-free children: A randomised controlled trial

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**Background:** Reducing the number of S. mutans is important for prevention of dental caries. Investigations are currently underway to develop alternative methods of caries prevention utilizing passive immunization. Immunoglobulin Y (IgY), an antibody found in chicken eggs, has been reported to inhibit adhesion of S. mutans to tooth surfaces. Recently probiotics have also gained popularity in caries prevention based on reports that they kill/inhibit growth of pathogens through production of bacteriocins, which are antagonistic towards pathogenic bacteria.

**Methods:** 60 healthy caries-free 5–12 year old children were randomly divided into 2 groups; Group 1: Immunoglobulin Y and Group 2: probiotics. Children in each group were given Immunoglobulin Y or probiotics tablets respectively for 15 days. S. mutans counts were evaluated at baseline, 15 days and 3 months using mutans sanguis agar. Plates were incubated for 48h in an atmosphere containing 5% CO<sub>2</sub> and 95% N<sub>2</sub> at 37°C. Colony forming units on plates were counted using a colony counter by a blinded assessor.

**Results:** Paired 't' test was applied to evaluate changes in S. mutans counts. Significant reductions were seen after 15 days using both Immunoglobulin Y and probiotics (p 0.05). However after 3 months, S. mutans counts were significantly reduced compared to baseline in the Immunoglobulin Y group (p 0.05), while the probiotic group did not show a significant decrease (p 0.05).

**Conclusions:** Both Immunoglobulin Y and probiotics can be used as effective means of caries prevention; however, in this study, immunoglobulin Y resulted in a relatively prolonged decrease in S. mutans counts.

## 1737 | What can impact the development of carious lesions in teeth with molar-incisor hypo mineralization (MIH)?

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**Background:** This study assessed whether the age, gender, the visible plaque index (IPV), gingival bleeding index (ISG), previous caries experience, MIH severity and number

of teeth affected by MIH could impact on the caries lesion development in teeth with MIH.

**Methods:** 476 schoolchildren at municipal schools (Bauru, São Paulo, Brazil), aged 6–10 years, were evaluated by two researchers trained and calibrated for MIH and caries diagnosis, using the Severity Scoring System (MIH-SSS) and the International Caries Detection and Assessment System (ICDAS), respectively. The IPV and ISG index were also evaluated. The children were examined with a mirror and under artificial light in a school environment. The data were evaluated using the Backward model for multiple linear regression analysis, which was performed to assess the impact of the independent variables (number of teeth affected by MIH, severity of MIH, past caries experience, IPV, ISG, age and gender) on dependent variable (presence of caries). The level of significance adopted was 5%.

**Results:** The results showed that multicollinearity was detected, and the independent variables (number of teeth affected by MIH and IPV) were excluded from the analysis. The coefficient of determination was (0.24) and the age, severity of MIH, past caries experience, and ISG influenced on the caries lesions developmental in teeth affected by MIH ( $P = 0.005$ )

**Conclusions:** In conclusion, the susceptibility to caries development of teeth with MIH is influenced not only by the severity of the condition, but also by age, past caries experience, and ISG.

**Funding:** The research project was supported by the São Paulo State Research Foundation (FAPESP-2019/02735-4).

## 158 | The use of diamine silver fluoride in early childhood caries: A review of literature

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**Background:** Currently Minimally Invasive Dentistry has been gaining more space in pediatric dentistry, as it follows the principle of recognising that restorative materials have a lower biological value than the original tissues, making their preservation essential. Diamine silver fluoride is a material used for the treatment of caries in children, being essential for the treatment of early childhood caries.

**Literature Review:** It is a colorless and odorless solution of silver, fluoride and ammonium ions. Which is composed of a high concentration of fluoride ions, which promote tooth desensitization by blocking dentinal tubules and paralyzing carious lesions, bacterial death, remineralization of

demineralized tooth and inhibition of dentin collagen degradation. Being effective against caries and has the aesthetic disadvantage left by the treatment. In the general interest, the treatment is effective in neutralizing and paralyzing caries disease.

**Conclusion:** It is concluded that silver diamine fluoride is a material with proven clinical success in the prevention and paralysis of dental caries; it has the advantages of low cost and easy application; treatment with diamine silver fluoride has controversies regarding the form of application and the frequency; the disadvantage is the blackened aspect of the teeth, but the anti-aesthetic aspect may have less significance since the child will have reduced sensitivity and controlled pathology.

## 1347 | Locus of control and biological factors of severe dental caries lesions of pre-school children

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**Background:** The aim of this study was to evaluate factors associated with the occurrence of severe dental caries lesions (with pulp exposure) in pre-school children.

**Methods:** The sample consisted of 115 pairs of parents and their 4 to 6 year-old children, attending 3 pre-schools in Belo Horizonte, Brazil. Parents self-completed questionnaires on their children's dietary and oral hygiene habits. The Locus of Control instrument was implemented to measure their beliefs whether the oral health of their children is or is not determined by their own behavior. Children were examined for diagnosis of dental caries with pulp exposure at their schools with natural light by two previously calibrated examiners ( $\kappa = 0.95$ ). Data analysis was carried out using the SPSS software and included chi-square test and multiple logistic regression (Stepwise Forward Procedure) ( $p \leq 0.05$ ).

**Results:** Caries with pulp exposure were observed in 16.5% of the children. It was taken for granted as independent associated factors for severe dental caries lesions the tooth loss due to dental caries (OR = 12.14; CI95%: 1.55–95.22), use of soft drinks in feeding bottle (OR = 12.14; CI95%: 1.55–95.22) and the absence of breastfeeding (OR = 8.48; CI95%: 1.53–47.11). No significant association between locus of

control and oral hygiene with the presence of severe dental caries was found ( $P = 0.05$ ).

**Conclusion:** Children that already had tooth extraction due to dental caries, drank soft drinks in their feeding bottle or that were not breastfed, presented a higher chance of the occurrence of severe dental caries lesions.

## 685 | Silver diamine fluoride for deep caries management in primary molars

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**Background:** In recent years, remineralization of caries lesions has gained acceptance in the practice of minimally invasive dentistry and caries arrest treatment is being promoted as part of the basic package of oral care. In this regard, topical application of silver diamine fluoride (SDF) solution has been shown to be effective in arresting active caries in primary teeth. The purpose of this study is to evaluate clinical and radiologic success rate of single application of SDF followed by placement of crown for deep caries management of primary teeth.

**Methods:** Thirty-two children aged 4–8 years, presenting deep carious lesions without pulp exposure in primary molars, were randomly assigned to receive either soft caries removal and restoration with stainless steel crown (SSC) (Treatment group A,  $n = 17$ ) or SDF application without caries removal and restoration with SSC using Hall's technique (Treatment group B,  $n = 25$ ). Clinical and radiological follow up was done at 3, 6 and 12-months intervals. Data was statistically analyzed using chi square test.

**Results:** Both the groups showed high clinical and radiologic success without any significant difference at the end of 12 months. Minor failures were seen in 11.8% of teeth in Group A and 4.2% in Group B. Major failures requiring further treatment like pulpectomy were seen in 4.2% of Group B and none in Group A.

**Conclusions:** SDF application with SSC without any removal of caries can be a viable option for management of deep carious lesions in primary teeth.

## 192 | Antibacterial efficacy of Camellia sinensis leaf mouth rinse in children with early childhood caries

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**Background:** This study was conducted to compare the antimicrobial efficacy of commercially available Camellia Sinensis Leaf green tea" (0.5%) mouth rinse to that of chlorhexidine (CHX) (0.125%) against Streptococcus mutans and Lactobacilli spp.

**Methods:** Forty-two children with early childhood caries were recruited in this study, and randomly divided, using lottery method, into three groups; group A: children using green tea mouthwash; group B: children using CHX (0.12%) mouthwash; group C: children using colored flavored unsweetened tap water. They were instructed to rinse the mouth for 1 min using 5 ml of the respective mouth rinses 30 min after tooth brushing, for 2 weeks. A volume of 2 ml saliva samples were collected prior to the commencement of mouth rinsing, and after 2 weeks rinsing. Data was collected and statistically analyzed.

**Results:** Both CHX and green tea mouth rinses showed a statistically significant fall in the colony counts of S. mutans and Lactobacilli spp. ( $P = 0.001$  and  $0.001$ ), while in the third group was not statistically significant ( $P = 0.003$  and  $0.183$ ) for S. mutans and Lactobacilli spp., respectively. When the antimicrobial efficacy of CHX and green tea was evaluated against both S. mutans and Lactobacillus spp., no statistically significant difference was found ( $P = 0.462$  and  $0.824$ , respectively).

**Conclusion:** From the results of our study, it can be concluded that a commercially available green tea mouth rinse could be effective as CHX mouth rinse. However, further studies are required to evaluate plaque rate formation, cost effectiveness, and acceptability.

## 1211 | Comparative evaluation of microleakage of ACP containing pit and fissure sealant and moisture tolerant pit and fissure sealant: An in vitro study

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**Background:** Pits and fissure sealants are widely used to prevent caries in children. Microleakage is one of the most important factors resulting in sealant compromise. Factors

pertaining to microleakage like, pretreatment of occlusal surfaces, moisture control, bonding systems, and flow ability of the sealant, will determine the longevity of treatment. Aegis is the new SMART material and Embrace is a new generation hydrophilic sealant. This study was undertaken to evaluate and compare the microleakage of ACP (Aegis®) containing pit and fissure sealant and moisture tolerant pit and fissure sealant (Embrace™ Wetbond™).

**Methods:** 26 permanent non carious premolars extracted for orthodontic treatment were used. The sealants used for analysis of microleakage were Aegis and Embrace Wetbond pit and fissure sealants. The premolars were divided in 2 groups of 13 each. After sealant application, the teeth were subjected to thermocycling for 24 hours, after which they were inserted in methylene blue dye. The teeth were sectioned buccolingually and dye penetration was studied under stereomicroscope.

**Results:** Both the groups were studied and statistically evaluated using Mann-Whitney U test. Aegis showed higher microleakage in (46.2%) than Embrace (38%) though not statistically significant.  $P = 0.089$ .

**Conclusions:** Both the materials showed microleakage, but more clinical trials are required in order to have concrete evidence of superiority of one material over the other.

## 1856 | Oil pulling for oral diseases: A randomized controlled study

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**Background:** Oil pulling has long been considered as a natural remedy for preventing oral diseases. Due to side effects of modern medicines and oral hygiene products, many people are increasingly attracted towards complementary and traditional practices. Sesame oil and coconut oil have nutritional qualities and are reported to have many desirable health effects. The aim of this study was to conduct a comparative evaluation of the antiplaque efficacy of sesame oil, coconut oil, chlorhexidine mouthwash and placebo amongst 15–18 year-old school children.

**Methods:** A randomized controlled study was carried out among 160 school children. 40 subjects each were randomly selected and assigned to Group 1 (sesame oil), Group 2 (coconut oil), Group 3 (chlorhexidine mouthwash) and Group 4 (placebo). Subjects were given their assigned constituents and advised to rinse for 5 minutes, once daily in the morning for a period of 15 days. Plaque index (PI) and modified gingival index (MGI) were assessed at baseline and on day 15 using Student Paired T-test at  $P = 0.05$  (SPSS software version 15).

**Results:** The results revealed that there were statistically significant reductions between baseline and post therapy

values of PI and MGI ( $P = 0.05$ ) in Group 1 (0.45; 0.16 0.11; 0.83 0.35; 0.26 0.20), Group 2 (0.48 ± 0.15; 0.18 ± 0.12; 0.86 ± 0.32; 0.25 ± 0.19) and Group 3 (0.50 ± 0.16; 0.15 ± 0.10; 0.97 ± 0.39; 0.27 ± 0.19) respectively. No significant reduction was seen in Group 4 ( $P = 0.05$ ).

**Conclusion:** Oil pulling using coconut oil and sesame oil lowered plaque index and modified gingival index scores in 15–18 year-old school children.

## 1930 | Natural products in prevention of early childhood caries

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**Background:** Early childhood caries (ECC) is the most prevalent infectious diseases affecting children worldwide. It is a biofilm mediated disease and dysbiosis of oral microflora is said to be responsible for caries development. Reversing the microbiome dysbiosis is crucial for long-term disease control. Various chemotherapeutic agents have been used for this purpose. But concerns like broad-spectrum of antibacterial action, antibiotic resistance, allergies and high cost are making researchers look at alternatives for prevention of ECC.

**Literature review:** Natural products with antibacterial effect against ECC associated pathogens like Streptococcus mutans, Candida albicans and lactobacilli are an attractive alternative for long-term caries prevention. Natural products like Acacia catechu, Acacia arabica, Azadirachta indica, Bauhinia forficata, Cacao bean, Camellia sinensis, Cinnamon zeylanicum, Coffea canephora, Cymbopogon, Vaccinium macrocarpon, Caesalpinia ferrea martius, Citrus sinensis, Crustacean shells, Cymbopogon citratus, Curcuma xanthorrhiza, Chitosans, Eurycoma longifolia, Galla chinensis, Zingiber officinale, Guajaverin, Javanese turmeric, Licorice root, Melia azedarach, Myristica fragrans, Ocimum sanctum, Peppermint, Pongamia pinnata, Propolis, Morus alba, Sidium cattleianum, Sanguinaria canadensis, Sterculia lychnophora, Stevia rebaudiana, Syzygium aromaticum, Quercus infectoria, Tamarix aphylla, Tea tree, Thuja orientalis, Vitis vinifera contain various bioactive phytochemicals which have bactericidal action against caries associated pathogens. Some of them also beneficially regulate the de/remineralization balance of dental hard tissues.

**Conclusions:** Natural products are promising alternatives for prevention of ECC. However, there is a need for well-designed randomized controlled trials to investigate the ecological effects of natural products. Exploring the vast therapeutic potential of natural products will benefit in preventing ECC, especially in the developing countries.

## 655 | Determination of optimal concentration of deglycyrrhizinated licorice root extract for preventing dental caries: An in vitro study

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**Background:** Dental caries is a multi-factorial and most common childhood disease. *Streptococcus mutans* (SM) and *Lactobacilli* (LB) are the main bacteria responsible for dental caries. Many antimicrobials have been used to prevent dental caries. Considering their disadvantages herbal remedies seem to be better alternatives. Licorice root extract has strong bactericidal effects against cavity-causing bacteria. It has anti-adherence, antimicrobial, and anti-inflammatory properties. This study was done to evaluate optimal concentration of deglycyrrhizinated licorice root extract (DG-LRE) against *Streptococcus mutans* (SM) and *Lactobacillus* (LB) for prevention of dental caries.

**Methods:** Clinical strains of SM and LB were obtained from IMTECH, Chandigarh. Both the strains were cultured on a Todd Hewitt broth. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) values were calculated using a microdilution assay according to the Clinical and Laboratory Standards Institute. Data was entered on an excel spread sheet and results were inferred.

**Results:** MIC of DG-LRE against MS and LB was found to be 20 mg/ml. MBC values for both strains were 1 to 4 times higher the MIC values. For SM, zone of inhibition seen at 19mm for 20mg/ml DG-LRE. For LB, zone of inhibition seen at 22mm for 20mg/ml DG-LRE.

**Conclusions:** DG-LRE showed antibacterial properties against SM and LB. Thus, it can be used as a potential alternative in various forms for the prevention of dental caries.

## 878 | Comparative evaluation of retention, longevity of two non-fluoridated pit and fissure sealants placed with and without use of bonding agents in young permanent molars affected by dental fluorosis: An in vivo study

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**Background:** Dental caries is an infectious disease of 12.5% children whereas 90% seen in occlusal pit and fissures. Thus, study was designed to evaluate the retention and longevity of two non-fluoridated pit and fissure sealants HELIOSEAL and FISSURIT placed with and without use of bonding agents in young permanent molar affected by dental fluorosis at various intervals.

**Methods:** After fulfillment of inclusion criteria, 45 Children were selected from the age group of 7–13 years of either gender with written informed consent. With split-mouth design, routine clinical fissure sealant application of increase in etching time to 35–40 sec for all the group. Helioseal sealant (Group IA & IB) was placed in the occlusal pits and fissures on the right side and Fissurit sealant (Group IIA & IIB) on the left side. Clinically retention rates were evaluated Mascarenhas et al (2008) criteria at recall intervals of 1 week and 1, 3, 6 and 12 months, tabulated and were subjected to statistical analysis with Mann–Whitney U test.

**Results:** HELIOSEAL (Group-IB) showed the higher retention rate when compared to HELIOSEAL (Group-IA), as well FISSURIT (Group-IIB) when compared to FISSURIT (Group-IIA) revealed better retentiveness after 6 and 12 months was not statistically significant. But on comparing the retention rates of with and without bonding agent application of HELIOSEAL and FISSURIT, FISSURIT revealed better retentiveness after 3, 6 and 12 months which was not statistically significant.

**Conclusions:** Though not contraindicated, considering the extra time and cost needed and the inconclusive importance in retention, routine use of bonding agent as part of the sealant application technique is not recommended on fluorosed molars needs further studies.

## 1887 | Microbiological composition of dental biofilm in different stages of early childhood caries: A longitudinal study

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**Background:** This longitudinal study aimed at investigating if the microbiological composition of dental biofilm formed over dental surfaces in different stages of early childhood caries (ECC) – early caries lesions (ECL) and cavitated caries lesions (CCL) as well as the presence of visible biofilm are relevant factors for initiation and for progression of ECC.

**Methods:** This was an observational longitudinal study in which 51 children aged 36–71 months were selected from five preschools in Piracicaba-SP (Brazil). Visible biofilm was recorded and caries assessment was performed according to Séllos and Soviero criteria. Biofilm samples were collected and the microbiological composition was determined by assessment of quantities of *Actinomyces naeslundii*, *Bifidobacterium* spp., *Streptococcus mutans*, *Veillonella* spp. and commensal group (*Streptococcus mitis* group and *Streptococcus gordonii*) using quantitative PCR analysis.

**Results:** The mean number of decayed, missing and filled surfaces (dmfs) and decayed, missing and filled teeth (dmft) at baseline were  $4.05 \pm 7.33$  and  $2.68 \pm 4.06$  respectively, and at follow-up were  $5.45 \pm 10.82$  and  $2.96 \pm 4.13$  respectively. High levels of *S. mutans* over ECL showed significant association with the early stage of caries (OR = 15.3) ( $P = 0.05$ ) as well as with cavitated caries lesion (OR = 45.5) ( $P = 0.05$ ). Furthermore, presence of visible biofilm (OR = 13.1) was significantly associated with CCL ( $P = 0.05$ ).

**Conclusions:** High levels of *S. mutans* over ECL as well as CCL are relevant factors for initiation and for progression of ECC. The presence of visible biofilm is an important clinical parameter for the ECC progression.

## 1029 | Dental caries: An ignored health barrier to learning in Nigerian slums

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**Background:** The study examined the caries experience, risk factors, indicators and their association with anthropometric indices among children in a Nigerian slum.

**Methods:** Cluster sampling technique was utilised for recruiting the study participants ( $n = 684$ ). Participants included children from four cluster areas of Makoko; North, Central, On water residents and South-East. Caries was recorded based on WHO criteria, while the weight for age (WAZ), height for age (HAZ), and weight for height (WHZ) measures were used to assess each child's nutritional status. Chi-square test was used to test bivariate associations. Statistical significance,  $p \leq 0.05$ .

**Results:** Out of the 684 children seen, 64(9.9%) had  $dmft \geq 1$  with range of 1–12; (127 primary teeth were decayed; 6 missing due to caries; 0 filled); while 45 (7.1%) had  $DMFT \geq 1$  with range of 1–6; (79 permanent teeth were decayed; 14 missing due to caries; 0 filled). Maternal and paternal educational level, child's age, consumption of cariogenic meals, history of dental visits were significantly associated with caries experience ( $P = 0.05$ ). For children with dental caries, mean WHZ, HAZ, WAZ, BMI-for-age z-scores were ( $0.33 \pm 2.6$ ;  $-1.49 \pm 1.8$  and  $-0.79 \pm 1.90.58$ ,  $-0.16$ ), respectively, and these z score values were lower than those in the caries-free children. The BMI-for-age z-scores were significantly lower in children with dental caries than in caries free children ( $P = 0.005$ ).

**Conclusions:** Dental caries, which was mainly untreated was moderately prevalent among the children surveyed in the urban slum. There was also a significant association between the presence of caries and low BMI. Targeted designed oral health interventions that takes status into consideration is required.

## 782 | The use of vertical bitewings compared to visual examination for dental caries diagnosis in paediatric dentistry – Preliminary results from a cross: Sectional study

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**Background:** Horizontal bitewing is often used in Paediatric Dentistry for coronal caries diagnosis; however, vertical bitewings can be helpful with the visualisation of furcal and apical areas. The aim of this study was to compare the clinical and radiographic caries diagnosis using vertical bitewings for occlusal and proximal surfaces in primary and second primary molars, distal surfaces of primary canines and mesial surfaces of first permanent molars.

**Methods:** After ethical approval (#2020507), 4–9 years old children were evaluated clinically and radiographically where caries diagnosis was divided into sound (0); enamel (E); outer to middle third dentine (D); inner dentine with unclear pulp status (UP) and clear pulp necrosis (PN).

**Results:** A total of 561 surfaces were evaluated clinically in 205 teeth (n children = 18; n vertical bitewings = 36). 86 surfaces were not evaluated radiographically (14.79%) due to proximal overlap (n = 19) or when not visible in the radiograph (n = 67). From the 475 surfaces evaluated, 139 (29%) had different clinical and radiographical diagnosis (49% changed from 0 to E only). From the D lesions evaluated clinically (n = 54), only 2 had unclear pulp status (UP) radiographically but no one presented radiographical signs of pulp necrosis. However, from the UP lesions detected clinically (n = 45), the vertical bitewing helped with the pulp diagnosis in 73.33% of the cases (23 had a clear dentine bridge and 10 presented signs of pulp necrosis radiographically), and only 26% remained unclear even after the radiograph exam. Pulp necrosis was confirmed radiographically in 97% of the PN lesions.

**Conclusions:** Vertical bitewings should be considered as a diagnostic tool for determining pulp involvement in deep dentine caries lesions.

## 1355 | Therapeutic decision in proximal carious lesions of primary teeth: A literature review, with ludic association between depth of the radiolucency and Pac-Man®

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**Background:** Therapeutic decision making for proximal caries lesions in primary teeth is based on clinical and radiographic criteria. The image of Pac-Man®, demonstrating the relationship between radiolucency in enamel and dentin in the proximal area and the possibility of cavitation of the lesion, facilitates the understanding of undergraduate students, patients, and their guardians.

**Literature Review:** Bitewing radiography has been used as the main complementary method for diagnosing the presence and extent of caries lesion on proximal surfaces, and it is often taken as a basis for making therapeutic decisions. The radiographic method, due to its high sensitivity, increases the number of false-positive diagnoses, leading to unnecessary operative treatment. The presence of radiolucency in enamel or external half of dentin does not mean cavitation. Temporary tooth separation and visual inspection are recommended for therapeutic decision making of radiolucent images located in external third / half of dentin. Non-invasive or micro-invasive treatments are effective alternatives for controlling and paralyzing non-cavitated proximal lesions. And, in cavitated lesions, minimally invasive procedures should be preferred.

**Conclusion:** The therapeutic decision must be based on the correct diagnosis of the carious lesion, considering its activity, extension and cavitation. Surgical intervention, when necessary, must follow the principles of minimal intervention. The ludic use of Pac-Man®, in pediatric dentistry, can be a facilitating tool in the communication of the professional-patient-guardian triad.

## 1401 | Oral health status of patients with inherited bone marrow failure syndromes

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**Background:** Inherited bone marrow failure syndromes (IBMFS) including Fanconi Anemia (FA), Diamond-Blackfan anemia (DBA) and congenital neutropenia (CN) are rare diseases related with hematopoietic cell lines in the bone marrow. The present research aimed to present the oral-dental status of patients with IBMFS.

**Methods:** This descriptive study was conducted with patients aged between 0–18 years, diagnosed with FA, DBA or CN. The data was collected in two stages; one via a structured and pre-tested questionnaire and the other by oral-dental examination clinically and if needed, radiographically. Dental caries with dmft/s, DMFT/S indices and International Caries Detection and Evaluation System (ICDAS-II) was evaluated. Oral hygiene status of the patients with plaque index and gingival health status with gingival index were recorded.

**Results:** In total, 27 patients diagnosed with IBMFS (11 FA, 9 DBA, 7 CN) participated. Of all group 77.8% (n = 21) patients had initial or cavitated dental caries according to the ICDAS-II index system. Various oral mucosal lesions (aphthous lesions, dry chipped lips, angular cheilitis, hairy and geographic tongue) and dental abnormalities (microdontia, taurodontism, rotation, ankylosis, hypoplastic teeth, germ deficiency, cingulum hypertropia, dens invaginatus, pulp stones, etc.) were detected. Further, half of all the patients (51.9%) did not have a regular brushing habit.

**Conclusions:** Extensive dental caries, gingival inflammation and inadequate oral health showed the necessity of early dental visits. Regular dental counselling adopting the multidisciplinary team approach for patients with IBMFS is necessary to ensure better general and oral health.

## 1389 | Perspectives of pediatric dentists and parents during the COVID-19 pandemic

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**Background:** At the beginning of December 2019 a new type of coronavirus (SARS-Cov-2) that eventually lead to coronavirus disease (COVID-19) was firstly isolated in Wuhan and

was announced and categorized as pandemic disease by World Health Organization on March 11, 2020. Even though the clinical symptoms of COVID-19 have been still argued, the majority of the symptoms is composed of fever, cough, diarrhea, headache, shortness of breath. Unfortunately, dental procedures provide a high risk of transmission regarding cross infection of virus.

**Literature Review:** According to the current literature knowledge, it was reported that children tend to be fewer in numbers, cough and pharyngeal erythema with milder symptoms compared to adults due to having more active innate immune response and healthier respiratory tracts. Generation of high-concentrated aerosols and droplets during dental treatments leads to cross infection through dentists and patients. Majority of the COVID-19 infected children are asymptomatic or mild symptomatic, which makes pediatric dentists at double risk of getting infected. At that point, pediatric dentists played a key role in the COVID-19 pandemic via developing oral hygiene motivation and preventive caries approaches. Fluoride varnishes, Casein Phospho peptide—Amorphous Calcium Phosphate (CPP-ACP), High Viscosity Glass Ionomer Cements (HVGIC) should be used for both the prevention and remineralization of carious lesions that make significant contribution in COVID-19 pandemic by giving opportunity of aerosol free consumption. Moreover, Silver Diamine Fluoride application should be recommended for the management of cavitated carious lesions.

**Conclusion:** As a result, it would be strongly argued that parents should be informed about the importance of home-based oral hygiene motivation to improve general health of their children during COVID-19 pandemic.

## 376 | Retention rate of hydrophilic and hydrophobic pit and fissure sealants in first permanent molars: A systematic review

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**Background:** To assess retention rate of hydrophilic sealant compared with hydrophobic sealant in first permanent molars.

**Literature review:** Electronic databases (Medline via PubMed, Cochrane Library, Google scholar, EbscoHost) and grey literature were searched between January 1, 2012 and September 30, 2020 for randomized controlled trials and clinical trials which assessed retention rate of pit and fissure sealants with at least 3 months of follow-up.

The initial search identified 329 articles. Following the first step of screening 275 articles were finally evaluated according to the framework of PRISMA-statement. After full-text

screening, eight articles that fulfilled the eligibility criteria were included. Two reviewers independently selected studies, extracted data, assessed risk of bias using the Cochrane Collaboration tool. Five of eight included studies showed statistically significant difference between two materials based on their retention rate, of which three studies favoured higher retention of hydrophobic sealant and two studies favoured higher retention of hydrophilic sealant and rest showed no significant difference between the two materials.

**Conclusion:** Available evidence shows effective retention of hydrophilic and hydrophobic pit and fissure sealants. Overall studies showed the moderate risk of bias.

### 364 | Kids cario test: A preliminary study to evaluate an easy-to-understand caries risk assessment app for smartphone

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**Background:** Prevention and risk-assessment of dental caries are fundamental to endeavor patient-specific management strategies. The aim of our study was to evaluate the efficacy of Kids Cario Test (KCT), a smartphone-based caries-risk assessment application for a personalized prevention plan than provide an easy-to-understand set of information for parents. **Methods:** Patients were evaluated with KCT for five risk indicators (DMFT, dietary habits, oral hygiene, fluoroprophyllaxis, general factors) which were given a 0–9 severity score. Then, a total score (0–45) indicated the overall caries-risk as [low (0–8), medium (9–15) and high (16–45)]. Ultimately, a patient-specific treatment plan indicating the number of visits/preventive treatments per year, and which factors need to be modified (i.e. diet, oral hygiene), was estimated by the app/provider for each patient.

**Results:** Eighty-nine patients received a KCT evaluation. The overall DMFT score was 3 (range 0–9), with 50 (56.2%) patients having a median of 4 (range: 1–12) caries, 2 (2.2%) patients with 3 missing teeth each, and 6 (6.7%) patients having their teeth restored, with a median of two teeth each (range: 1–12). No patient was following a specific diet, but 53 (59.5%) patients were eating sugary foods. Overall, only one third of the patients had an optimal oral hygiene but more than 10% of all patients were not using any fluoride products despite their need. The overall median KCT score was 15 (3–45), with a median of suggested annually encounters of 4 (range: 2–6). 76.4% patients accepted to pursue their treatment plan.

**Conclusions:** In this preliminary study the efficacy of KCT as a valid and thorough instrument for communication and

motivation for the patient's parents has been determined. Future prospective studies are needed to evaluate its efficacy in the long term.

### 220 | Kids digital crown technique: An innovative workflow to restore primary teeth

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**Background:** The aim of this clinical case was to present the Kids Digital Crown Technique (KDCT), an innovative technique to restore primary teeth with customized prosthetic crowns.

**Case Report:** A ten-year-old patient with unremarkable medical history presented to our clinic in May 2018 following a 7-day history of a dull and continuous pain on his left mandibular area which only partially diminished on NSAIDs. Intraoral exam showed an extensive, dated, composite restoration involving the occlusal and distal aspect of tooth #L. When a panoramic radiograph was performed, an infiltrated, yet recurring carious process underneath the composite restoration was highlighted, and a diagnosis of acute pulpitis was made. An endodontic treatment was planned, and an intraoral digital impression was performed with the aim to fully restore the tooth with a zirconia crown. When the root canal was performed, the personalized crown was applied with a dual resin-based, self-curing cement following a minimal tooth preparation. Clinical and radiographic examination showed exceptional cervical margin sealings.

**Discussion:** KDCT is an innovative technique used to restore deciduous teeth with aesthetic crowns using a digital impression of the tooth before its preparation. The procedure permits the realization of a customized prosthetic crown ready to be applied immediately after the endodontic therapy. The protocol follows an easy, and kids' friendly workflow, which reduces the operative time and maintains the advantages of other procedures.

**Conclusions:** The KDCT is an easy yet very excellent restoration technique for pediatric patients with highly decayed teeth or important enamel structure defects.

## 1592 | Parental schooling and children's age influence the use of fluoridated toothpastes by children

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**Background:** The literature is scarce on the influence of parental knowledge about the effects of fluoride (beneficial/harmful) and the use of fluoridated toothpastes by their children. Thus, this study assessed the relationship between parental knowledge on the effects of fluoride, their education level and their children's age, on the use of fluoridated toothpastes by 0–7 year-old children.

**Methods:** Interviews (n = 704) were conducted at three vaccination centers in the city of Araçatuba, Brazil, using a structured questionnaire comprising 16 items related to interviewees' education level, children's age/gender, brushing habits, use of fluoridated toothpaste, and questions on preventive/adverse effects of fluoride. The results were submitted to Mann Whitney, Kruskal Wallis and Dunn's tests, and by Spearman's correlation coefficient ( $P = 0.05$ ).

**Results:** The interviewees' education level was directly related to their knowledge on preventive and adverse effects of fluoride, and inversely related to the amount of toothpaste used by the child. Furthermore, the type of toothpaste used by the children was also influenced by the interviewee's schooling and by children's age. Overall, interviewees with higher education level reported more frequently the use of fluoride-free and low-fluoride toothpastes by their children; toothpastes with special packaging/flavoring were used more often by younger children. Children's age was also inversely related to toothpaste ingestion (during toothbrushing and from the tube).

**Conclusions:** Parental knowledge and children's age influence the use of fluoridated toothpastes by children, emphasizing the need for instructing parents/caregivers on the correct use of fluoride toothpaste, in order to achieve maximum preventive effects with minimum unwanted side-effects.

**Funding:** The study was supported by Coordination for the Improvement of Higher Education Personnel (CAPES, Finance code 001) and PROCAD/CAPES (Grant 88881.068437/2014-01).

## 1639 | Early childhood caries: Prevention and treatments: Systematic review

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**Background:** Dental caries is a sugar and biofilm dependent disease of multifactorial origin caused by microorganisms that affect the hard tissues of the tooth giving rise to cavitation and dental loss, it is related to the lack of oral hygiene and the excessive intake of sugars. Early childhood caries is a bacterial disease that occurs in children under 71 months of age, with a prevalence that can reach up to 90%.

**Methods:** A systematic review study was presented, with a qualitative approach with a retrospective and cross-sectional type of research, to obtain data, 79 articles were used, the data evaluated were: etiology, diet, prevention, treatments, and oral health.

**Results:** It was analyzed that the main etiological factor of ECC is *S. Mutans* with a percentage of 83.64%. It was also possible to determine that excessive sugar consumption is the main factor of cavities. It was possible to determine that the habit of daily oral hygiene is the key factor for the prevention of ECC with 38.33% followed by regular and adequate use of fluoride with 27.50%. The ideal treatment for the prevention is the application of fluoride with 48.53% followed by restorative treatments and sealants. Parents are involved in brushing their child's teeth, but there is a lack of oral knowledge around 51.28%.

**Conclusions:** to prevent ECC, the organization of bacterial plaque must be prevented, promoting the habit of oral hygiene with the regular and adequate use of fluoride, as well as visits to the dentist and a balanced diet.

## 1212 | Comparative evaluation of the antimicrobial properties of three different bioactive compounds of cassia species and 0.2% chlorhexidine against *S. mutans* serotype C (ATCC 25175)

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**Background:** Cassia species (Caesalpinaceae) is a medicinal plant used traditionally for various ailments. This study evaluated and compared the antimicrobial properties of three

different Bioactive Compounds of Cassia species and 0.2% chlorhexidine against *S. mutans* serotype C (ATCC 25175).

**Methods:** The three different Bioactive compounds of two medicinal plant species Cassia tora and Cassia fistula were obtained. Microbiological assay of well diffusion method was done to determine zone of inhibition against pure forms of *S. mutans* serotype C (ATCC25175). This study was conducted as a triple blind study to identify their effectiveness.

**Results:** All the Bioactive Compounds had good antimicrobial activities based on their zones of inhibition; the highest zone of inhibition in mm was formed by Extract 8 which was Cassia Flower extract having mean inhibitory zone of 9.93mm +0.76. Statistical analysis of the results with Kruskal Wallis and Mann Whitney Post Hoc test which proved that at any concentration of Extract 8 the inhibition results are comparable to that of 0.2% chlorhexidine with  $P = 0.05$ . The results confirmed the antimicrobial potential of the Bioactive Compound of Cassia Flower and hence it can be used as a preventive means for dental caries.

**Conclusion:** The Bioactive Compound of Cassia Flower extract derived from cassia plants are only required in minute quantities as compared to their crude extracts. The study confirmed the antimicrobial potential of the plant at different concentrations can be used as preventive and therapeutic measure in preventive dentistry and due to its reduced potency can be used in children effectively.

## 545 | Stem cells of human exfoliated deciduous teeth: An overview of future dentistry

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**Background:** The SHED has a unique potential of self-renewal capacity and are able to differentiate into various types of cells in the body.

**AIM:** To study the antibacterial properties on *Streptococcus mutans* and to analyse the immunomodulatory properties of IL2 and IL6 of SHED.

**Methods:** The primary cultures of SHED (N = 6) were used to assess the antibacterial properties on *S. mutans* strains using Mutans-Sanguis Agar. Colonies were counted after overnight incubation at 37°C. The immunomodulatory properties of SHED on IL-2 and IL-6 was analysed by ELISA method. All data were expressed as the mean  $\pm$  standard deviation (SD) from at least three independent experiments and one-way or two-way ANOVA was performed. Significance was set at  $p < 0.05$ .

**Results:** The number of *S. mutans* was significantly reduced in presence of SHED and it was almost equal to *S. mutans* treated with antibiotics groups.

Levels of IL-2, IL-6 after stimulation with *S. mutans* were not statistically significant ( $P = 0.05$ )

**Conclusions:** In conclusion, SHED exhibited antibacterial properties against *S. mutans* by significantly reducing its CFU. It also played a role in suppressing or maintaining the levels of IL-2 and IL-6 at constant levels that were comparable to the control. This study suggest that SHED could be of benefit for suppressing or limiting the infection through their antibacterial activity, and can offer immunomodulatory actions by regulating the cytokines expression. However, further studies are warranted to evaluate these properties of SHED in an in vivo context to realize their enhanced potential in therapeutic applications.

## 1754 | The role of dental aesthetics in the social behavior of children

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**Background:** Smile is one of the most remarkable features on the face. It has been well documented that considerable importance is placed on dental aesthetics among adults and teenagers, but there are only a few studies available regarding younger children. The purpose of this study is to confirm that dental appearance plays a significant role in the social behavior of preschool children.

**Methods:** Fifty-eight three- to six-year-old participants were involved in the study. To assess the social perception of dental aesthetics, photographs of smiling children were presented to the volunteers. Photos were modified showing healthy dentition, carious incisors, fractured or missing teeth. Photograph selection and modification were based on psychological studies. The participants were asked which child they preferred to be friends with. PsychoPy3 software was used for evaluation. Preference order was set up using Repeated Measures ANOVA and post-hoc test.

**Results:** The participants preferred the healthy teeth over the alterations, the least favored were the carious teeth. Further analysis showed that boys and girls gave significantly different answers. According to Spearman correlation, older children were more likely to select the faces with missing tooth.

**Conclusions:** Preschool children can instinctively or consciously recognize and differentiate healthy and abnormal teeth. Besides several negative effects, untreated dental alterations can lead to psychological and social problems in children. This study can emphasize the importance of

education regarding oral health. Pediatric dentists should be committed to performing dental reconstructions not only to restore the function but the aesthetics of the primary front teeth.

## 1088 | Caries prevalence in children and adolescents with type 1 diabetes mellitus: A review of literature

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**Background:** type 1 diabetes mellitus is a chronic disease with high prevalence that appear in children and adolescents. The international diabetes federation indicates that 10% of diabetes mellitus cases in the world are type 1 diabetes mellitus, and similar results have been reported in Chile. Diabetes mellitus induces different alterations caused by maintained hyperglycemic state and this is the case of the oral health and caries prevalence. On the other hand, caries is a multifactorial disease that affects all ages, begin in childhood and its been increasing in the last years. Knowing that type 1 diabetes and caries are chronic processes, is important to make multidisciplinary approach, diagnosis, prevention and control.

**Literature Review:** type 1 diabetes mellitus and caries are chronic multifactorial diseases, begin in childhood and can be lifestyle-modified. The principal factor for caries are food intake and oral hygiene, meanwhile type 1 diabetes mellitus is insulin deficit and can be modified by food intake and glycemic control. Thereby, cases with higher prevalence of caries have been reported in children and adolescents with type 1 diabetes mellitus in the last years.

**Conclusions:** There is a possible relationship between type 1 diabetes mellitus and high prevalence of caries in children and adolescents. Future studies must be carried out in order to establish a causal relationship.

## 1752 | Infiltrant resins: Minimally invasive treatment of enamel hypomineralization in anterior teeth

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**Background:** With the advance of dentistry, there is a tendency to treat caries taking into account demineralization and

remineralization depending on the pH of the oral environment and salivary flow. This treatment is included in the term Minimally Invasive Dentistry, based on caries prevention, early diagnosis, remineralization of the enamel and restoration of the lesions under the premises of minimal intervention.

**Literature review:** White lesions of the enamel have as a common characteristic the hypomineralization of the tissue, showing opaque spots due to the refraction of light in multiple directions. The use of infiltrating resins increases the resistance of the hypomineralized enamel and attenuates the lesions, so they can be a suitable option to avoid the use of more aggressive techniques. The caries infiltration technique consists of the penetration of resin into the enamel lesion, which, thanks to its low viscosity and high impregnation coefficient, is driven by capillary forces. This technique has been shown to block or even arrest the progression of caries in vitro. The results obtained in the attenuation of incipient caries lesions or defects following the use of fixed orthodontics are promising, whereas in MIH lesions only some of the lesions were attenuated and did not disappear completely.

**Conclusions:** The masking potential of infiltrating resins is dependent on histology and lesion severity, especially in mild to moderate developmental alterations; in more severe cases, color masking is not good enough and more aggressive techniques will be necessary.

## 968 | Salivary C-Reactive protein levels in children with early childhood caries

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**Background:** C-reactive protein (CRP) is one of the most commonly assayed biomarkers whose production is stimulated by IL-6. CRP has two isoforms, one of which produced locally in inflamed/ damaged tissues. The other isoform is routinely produced in absence of inflammation and may have net anti-inflammatory effects. Pulpitis is the sequelae of dental caries characterised by inflammatory mediators. Children with ECC were found to have increased IL-6 which has a strong correlation with severity and extent of carious lesions in the oral cavity, and therefore, minimizing its levels will help in improving the inflammatory condition in the oral cavity.

The aim of this study was to assess the level of CRP in children with Early Childhood Caries.

**Methods:** A total of 30 children was divided into 3 groups of 10 children each of caries free children, Early Childhood Caries (ECC) and Severe Early childhood caries (S-ECC). Unstimulated saliva was collected and transported to laboratory where it was centrifuged at 4000rpm for 15mins.

The supernatants were stored at  $-80^{\circ}\text{C}$ . CRP was measured using CRP LEIT (Light energized irrigation technology) kit. Intergroup comparison of the results was analysed by one way ANOVA test.

**Results:** The level of salivary CRP was found to be  $1.3 \pm 0.93$  in control group, increased to  $5.31 \pm 1.14$  in ECC group and  $8.61 \pm 1.53$  in S-ECC group respectively. The increase was statistically significant ( $P = 0.001$ ).

**Conclusions:** Salivary C-reactive protein can be a potential non-invasive diagnostic and/or prognostic inflammatory biomarker in Early Childhood Caries.

### 1377 | Influence of cavity size on the progression of atypical carious lesions in primary teeth treated with the Hall technique: Preliminary results of a randomized clinical trial in Goiânia-GO

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**Introduction:** This work is part of a clinical study randomized by multi-operators using the Hall Technique

**Methods:** This technique uses a prefabricated metallic crown for the treatment of decayed molars, which is based on the non-removal of the carious lesion, the non-preparation of the tooth and or the use of local anesthesia. In this project, children with the following characteristics were selected: good general health, and at least one molar with an atypical lesion for dental treatment and follow-up for 6 and 12 months. These children were divided into two groups: composite resin (RC) restoration in the control group (10 children) and prefabricated metallic crown restoration based on Hall Technique (HT) (10 children). This project was carried out at the Public Health Service (Cais-Cândida de Moraes), located in the city of Goiânia - Goiás.

**Results:** The results obtained, in this work, for 6 months for Hall Technique in relation to the progression of the caries disease taking into account the size of the lesion.

**Conclusion:** The size of the atypical caries lesions treated with CR and HT seems to have no influence on the progression of caries over a period of six months.

### 1381 | Effect of varied formulations of fluoride varnish on demineralization inhibitory effect and antibacterial effect: A comparative in vitro study

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**Background:** Dental caries is a global burden that affects a large proportion of the world. Caries-prone children do not only suffer from tooth pain and infection, but the overall growth and development is influenced. It poses a challenge for young children to tolerate the lengthy and complicated procedures of restorative treatment. Hence, a non-invasive and unsophisticated preventive treatment modality is indispensable to tackle the burden of caries in children. Fluoride varnish has been shown to play a dominant role in this process and formulations with added ingredients have been investigated to check their clinical outcome.

**Methods:** A buccal window was prepared in forty extracted premolars for fluoride treatment. These were categorized as Group 1 – Vanish™, Group 2 – Embrace™ Varnish, Group 3 – Fluor Protector®, and Group 4 – No fluoride application. The samples were then immersed in 3 ml of demineralizing solution for 48 hours at room temperature. Thin sections measuring  $100\mu\text{m}$  were obtained using a hard tissue microtome and examined under polarized light microscope and the depth of demineralization was measured using ImageJ.

The antibacterial effect was analysed using broth microdilution assay. MIC was recorded as the lowest concentration which did not permit the growth of *S. mutans*.

**Results:** The demineralization inhibition efficacy of Vanish™ over Fluor protector® was statistically significant. MIC values of Vanish™ and Embrace™ were at 2.5% and 0.04% respectively which showcases the better antibacterial efficacy of Embrace™ over Vanish™ and Fluor protector®.

**Conclusion:** Fluoride varnishes with active agents like TCP and Xylitol could be included in the preventive protocol owing to their versatile properties in influencing the demineralizing activity as well as their impact of the cariogenic pathogens. This could be considered as an effective preventive protocol which could be employed on a regular basis with the motive of reducing the global burden caused by dental caries.

### 1310 | Bacterial reduction after selective caries removal: A systematic review and meta-analysis

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**Background:** The purpose of this study was to verify whether the time factor interferes in the reduction of the microbiota after the sealing of caries lesions when the technique of selective removal of caries lesions was used.

**Methods:** A search was performed in the PubMed and Scopus databases, with the inclusion criteria being randomized clinical trials, in human teeth that used selective caries removal. Exclusion criteria were: studies without longitudinal follow-up, which did not have standardized microbiological analysis, studies that used chemical methods that may interfere with microbial counting.

**Results:** There was no language restriction or year of publication, identifying 1265 references. Two reviewers selected and extracted the data independently, according to PRISMA protocol, evaluating the quality of the studies following the Cochrane Handbook and the GRID system. Seventeen studies were selected, twelve considered for quantitative analysis, classified as low risk of bias. The study compiled microbiological evaluations of total microbial count, Streptococcus mutans and Lactobacillus.

**Conclusion:** There is no significant difference in the reduction of microorganisms when comparing the techniques of selective and non-selective removal of decayed tissue. However, there was a significant difference in the reduction of microorganisms observed in the reopening of cavities after selective removal of caries, and the microbial reduction was significant in the first hundred days after cavity sealing in these cases.

### 1373 | Factors affecting children's brushing habits and amount of toothpaste applied on the toothbrush

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**Background:** This study evaluated the use of fluoridated toothpastes by children and estimated the amount of toothpaste applied on the toothbrush by their parents/guardians according to descriptions typically recommended by scientific societies.

**Methods:** Parents/caregivers of children (0–7 years old; n = 306) attending vaccination centres in the city of Araçatuba (Brazil), answered to a structured questionnaire comprising items related to interviewees' education, child's age, gender, data on brushing habits and use of fluoridated toothpaste. In addition, a portable scale was used to estimate the amount of toothpaste used by children during toothbrushing. The results were submitted to Mann Whitney's, Kruskal-Wallis' and Friedman's tests, and Spearman's correlation coefficient ( $P = 0.05$ ).

**Results:** The type of toothpaste and the amount of product used at home were not affected by the respondents' educational level or family income. However, child's age was significantly correlated with the amount of toothpaste placed on the toothbrush ( $r = 0.324$ ,  $P = 0.001$ ). Also, the amount of toothpaste placed on the toothbrush increased according to what would be expected from the descriptions, although wide variations were observed within each description.

**Conclusion:** It was concluded that verbal instructions regarding the amount of toothpaste to be used by children might not be an effective strategy for ensuring optimum exposure to fluoride, considering risk and benefits.

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### 641 | Estimation of fluoride ion concentration in urine after application of silver diamine fluoride in S-ECC patients

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**Background:** Silver diamine fluoride (SDF) is a topical solution that has been used for caries management. Though its

use is approved for arresting the dentinal caries, literature available on systemic absorption is limited and inconclusive. The aim of the study is to evaluate if high concentration of fluoride in SDF solution will have any systemic absorption in young children.

**Methods:** Patients diagnosed with S-ECC caries between the ages of 3–6 years requiring dental rehabilitation were recruited for the study. Before applying SDF, the base line urine samples were collected. SDF was applied for a minimum of 5 dentinal carious teeth, according to AAPD protocol. Urine samples were collected after 2 and 24 hrs of application of SDF, fluoride ion concentration was estimated using fluoride ion selective electrode.

**Results:** The results showed that urinary fluoride concentration before the application of SDF was 0.66 mg/L + 0.25 mg/L and after 2hrs it was 1.13mg/L + 0.28. however after 24hr it reached to 0.63mg/L + 0.19 which is close to the base line value.

**Conclusions:** There is no statistically significant difference in the fluoride ion concentration before and after 24 hrs of application. Therefore there may not be any systemic absorption of fluoride after topical application of SDF.

### 1952 | Dental caries experience and treatment needed using ICDAS II criteria among school children in Iasi, Romania

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**Background:** The study was carried out to determine the caries experience, caries prevalence and dental treatment needs in 6-8 and 11-13 years-old school children from Iasi, Romania.

**Methods:** A cross-sectional oral health survey of school children was conducted for 6–8 and 11–13 years old children, using the ICDAS II system.

**Results:** The children from the age stage 6-8 year-old, 88.4% had experienced carious lesions, with a mean d1-6mft and d3-6mft of 5.12 (SD = 3.16) respectively 4.94 (SD = 3.11). No gender differences in caries experience or in its components were found (p 0.05 in all cases). Among the 11-13 year-old children, 96.4% had caries experience with mean D1-6MFT and D3-6MFT of 5.27 (SD = 3.66) respectively 4.04 (SD = 2.88). For this age stage, significant statistical differences were observed in caries experienced by gender.

The ratio of first- and sixth-grade children with treatment need was of 85.8% and 82.7%.

**Conclusion:** Caries prevalence was very high in both age stages, the established carious lesions being the main contributors to children's caries experience, indicating an increased need for preventive and restorative treatment in both age groups.

### 733 | Accuracy of different clinical methods for detection of non-cavitated lesion in primary teeth: A systematic review

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**Background:** Non-cavitated refers to initial caries lesion development, before cavitation. They are characterized by a change in color, glossiness or surface structure as a result of demineralization. Detecting them early might prevent the invasive treatment and likely protect from further damage to dental tissues. For their detection of caries, we have relied mostly on visual examination, with or without tactile sensation, aided by radiography. Often, the end result is low sensitivity and high specificity, meaning a large number of lesions may be missed. These technologies include quantitative laser or fluorescence based methods, electrical conductance measurements, digital radiography and Trans-Illumination (DIFOTI).

**Literature review:** Databases search was carried out from inception to the present for four electronic databases- PubMed/ Medline, EBSCOhost, google scholar and The Cochrane library. A total of 834 studies were identified throughout search. After the removal of duplicates 818 remained. After screening of title and abstract 35 studies were suitable as per the inclusion criteria. They were analyzed qualitatively by applying the QUADAS-2 tool.

**Conclusions:** There are ample studies demonstrating the efficacy of laser fluorescence for detection of non-cavitated lesions they can be used to rule in the disease based on good sensitivity scores but more high quality and low bias in vivo studies needs to be done to know the accuracy of ACIS, light-fluorescence and transillumination.

## 552 | Fluoride varnish for caries prevention in South African children: A cluster-randomized controlled community trial

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**Background:** This cluster-randomized controlled community trial aimed to assess the efficacy of fluoride varnish (FV) application for caries prevention as part of a tooth-brushing program in a high-risk population in South Africa. Additionally, the cost-effectiveness was assessed.

**Methods:** 513 children aged 4–8 years from two schools in a rural township in South Africa were class-wise cluster-randomized to the FV or Control (CO) groups. In addition to supervised toothbrushing in both groups, FV was applied in 3-monthly intervals. Intraoral examinations were conducted at baseline, 12, 21 and 24 months. The primary outcome was the increment of cavitated lesions (i.e. newly developed ones or progressed, formerly non-cavitated lesions), requiring restorations or extraction. Additionally, treatment and re-treatment costs were analysed. This trial was registered (ClinicalTrials.gov/NCT03429829).

**Results:** The 513 children (mean  $\pm$  SD baseline d1-4mft  $5.9 \pm 4.3$ ) were randomized to FV ( $n = 287$ ) or CO ( $n = 226$ ). 4.7% FV and 4.7% CO teeth received or required a filling; 2.0% FV and 2.1% CO were extracted, without significant differences between groups ( $P = 0.05$ ) and in multivariable analysis, neither group allocation nor age or sex were significantly associated with outcomes ( $P = 0.05$ ). While FV generated high initial costs, follow-up costs were similar in both groups, resulting in FV being significantly more expensive than CO ( $1524 \pm 956$  ZAR vs.  $806 \pm 818$  ZAR,  $P = 0.001$ ).

**Conclusions:** Regular FV application was not cost-effective and had no significant caries-preventive effect in a primary school setting within a rural, high-risk community in South Africa.

## 751 | Changes in the appearance of dental fluorosis in children after one year

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**Background:** The aim of this study was to evaluate the changes in the appearance of dental fluorosis (DF) after one-year period in a cohort of 30 children living in an area of high fluoride level in the drinking water.

**Methods:** 30 children aged between 7 to 12 years from Hanliyenice, a small town in Edirne, Turkey were included in the study. Inhabitants of this town were using tap water for drinking and it contained 2.3 to 3 ppm fluoride. All children were examined by two calibrated pediatric dentists, all erupted primary and permanent teeth were inscribed, and DF was assessed with Thylstrup-Fejerskov Index (TF). After One year they ( $n = 21$ ), were re-evaluated by the same pediatric dentists for the DF examination and all the present teeth were evaluated. Prevalence ratios associated with changes in each score of TF and 95% CIs were reported and evaluated with Mann-Whitney U test.

**Results:** In the cohort group, the increase of permanent teeth was 45% and the decrease of primary teeth was 20.7% in one year. Mean TF0 scores were 25.7% and 98% in the 1st and 2nd examinations respectively and the difference was statistically significant ( $P = 0.010$ ). For TF1-2 and for TF5-8 there were not significant differences (TF1-2 3, 7, 4.4% and 30.9%  $P = 0.191$ ; TF5-8, 19.5% and 13.4%  $P = 0.814$  in 1st and 2nd examinations respectively), whereas for TF3-4 the ratio of DF increased from 18.4% to 45.9% after one year and the difference was significant ( $P = 0.001$ ).

**Conclusions:** This study showed that the appearance of DF degraded after one year as the children grew up.

**Funding:** The study was supported by The Marmara University Scientific Research Committee (BAPKO) with project number SAG-C-DUP-090518-0217.

## 1208 | Can every tooth should have silver lining???... the SMART way!

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**Background:** “Prevention is better than cure” the preventive aspect of dentistry is evolving day by day so as to achieve

the goal of total caries control. There are so many other reviews available on various preventive strategies. It is most important to avoid complications of caries progression as it may compromise children's ability to eat, sleep and may also restrict life activity. Silver diamine fluoride has gained popularity in arrest of caries. SMART (Silver modified Atraumatic restorative technique) is new technique, in which SDF is accompanied with Atraumatic Restorative Treatment. SMART is a non-aerosol based, ascertained and it is significant technique that involves minimal exposure to the patient during this COVID-19 situation. The Aim of this review is to summarize all the details about SMART and create awareness during this COVID-19 to use this technique precisely by clinicians/public health workers.

**Literature Review:** A Review of pertinent literature was based on articles searched through PubMed, EBSCO, Google Scholar, Inside Dentistry and medRxiv electronic Databases published in English language from year 2016 to year 2021 by using mesh terms and free text terms and also some basic Reference Manual related to Pediatric & Preventive Dentistry and COVID-19 to gather up-dated Information required for research. The only case reports and reference manual which evaluated the effectiveness of SMART technique in preventive dentistry amongst children. Initial search using terms gave total 30 number of articles among which 8 were selected Based on eligibility criteria.

Dental caries is most common chronic childhood diseases and involves complex process of De and Remineralization. Introduction of Silver Modified Atraumatic Restorative Technique as an alternative caries prevention tool enhances the current dental armamentarium. Minimal interventional dentistry is the best early preventive technique to arrest caries which includes a recently introduced technique called as SMART (Silver modified Atraumatic restorative technique). It is technique in which decay is halted by using Silver Diamine fluoride and then restored with Glass Ionomer cement to seal the tooth and mask the black stain caused by SDF. SMART is an inexpensive, non-invasive and effective way to control caries at an early stage with conservative cavity preparation. SMART helps in significant reduction of child's traumatic dental experience and therefore conveying manageable child behavior in dental office. In this COVID-19 situation it is difficult to carry out aerosol-based. So, SMART can be opportunity to prevent caries in a single visit with minimal exposure of clinician to patient.

**Conclusion:** SMART is a benefit for both practitioner as well as patient. In this current review we will be giving brief idea about SMART technique and focusing on its superiority over traditional caries management techniques. As we know dentists are at a higher risk in current COVID-19 situation so by Adhering to the principles of infection control and the non-aerosol based practices such as SMART helps in resume the dental practices and in reduction of risk associated with disease transmission.

## 627 | Evaluation of salivary pH changes after consumption of different berry juices

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**Background:** Purpose of the study is to assess the salivary pH changes at different intervals after consumption of 100 ml of freshly prepared different berry drinks.

**Methods:** 30 volunteers aged 6 yr were assessed for salivary pH changes at 4 different days at 0min, 5min, 15min and 30min time interval after consumption of 100ml of 3 types of freshly prepared berry juices, that is Strawberry (Group 1), Blueberry (Group 2) and Cranberry (Group 3) and distilled water (Control). Intrinsic pH of all the berry juices were recorded initially before consumption using digital pH meter. The salivary pH changes were assessed after the consumption of 100ml of berry juices at different intervals using digital pH meter.

**Results:** At baseline the pH for Group 1, Group 2 and Group 3 was 7.063, 7.134 and 7.11. After 30 min, the Group 1 showed increased pH (7.184) which was equal to control group (7.112). Group 2 showed moderate drop in the pH (6.857) and Group 3 showed significant drop in pH (6.985) after consumption. Control group showed slight increase in salivary pH after intake of distilled water. None of the test drinks showed drop in salivary pH values below critical pH. Statistically there was no significant difference between groups at different time intervals.

**Conclusion:** The freshly prepared strawberry juice has the least acidogenic potential when compared with other juices. Hence among 3 types of berry juices strawberry juice can be considered as safe, suggesting less cariogenicity.

**Funding:** The present research project was self-funded.

## 1688 | Baking soda as a preventive oral care measure

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**Background:** Microbial fermentation by dietary sugars and subsequent decrease in biofilm pH below critical pH is the bedrock of the caries process. Use of baking soda for rapid alkalization of the biofilm has evoked interest in researchers and can be one of the main drivers in caries preventive strategies

**Literature review:** The earliest use of sodium bicarbonate was in dentifrices, having an effect on the numbers of Mutans Streptococci. Addition of sodium bicarbonate in chewing gums has also been used to elevate the interproximal plaque pH previously lowered by exposure to fermentable carbohydrate. When bicarbonate was used in an oral rinse, it was shown to have a significant effect on the salivary pH and also resulted in a marginal decrease in pathogenic oral microflora. Patients with Acute leukemia undergoing chemotherapy have also been administered baking soda solution as an adjunctive oral care measure. Baking soda wipes and rinses are recommended methods for caries management in 0-5 year old children at extreme risk of dental caries by CAMBRA

**Conclusion:** As the studies have shown, Baking soda in various forms can be used to modify biofilm pH and can be used as a preventive oral care measure but more scientific research is required to establish its role in caries incidence reduction.

### 1689 | Association between single nucleotide polymorphisms of enamel formation genes and early childhood caries: A systematic review and meta-analysis

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**Background:** Early Childhood Caries (ECC) is a common chronic condition affecting more than 600 million children globally and is characterised by interaction between genetic and environmental factors. Single Nucleotide Polymorphisms (SNPs) are one of the most common variations occurring in the human genome. This systematic review aims to evaluate the association between SNPs of enamel formation genes and ECC.

**Methods:** An extensive search was conducted across electronic databases and Genome Wide Association Studies (GWAS) databases from January 2003 till April 2020. Observational studies assessing the association between SNPs of enamel formation genes and ECC were included. Two researchers independently assessed the studies, extracted the data and performed Risk of Bias assessment using the Q-Genie tool.

**Results:** A total of 5734 articles were identified and 17 studies assessing the association between SNPs of genes regulating enamel formation, maturation and ECC were included

of which nine studies qualified for meta-analysis. One study scored less than 45 and was classified as moderate quality study and the other sixteen studies scored more than 45 and were qualified as good quality studies.

**Conclusions:** Despite 90 SNPs of enamel formation genes being analysed for predisposition to ECC, Meta-Analysis revealed that genotype AA of polymorphism rs12640848 of ENAM gene was found to be significantly higher in patients with ECC with an odds ratio of 2.36 (1.00, 5.57). Further research is warranted to understand genetic predisposition to ECC.

### 152 | Non-removal of carious lesion a possible option during COVID-19: A review of literature

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**Background:** Today, the world is fighting against the COVID-19 pandemic. Dental professionals are at higher risk of cross infection and exposure due to aerosol generating procedures. Therefore, alternatives that do not include use of handpieces are recommended. Non-Restorative Cavity Control (NRCC) technique can be used as an alternative option in clinical practice for caries management.

**Literature Review:** NRCC is management of a carious lesion without removing it. The technique is minimally invasive and grounded on the aetiology of dental caries disease development occurring at the level of the plaque biofilm. It aims to control activity of biofilm on tooth and lesion surface by preventing the plaque biofilm formation or by causing disruption of maturation of plaque. Thus, the technique simultaneously prevents demineralization and promotes remineralization of tooth structure. The technique is particularly useful in young pre-cooperative anxious paediatric patients and for individuals with special healthcare needs. It includes simple steps like reinforcing good home oral care, good professional care, and regular follow-ups which are critical for the success of the procedure. However, failure in any of the above can lead to an adverse outcome.

**Conclusion:** The current pandemic has challenged paediatric dentist to amalgamate newer approaches for caries control and the NRCC approach gives the benefit of aerosol free treatment. For an NRCC technique of caries lesion management to become successful, a paradigm shift in the minds of dental practitioners is needed, along-with compliance and motivation of the parents.

### 839 | Application of the CAMBRA protocol by dentists in the clinical care of infant patients

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**Background:** The CAMBRA protocol represents an evidence-based method to prevent, reverse and treat dental caries. It aims to use strategies that reduce caries risk factors and increase protection factors. In a first stage, it is based on the prevention and treatment of causes of dental caries in order to prevent irreversible damage. Through a set of criteria, it is possible to assess the patient risk of future demineralization, considering all the disease indicators and risk factors, in relation to the protective factors.

**Methods:** The objective of the present work was to evaluate the knowledge and the use of the CAMBRA protocol, by dentists who develop their professional activity in the city of Oporto, Portugal, by completing a questionnaire, and understand the advantages and disadvantages of this method. The sample of the present investigation was formed by dentists who accepted to participate in the study.

**Results:** 48 responses to the questionnaire were obtained. The evaluation of the results showed that in most cases (56%) of the studied sample, the CAMBRA protocol is not widely known. Among the respondents who say they know the protocol (44%), only 21% report using or have used this protocol in their clinical practice.

**Conclusions:** The CAMBRA protocol is still not widely known or used in the care of infant patients in the studied sample.

### 1116 | Oral health and anthropometric profile in pediatric ages: A systematic review

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**Background:** This work checked the way food intake and the type of food taken are related to oral health and body mass index, body weight, height and body composition.

A systematic review was done, including several scientific investigations developed in countries from all the continents, searching to specify that relationship in children 2 to 18 years, attending public and private schools, belonging to families from different social, economic, and regional origin.

**Literature Review:** A weaker global oral health is observed in children presenting lower body mass index and obesity, and also in those belonging to less favored social and economic environments, with habits of bigger sugar ingestion and poorer nourishment regarding to healthy nutrients, causing pathologies such as dental caries.

The relation of dental caries prevalence and the intake of sugary foods was verified in children with high body mass index, but also with low weight. Poor oral hygiene was also found to cause dental caries. There was a clear negative impact of the most disadvantaged socio-economic environments.

**Conclusions:** Although it was not possible to establish an unequivocal relationship between anthropometric data, such as obesity, and socioeconomic status in the prevalence of dental caries in children, there is a major focus on the need to promote a wider education for oral health in schools and near families, by health authorities and teachers, stressing the important role of family doctors.

### 1813 | Comparative evaluation of CPP-ACP cream and fluoride varnish in remineralization of MIH-affected teeth using laser fluorescence

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**Background:** Molar incisor hypomineralization (MIH) affected teeth have enamel with altered mineral content, including decreased calcium and phosphorous and increased carbon, leading to porous enamel and subsequent post-eruptive breakdown. Treatment is aimed at the prevention of that breakdown. Various remineralization strategies originally employed for initial carious lesions have been extrapolated for use on these defects. The aim of this study was to evaluate the remineralization potential of CPP-ACP-based cream and fluoride varnish on MIH-affected teeth using laser fluorescence.

**Methods:** Thirty children aged 8–14 years who exhibited intact, demarcated opacities on their first permanent molars or permanent incisors were randomly divided into two groups using simple randomization. Group A received professional application of fluoride varnish (n = 15); Group B received daily single applications of CPP-ACP cream (n = 15). The mineral density was assessed before and after 15 days of application with DIAGNOdent™ pen (KaVo).

**Results:** The mean change in laser fluorescence values depicting a change in the mineral density scores was  $8.933 \pm 5.05$  for the fluoride varnish group and  $7.133 \pm 4.17$  for the CPP-ACP group. This decrease was statistically significant for both groups. However, no significant difference was found between the two groups in terms of these changes.

**Conclusion:** In this study, CPP-ACP cream and fluoride varnish were equally effective in achieving remineralization of MIH-affected teeth.

## 170 | A retrospective investigation of paediatric caries management under general anaesthesia at Hospital Canselor Tuanku Muhriz, Kuala Lumpur, Malaysia

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**Background:** Studies have reported that there is a growing trend among parents' preferences towards accepting dental treatment under general anaesthesia (GA). The aim of this study is to investigate the types of treatments provided, the time taken for treatment and post-operative complications.

**Method:** It is a retrospective study from 2017 to 2019 at Hospital Canselor Tuanku Muhriz (HCTM). Clinical notes of caries management under GA with ICD Code CM K02.9 for paediatric patients were retrieved. Detailed information regarding patient's demographic, GA year, referral source, medical history, type of treatment, time taken for treatment and post-operative complications were collected.

**Results:** A total of 140 medical records were retrieved. The mean age of patient was 5.9 years with more male patients 62.1%. Highest treatment was done in 2019 with 39.3%. The bulk of the patients are for internal referral 65% and 60% of these children has medical illness. The most treatment done during GA was extraction of deciduous teeth followed by fissure sealant of deciduous teeth. The average time taken per child is 52.87 minutes. No post-operative complications were recorded.

**Conclusion:** Majority of paediatric caries management under GA in HCTM involved preschool children aged 5–6 years old boys with medical illness. More than half of the cases required extraction of deciduous teeth. Oral health of children with medical illness is often overlooked because of their systemic disease and ongoing medical treatment. Hence, it is important for our paediatrician colleagues to refer the child early for oral health prevention.

## 695 | Effect of fluoride varnishes on remineralization of artificial enamel lesions: An in vitro study

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**Background:** In this in vitro study, evaluation of the remineralizing effect of seven fluoride varnishes on artificial carious lesions using surface microhardness was performed.

**Methods:** 4mm x 4mm blocks of bovine incisors (n = 80) were randomly divided into 8 groups (n = 10 each group): G1: control, G2: Duraphat, G3: MI Varnish, G4: Clinpro White Varnish, G5: Enamel Pro Varnish, G6: Duofluorid XII, G7: Profluorid Varnish, G8: Enamelast. All the samples were subjected to acid challenge for 96 hours at 37 °C to create the artificial lesion, varnishes were applied to the samples and samples were left in artificial saliva for 6 hours. The varnish residues from the samples were removed and samples were subjected to remineralization model, 3 hours in demineralizing solution and 21 hours in remineralizing solution for 5 days. Vickers surface microhardness (VHN) test was performed in all three stages of procedure.

**Results:** The recovery potential in remineralization was insufficient in the control group (-61.66%) and the Enamelpro group (-7.67%). In the other groups a mineral gain was observed, in Duraphat (4.43%), Clinpro White Varnish (0.82%), Enamelast (1.49%), Duofluorid XII (4.21%), MI Varnish and Profluorid groups the ones that showed the highest remineralization with 22.94% and 24.93 % respectively.

**Conclusions:** Profluorid is the most effective varnish in the remineralization of enamel lesions in bovine teeth, followed by MI Varnish.

## 747 | Caries as a risk factor for worsening masticatory performance: A seven-year longitudinal study

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**Background:** The literature shows a strong association between masticatory performance (MP) and dental caries, which is the most prevalent chronic oral disease in the population. The aim was to assess whether caries is a risk factor for worsening MP in adolescents.

**Methods:** A longitudinal study was carried out with 324 adolescents between 13 and 19 years old in 2019 (follow up), which were previously evaluated in 2012 (baseline), in the city of Diamantina / Brazil. The evaluation of dental caries was performed at both moments of data collection, using the DMF-T/def-t index and was classified into caries free at both moments, presence of caries only at the baseline, presence of caries only at the follow up, and presence of caries at both moments. For follow-up, a clinical oral assessment of malocclusion was performed using the Angle Classification and the number of masticatory units. Questionnaire about age, sex and harmful oral habits was filled. All evaluations were performed by two examiners calibrated for the clinical oral conditions. The MP was evaluated using Optical test material and was based on the median particle size. For data analysis, Simple and Multiple Linear Regression, and a 95% confidence interval, were considered.

**Results:** The MP mean was 2.68mm. The variables associated with a worsening MP were caries ( $B = +0.11$ ;  $P = 0.04$ ); malocclusion ( $B = 0.16$ ;  $P = 0.01$ ) and masticatory units ( $B = -0.13$ ;  $p 0.001$ ).

**Conclusions:** Caries is a risk factor for worsening MP in adolescents.

## 763 | Salivary biomarkers for early childhood caries risk assessment

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**Background:** Early childhood caries (ECC) is one of the most common chronic childhood diseases. Despite of advances in dental care, identification of children at risk for ECC before the onset of Cavitation remains challenging. Saliva as a host factor plays an essential role in maintaining the integrity of oral structures. Therefore, in recent studies, saliva was used to evaluate the incidence and resistance or susceptibility to caries by examining some of the promising biomarkers like microbiological species, electrolytes in saliva, antibodies, inflammatory mediators, glucosyltransferase and physical characteristics of saliva. Utilization of these biomarkers in clinical practice might help the clinicians in improving the oral health status of the child.

**Literature review:** Salivary biomarkers in early childhood caries can be classified as, Biological constituents of saliva (Microorganisms), Physical properties and Chemical constituents of saliva. Several studies have reported higher concentrations of sIgA and Lysozyme in caries-free children than in ECC. Salivary proteins also modulate the oral microflora by innate defense mechanisms. Therefore, the protein composition of saliva can be a sensitive indicator for dental health. Recent Studies have also reported role of cytokines as a marker in the oral inflammatory process in ECC.

**Conclusion:** The literature supports relation between caries prevalence in children with levels of salivary microbes, salivary proteins, salivary IL 6 and also the physical and chemical characteristics of saliva. Therefore, salivary components can be used as one of the biomarkers for dental caries detection, risk assessment, diagnosis, prognosis and disease monitoring, and evaluation in ECC.

### 835 | Correlation between oral health knowledge and practices, dietary behavior and caries prevalence among institutionalized children in Targu Mures, Romania

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**Background:** The aim of our study was to assess the oral health knowledge and practices, dietary behavior and the prevalence of dental caries among institutionalized children, in Targu Mures, Romania.

**Methods:** A descriptive cross-sectional study was carried out on 355 children, aged 10–14, recruited from three orphanages. The data was collected on a structured questionnaire which included 25 closed ended multiple-choice questions on perceived knowledge and attitude towards oral health, oral hygiene practices and dietary habits. The dental status was analysed at the Department of Paediatric Dentistry in Targu Mures, using decayed, missing and filled tooth index (DMFT), for each subject. The statistical software SPSS (version 27.0) was used for the analysis of the data.

**Results:** Dental caries prevalence was 89.5% with a mean DMFT of  $5.13 \pm 2.0$ , without significant differences between females and males ( $P = 0.253$ ), but increased prevalence of caries with age ( $P = 0.023$ ). 87.4% of subjects had good knowledge regarding use of fluoridated toothpaste and importance in maintaining good oral hygiene, however 78.7% had poor practice and low access to additional methods of dental hygiene, leading to higher caries prevalence ( $P = 0.028$ ). 91.1% of the subjects showed poor dietary intake with high consumption of sugar-sweetened beverages and foods which directly influences the DMFT index ( $P = 0.030$ ).

**Conclusions:** The study showed good knowledge of oral health, but poor oral health practices and unhealthy eating behavior, all leading to high prevalence of dental caries. There is a clear need for preventive and curative oral health programs in this section of the society.

### 1971 | Inadequate care of shallow caries of young permanent teeth can lead to endodontic treatment: A case report

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**Introduction:** Nowadays, composite fillings are considered the method of choice for the treatment of caries. It is of greater importance to work in a dry environment to achieve maximum adhesive strength between restorative materials, enamel and dentin, and therefore the use of a dental dam in pediatric dentistry is mandatory. Inadequate care of shallow caries can lead to necrosis of the dental pulp of young permanent teeth.

**Case Report:** In this case report presents a 9-year-old girl who came to another dentist office due to vestibular swelling of the tooth 16; an antibiotic was prescribed. During the clinical examination a week later, the tooth reacted to a cold-sensitivity test, and premolars had just erupted. Preoperative radiograph revealed a filling that extends into the outer half of the dentin. It turned out that during the initial caries removal, the pulpal mesiobuccal diverticulum was trepanned, and the pulp tissue, with the exception of the palatal root, was necrotic. Endodontic treatment followed.

**Discussion:** Young permanent teeth have a wide pulp chamber; the treatment of caries requires special attention. In the case of pulp chamber trepanation during caries removal, the method of choice for direct or indirect pulp capping should be calcium-silicate based materials and not composites. Inadequate care, even in shallow fillings, can lead to pulp necrosis and accompanying complications such as pain, swelling, and fever.

**Conclusion:** Treatment of young permanent teeth is challenging due to the size of the pulp chamber and patients' cooperation. Inaccurate treatment methods could result in unnecessary endodontic treatment.

## 847 | Treating early childhood caries during COVID 19 pandemic, using digital workflow to avoid aerosol production

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**Introduction:** Early Childhood Caries management and treatment are complex and difficult to navigate in pediatric dentistry, and now with the pandemic situation worldwide, it makes it even harder for pediatric dentists to solve this complicated health situation, both in the challenge of treating ECC with functional and esthetic restorations and minimizing possible exposure to COVID-19.

**Case Report:** A 3-year-old patient with ECC, parents strongly opposed General Anesthesia, was treated with this alternative treatment. Using technology routinely used in prosthodontics, following all the health guidelines, a satisfactory and relatively inexpensive restorative and esthetic treatment was accomplished.

**Discussion:** Treating ECC has always been challenging for pediatric dentists, being able to restore function and fulfilling esthetic demands while not causing a negative impact on the dentist-patient relation. General Anesthesia, strip crowns, zirconia crowns and SSC have been options treatment for dentists all over the world to treat ECC pre COVID-19 pandemic. Taking into consideration the new health and security protocols for medical personnel, waiting lists for operating rooms and the parent's negative views on general anesthesia, we have to come up with protocol secure treatments that can accomplish the restorative function and esthetic demands without exposing ourselves to aerosol production and complying with minimal invasive treatments. In this case report, the aim is to provide pediatric dentists with an option that minimizes exposure potential, while still achieving the treatment goals thru the use of an oral scanner and 3D printer using biocompatible resin.

**Conclusions:** This Case Report aims to give pediatric dentists a viable alternative to treating ECC, complying with health guidelines and safety protocols, achieving functional and esthetic restorations on a young patient who might otherwise been treated with non-esthetic restorations or delayed treatment due to the Covid 19 pandemic with usage of Digital Workflow to fulfill the treatment.

## 1557 | Silver diamine fluoride: A review of literature

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**Background:** There are many preventive interventions that can be used as an alternative to traditional restorative procedures, and one of them is the use of silver diamine fluoride. It halts the caries progression and prevents new lesion development and appears to be almost twice as effective as fluoride varnish

**Literature Review:** Silver diamine fluoride is available in different concentrations (10%, 12%, 30% and 38%). Various authors recommend the use of 38% concentration for effective prevention and arrest of dental caries in children. Caries arrest rate of 38% concentration was also found to be higher with biannual application as compared to annual application.

**Conclusion:** Silver diamine fluoride (SDF) has been shown to be a successful treatment for arresting caries and also prevent the occurrence of new carious lesions. It has great potential, especially for early childhood caries, fearful adults, special needs children and adults, patients with salivary dysfunction, and patients with treatment challenged by behavioural or medical issues.

## 764 | Applications of zinc oxide nanoparticles in dentistry: A review of literature

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**Background:** Zinc is an essential trace element that plays an important role in the systemic health due to its antioxidant properties. It is found naturally in the teeth, saliva and plaque. Zinc Oxide Nanoparticle (ZnO-NP) is a white odourless powder whose extensive applications in dentistry is attributed to its unique electrical, optical, catalytic and photochemical properties which are favourable in various domains of dentistry such as in prevention, prognosis, tissue regeneration and restoration.

**Literature Review:** The incorporation of ZnO-NPs into adhesive systems, composites, interim cements, intracanal medicaments and tissue conditioners enhances the anti-microbial activity against *Streptococcus sobrinus*, *Streptococcus mutans*, *Lactobacillus*, *Enterococcus faecalis* and *Candida albicans*. It decreases the microleakage in flow

able composites and nano-sealers and improves the colour stability of silicone prosthesis. Incorporation in endodontics irrigants improves the fracture resistance of endodontically treated roots. It decreases biofilm growth in guided tissue regeneration and enhances stability of drugs in controlled drug delivery. Incorporation in Nickel-Titanium wires reduces frictional forces and improves corrosion resistance. The applications in cancer therapy are due to its ability to detect low-level biomarkers and produce reactive oxygen species. It enhances dental waste-water purification in filters by selective adsorption. In dentifrices and nanogels, it causes dentinal tubule occlusion and promotes dentin re-mineralization.

**Conclusions:** The development of ZnO-NPs has opened new perspectives for innovation in oral care. Its use represents an expanding domain for diagnosis, treatment and prevention of various oral diseases, and in enhancing characteristics of existing dental materials. Further research is necessary to explore its complete in vivo potential.

### 1800 | Fluoride effect on activity of matrix-metalloproteinase-20 (MMP-20) during the amelogenesis process

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**Background:** Amelogenesis is a biologic process of enamel development in which 90% of the protein that comprises matrix enamel is amelogenin and the other 10% is ameloblastin, enamelin and tuftelin. These proteins will be degraded by enamel protease, which is known as Matrix Metalloproteinase – 20 (MMP-20) to allow the formation of a mineralized enamel. Fluoride in the right concentration can be used for dental caries prevention, but excessive fluoride intake can result in hypoplastic enamel. This literature review aims to analyze the effect of fluoride induced activity of MMP-20 during the amelogenesis process.

**Literature Review:** Amelogenesis is a two-step process consisting of a secretory phase and a maturation phase. Amelogenin is secreted in the secretory phase and will be degraded by MMP-20. This is a critical phase of enamel biomineralization; and MMP-20 activity has an important role in the amelogenesis process. Fluoride intake in excessive concentration during enamel formation inhibits MMP-20's ability to degrade amelogenin. Several researchers report that fluoride incorporation into enamel apatite and amelogenin changes the protein structure. A change in protein structure could affect MMP-20 accessibility to degrade amelogenin. Delay of the degradation process can delay final mineralization of the

enamel matrix. This can result in a thin, porous and brittle enamel.

**Conclusion:** Excessive fluoride intake can inhibit MMP-20 proteinase activity during amelogenesis.

### 1707 | Improving the oral health of expectant mothers: A review of literature

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**Background:** Pregnancy is an ideal time to promote primary prevention of Early Childhood Caries (ECC). The physiologic changes that occur in the body during pregnancy, can affect the oral health of the expectant mother. Along with the changes that occur in the oral cavity such as increased acidity in the mouth and reduction in saliva production, other factors like increased craving for sweets, hyperemesis and fear of dental treatment during pregnancy, makes the expectant mother more susceptible to dental diseases.

**Literature review:** Utilization of prenatal oral health care is limited in both developed and developing countries. Increasing evidence suggests that poor oral health during pregnancy may have adverse effect on the pregnancy outcome. Periodontal diseases during pregnancy increases the risk of preterm birth, preeclampsia, and delivering small-for-gestational-age infants. Studies have shown an association between maternal poor oral health and increased risk for ECC. Mothers who received prenatal oral health care during pregnancy, showed a reduced incidence of ECC in their children. Prevention and treatment of gingival and periodontal diseases and dental caries before, during and after gestation are the best ways to protect and optimise oral health in mothers, new-borns and their community.

**Conclusions:** Pregnancy is not a reason to defer dental care or treatment. Expectant mothers should be provided with appropriate and timely oral health care, including oral health education. Improving the knowledge on oral health care, maintenance of good oral health and utilization of dental care during pregnancy are critical and promising steps towards prevention of ECC.

## 1711 | Prenatal counselling: A review of literature

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**Background:** Prenatal oral health counselling marks the beginning of infant oral health care. The purpose of this is to generate awareness among expectant mothers about the dental disease that occur during pregnancy and in early childhood, the prevention modalities and the means to provide a suitable environment for the child to develop.

**Literature review:** Early Childhood Caries (ECC) is an early arising, virulent form of dental caries which may result in pain, infection, and impairment of oral function. It not only affects the oral health but can also lead to malnutrition and diminished quality of life. Both poor nutrition and low birth weight are potential risk factors for enamel hypoplasia and development of ECC. The expectant mothers should be therefore be counselled to optimize nutrition during pregnancy and the infant's first year, when the enamel is undergoing maturation. Oral health status of the parent must be assessed and parent's risk of dental caries should be evaluated. Uncontrolled caries in the expectant mother reflects a high level of Mutans streptococcus, which can be transferred to the infant later. Hence the dentist should educate on maintaining good oral health, discuss the transmissibility of Mutans streptococcus to the infant and provide preventive treatment along with this the concept of "Dental Home" and "First Dental Visit" must also be introduced.

**Conclusions:** Regular monitoring on effective oral hygiene and dietary habits, improvement of the mother's oral hygiene, diet and use of mouth rinses have a significant impact on the child's caries rate in the future.

## 1435 | Preventive measures in permanent molar caries control: A longitudinal study

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**Background:** This longitudinal study aimed to analyse evolution, stabilization or setback of caries lesions in pigmented

fissures of first permanent molars, comparing to different preventive measures.

**Methods:** For this study, 60 children from a public school were evaluated concerning buccal condition and according to the presence of pigmented fissures in first permanent molars. Intervention was done using different methods: control of the fissure, duofluorid varnish, Fluoride varnish and fluoride gel. After 6 months, evaluation was done in order to verify condition of the teeth (analyse evolution, stabilization or setback). Data was submitted for statistical analysis.

**Results:** Preventive measures as control, fluoride varnish and fluoride gel showed similar results. Duofluorid varnish leads to evolution of caries cavities.

**Conclusions:** In pit and fissures lesions in permanent molars, preventive measures could lead to stabilization of caries progression, although its protector effect will depend on the caries risk of the patient.

## 1298 | Dental caries experience in children and adolescents with autism spectrum disorder

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**Background:** Behavior related to Autism Spectrum Disorder (ASD), such as difficulty in oral hygiene and preference for a sugary diet can increase the susceptibility of these individuals to oral problems. The oral health conditions of individuals with ASD is a controversial topic in the literature. The aim of this study was to evaluate dental caries experience and clinical consequences of untreated dental caries in children/adolescents with ASD, as well their socioeconomic characteristics and oral health habits.

**Methods:** Forty-four (44) individuals with ASD participated in this cross-sectional study, with ages between three and 16 years, attended by the Department of Children's and Adolescents' Health of Juiz de Fora, Brazil. Children/adolescents with ASD were clinically examined for dental caries experience (DMFT/dmft) and clinical consequences of untreated dental caries (PUFA/pufa). Parents/caregivers answered questionnaires about socioeconomic information and children's oral health habits. Descriptive statistics were performed.

**Results:** The mean age of the children/adolescents was 6.4 ( $\pm 3.2$ ) years and most were male (90.9%). Most children/adolescents with ASD had never visited the dentist (63.6%) and 43.2% experienced dental caries. The mean DMFT/dmft

was 1.52 ( $\pm$  2.46), with the mean of the decayed component being the highest one ( $1.2 \pm 1.9$ ), followed by filled ( $0.3 \pm 1.1$ ), and missing ( $0.1 \pm 0.5$ ). Most of the individuals did not present clinical consequences of untreated dental caries (95.5%).

**Conclusions:** The prevalence of dental caries in children/adolescents with ASD was 43.2%. Most of the children/adolescents never had visited the dentist and had a need for treatment concentrated on teeth with untreated cavitated lesions. Funding: The research project was supported by the Higher Education Personnel Improvement Coordination (CAPES) and to the Minas Gerais State Research Support Foundation (FAPEMIG).

### 1834 | Early childhood caries in children up to 6 years of Wardha district as influenced by maternal characteristics: A cross-sectional study

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**Background:** Early childhood caries (ECC) has multifactorial etiology. Mother has an important role in her child's health. Untreated caries leads to poor oral health, which affects the quality of life in children and parents. Present study was conducted to determine the impact of maternal characteristics which influence ECC in children up to 6 years of age.

**Methods:** 540 children up to 6 years attending OPD of Pediatrics and Pedodontics were included in study. Structured questionnaire consisted questions related to maternal factors such as educational, socio-economic status and feeding practices affecting ECC were considered. Software used was SPSS, version 12.0 for analysis. Chi-square test was used for comparing categorical data.

**Results:** Maximum children were from 3–4-year age group [28% (151)] followed by 5–6 years age group [23.33% (126)]. Least number of children were from 6 months to 1-year age group [4% (22)]. As the education of mothers increased, children affected with caries were less, but severity was more with involvement of maximum number of teeth. Total caries experience in children of working mothers was less [5.34% (29)]. Overall caries experience was more in average socio-economic status [29.33% (158)]. In both breast as well as bottle feeding, 4% (22) children had 2 teeth affected followed by 3.33% (18) children with involvement of 1 tooth.

**Conclusions:** Maternal characters such as educational, socio-economic status and feeding practices of mothers can act as beneficial parameters to evaluate the nature and severity of ECC.

### 828 | The effect of fluoride varnish on early childhood caries lesions

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**Background:** The aim was to evaluate the effect of fluoride varnish, applied along with advice on proper nutrition and tooth brushing with fluoride toothpaste, on early childhood caries lesions.

**Methods:** Fifty-two children aged between 14 and 33 months, without fillings or extracted teeth and with at least one carious lesion in enamel or dentin, assessed with ICDAS, were included. Children were clinically examined every 3 months, seven times. All parents were instructed on proper nutrition and teeth brushing with fluoride toothpaste. At each check-up, the test group (N = 26) was treated with Fluor Protector S and the control group (N = 26) with water (placebo). The analysis of variance was used to determine differences in proportions of tooth surfaces with carious lesions between study groups and between first examination and check-ups.

**Results:** At individual check-ups, there were no statistically significant differences in the proportions of surfaces scored ICDAS 1–6 ( $P = 0.778$ ), ICDAS 1–2 ( $P = 0.741$ ) and ICDAS 4–6 ( $P = 0.832$ ) between the study groups. The proportions of surfaces scored ICDAS 1–6 ( $P = 0.001$ ) and ICDAS 1–2 ( $p 0.001$ ) were statistically significantly lower at all check-ups in comparison to the first examination. The proportions of surfaces scored ICDAS 4–6 differed statistically significantly between check-ups ( $P = 0.047$ ), but statistically significant differences were observed only between the first examination and second, fourth and fifth check-up.

**Conclusions:** The preventive measures applied contributed to reducing the incidence and arresting of early childhood caries lesions in our study groups; however, the additional effect of fluoride varnish was not confirmed.

## 1046 | Comparison of the efficacy of three different oral hygiene teaching methods

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**Background:** Dental caries is one of the most prevalent diseases worldwide. The presence of bacterial plaque is a crucial condition for developing tooth decay. For this reason, it is important to control dental plaque to prevent dental disease. The aim of this study was to determine which oral hygiene teaching method is the most effective in reducing the bacterial plaque index in children aged 3 to 5 years who study in schools in Catalonia (Spain).

**Methods:** A prospective longitudinal study was carried out in children aged 3 to 5 years from a school in Catalonia, Spain. The study was carried out in three parts: in the first phase, a dental examination was performed to evaluate the bacterial plaque index using the O'Leary Index. The second phase was based on educational sessions on oral hygiene, and each school group was shown a different oral hygiene teaching method. The three oral hygiene teaching methods consisted of an explanatory video, a presentation using PowerPoint® slides and a practical session with denture models. Finally, a third phase was carried out 2 months later, in which the bacterial plaque index was again evaluated using the O'Leary Index to assess which learning technique was the most effective.

**Results:** A total of 157 children were included in the study (20% males and 80% females). There are no statistical differences regarding the applied oral hygiene teaching method (*P* value 0.01). There are also no significant differences between age and sex (*P* value 0.01).

**Conclusions:** Although there is not a more effective oral hygiene teaching method, it is essential to emphasize the importance of oral prevention. The educational talks on health encourage the younger population to re-educate their habits.

## 205 | Fluoride content in dentifrices commercialized for children in Brazil

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**Background:** The aim of this study was to determine the total, soluble and ionic fluoride concentration in toothpastes for children.

**Methods:** Fifteen different brands of toothpastes were purchased in different cities of Brazil. The total fluoride (TF), total soluble fluoride (TSF) and ionic fluoride (IF) of two samples of each brand were determined (µg/g F).

**Results:** Measured TF was less than that declared by the manufacturer in all the products. The concentration of TF found in the fluoride toothpastes ranged from 324.4 to 1608.2 µg/g F, TSF ranged from 214.6 to 1557.7 µg/g F and IF ranged from 108.3 to 1329.5 µg/g F. TSF ranged between and IF. Most of toothpastes were formulated with Sodium Fluoride (NaF), and only one MFP. **Conclusions:** The concentrations of total fluoride were below the reported values. TSF and IF were below than the total fluoride concentration. Most of the samples studied have TSF concentration that provide anti-caries effect. Additional studies with a larger number of samples are suggested to obtain more data.

## 854 | Groundwater fluoride and the risk of fluorosis

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**Background:** Fluorosis is a worldwide public health problem and the type of water consumed is one of the factors related to it, such as the consumption of well water. Well water is still the main source of drinking water in many communities, being the main source of fluoride intake. The high concentration of fluoride in these waters can be justified by contamination by local industries, where some studies correlate the consumption of groundwater with a high prevalence of fluorosis, since

fluoride, together with arsenic, are considered the main pollutants in these waters. Objective: The objective is to carry out a systematic review relating the risk of fluorosis in children exposed to water consumption from wells.

**Literature Review:** This systematic review was conducted in accordance with the guidelines of the Cochrane handbook for systematic review of Interventions following the four-phase diagram of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA). The study protocol was registered at the National Institute of Health Research Database (CRD42021227298). The research question was adapted from PECO framework to systematically review the clinical studies: Population: Patients up to 18 years; Exposition: Ground water; Comparison: -; Outcome: Fluorosis. A comprehensive search was conducted to identify potentially relevant studies by exploring a range of electronic databases (Medline via PubMed, Scopus, Cochrane library, Science Direct, Web of Science Core Collection, Medline via Ovid, Lilacs and Embase). Additionally, a Google scholar and reference search on grey literature were undertaken to identify any other relevant published work. The search was carried out without applying any time limits or language restrictions. The search strategy includes the terms: "Children", "child" and "Fluoride", "Fluorine", "Water Well\*", and "Water Ground\*"; and "Fluoridated water", "water fluoridation" and "Enamel defect\*", "Fluorosis". We found 2188 articles, after reading title and abstracts we selected 63 references to screen and finally the data was extracted from 24 articles.

**Conclusions:** A relationship was identified between the consumption of water from wells and the prevalence of fluorosis in individuals up to 18 years of age, this study being the first to systematically assess this worldwide.

### 1797 | Remineralization potential and application of casein phosphopeptide-amorphous calcium phosphate in pediatric dentistry: A review of literature

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**Background:** Minimal invasive dentistry is the new paradigm in oral health care that integrates the ideology of prevention and remineralization with little or nil invasive procedures. Non-fluoridated products such as casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) have been introduced and play an integral part in caries prevention by initiating remineralization at an early stage. With no risk of ingestion in children as an added advantage over fluoridated products, it plays an integral role in preventive pediatric dental care.

**Literature Review:** Intra-orally, CPP-ACP can act as a calcium-phosphate reservoir and also buffer acid and delay biofilm formation, leading to sub-surface remineralization of early enamel lesions. This remineralization potential of CPP-ACP makes its application in various conditions possible, including reversal of white spot lesions, dental erosion, dentine hypersensitivity, adjunct in tooth bleaching and molar incisor hypomineralisation. Recently, various authors have introduced new agents by incorporating fluoride, propolis, chitosan, and other products to CPP-ACP to enhance the remineralization potential and the applications of CPP-ACP.

**Conclusion:** A review of literature supports the role of CPP-ACP in the non-invasive management of early caries lesion, dental erosion, and various other conditions, and its being accepted as an effective preventive measure in various forms in pediatric dental care.

### 1895 | Comparative evaluation of the bond strengths of glass ionomer cement to eroded dentine surfaces following treatment with silver diamine fluoride with and without the application of potassium iodide

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**Background:** Silver diamine fluoride (SDF) is currently recognized as a safe, effective, and easy-to-use remineralization agent. The only drawback which limits its use is its potential black staining. Studies have introduced the application of potassium iodide (KI) following the use of SDF to reverse this black staining and increase treatment acceptance. A lacuna, however, exists on the potential effect on bond strength of permanent restorations such as GIC to eroded surfaces treated with SDF and KI.

**Method:** 30 1st maxillary premolars were selected and an occlusal cavity of approximately 2mm diameter 1mm depth into dentine was prepared. All the samples underwent an acid-pH cycle (3 cycles) which involved immersion in carbonated beverage for 3minutes followed by immersion in artificial saliva for 1 minute. They were then segregated into 3 groups of 10 each. Group 1: SDF application followed by GIC; Group 2: SDF application immediately followed by application of KI and GIC; Group 3(Control): GIC directly applied. A 2mm loop stainless steel wire was inserted into the cavity prior to GIC application to obtain datum for calculation of bond strength. All samples were subjected to a micro tensile bond strength test using a universal testing machine (UTM).

**Results:** The mean micro tensile strength for Group 2 (SDF) was 5.15 MPa ( ± 1.45), Group 3(SDF+KI) was 10.42MPa

( $\pm 2.07$ ), as compared to 4.5 ( $\pm 0.9$ ) for the control group ( $P = 0.001$ ).

**Conclusions:** The application of KI significantly increased the bond strength of GIC to eroded dentine treated with SDF.

## 617 | Minimal intervention technique for managing carious primary molars: Hall technique

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**Background:** Dental caries in preschool children is more complex disease effecting around 60- 90% of worldwide population (WHO 2019). Primary molars are the most commonly affected, if left untreated caries may progress to involve pulp leading to infection and pain. In children, who are young and apprehensive tooth preparation may lead to structurally weakened teeth and is really a challenging procedure. Dr Hall described a novel method of managing carious primary molars by cementing preformed metal crowns also known as stainless steel crowns, without any local anaesthesia, caries removal or tooth preparation.

**Literature Review:** Timely management of carious primary molars should be done to prevent premature tooth loss, to maintain physiological space for developing permanent molars. Recently, Hall technique has been introduced, which is based on the scientific evidence that caries progression is arrested once an effective marginal seal is achieved. Innes et al, Santamaria et al, Ludwig et al. conducted studies and inferred that Hall technique as a successful treatment modality for the management of carious primary molars compared with traditional techniques which required caries removal under the local anaesthesia.

**Conclusions:** Present review concluded that Hall technique is superior to conventional method of treatment and the success rate is 5 times higher than conventional restorative techniques. Hall technique is a minimal intervention technique and child friendly approach of managing carious primary molars.

## 1808 | Bringing back the smile in infants and toddlers-A review of literature

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**Background:** An infant smile is always captivating. Early childhood caries (ECC) is one entity which can take away the smile. It is a serious public health problem which begins in

early life soon after eruption of the teeth, progressing rapidly, and can lead to more widespread health issues.

**Literature Review:** Even though it is a preventable condition, ECC remains one of the most common childhood diseases. Improper feeding practices, familial social background, lack of parental education and lack of access to dental care are major contributing factors in the etiology of the disease. This poster will give an overview of the consequences of ECC and various measures to be taken to treat the disease. The most important aspect in the management of ECC should be prevention, since this alone can eradicate the disease. The most cost effective regimens of fluorides in all forms, with emphasis on the use of fluoride varnishes, new formulations of fluoride toothpastes, fluoride releasing restoratives and tooth mousse will be discussed. In addition to the optimal use of fluorides, early visits to a dentist will also be included.

**Conclusion:** Development of ECC among children should be properly controlled and prevented to maintain effective eating, speech development and formation of a positive self-image.

## 952 | Silver diamine fluoride: A paradigm shift in the management of early childhood caries

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**Introduction:** Early childhood caries (ECC) is one of the most prevalent chronic diseases worldwide and may predispose to pain, sepsis and poor general health. Due to their young age, restorative treatment for children with ECC can be challenging. Silver diamine fluoride (SDF) represents a non-invasive biological approach which can inhibit demineralisation and arrest carious lesions.

**Case report:** A 1-year-old girl presented with asymptomatic ECC affecting her upper primary incisors. Her medical history was unremarkable. Clinical examination revealed labial caries of her URA, ULA and ULB. Cooperation was limited. Treatment options discussed included extraction/restoration of carious teeth under general anaesthesia (GA). However, as her parents wished to avoid this, SDF was chosen as an alternative. After informed consent was gained regarding its associated tooth discolouration, SDF was applied topically to all carious lesions. On three month recall, all caries were arrested.

**Discussion:** The pre-cooperative nature of many children presenting with ECC may necessitate treatment under GA. SDF is a safe and effective alternative, which can minimise the need for GA and avoid premature loss of primary teeth.

With the current climate encouraging a minimally invasive approach to dentistry, SDF is a pragmatic strategy for caries management in the paediatric patient. It is therefore vital that practitioners are aware of its aesthetic compromise and off-licence use to aid informed consent.

**Conclusion:** This case highlights the use of SDF as an effective caries management technique in a patient where age and cooperation would otherwise commit them to treatment under GA.

### 1309 | Antimicrobial photodynamic therapy in pediatric dentistry

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**Background:** Antimicrobial Photodynamic Therapy is effective in the treatment of bacterial, fungal and viral infections; recognized as a new therapeutic approach in the management of biofilms. In pediatric dentistry, aPDT is generally used for the purpose of remineralization by disinfection of affected dentin on deep carious lesions, and has many different uses in dentistry.

**Literature Review:** Antimicrobial Photodynamic Therapy is promising and emerging as adjuvant therapy in an attempt to eliminate the microorganisms persistent to chemo-mechanical preparation. Since there is presence of oxygen in cells, photosensitizer activated by light can react with molecules in its vicinity by electrons transfer, leading to microorganism death. Bactericidal effects on saliva to *Streptococcus mutans* have been proven by studies in children with severe early childhood caries. Also a PDT can be applied as preventive protocol in patients with high caries risk for successful restorations in which the formation of secondary caries is prevented and the dental tissue is preserved at the maximum level. The effects of aPDT on periodontal pathogens were determined by studies, and it was emphasized that this method could accelerate healing in addition to mechanical debridement. Besides biofilm disinfection, this method can be used therapeutically in lesions caused by *Candida albicans* and Herpes Simplex virus.

**Conclusions:** In addition to its low toxicity and cell selectivity, it is suggested that aPDT can be considered as a solution to high adaptation capacity of microorganisms to antimicrobial agents. However more clinical studies are needed to

confirm the efficacy and long-term success of this treatment method.

### 772 | Is silver diamine fluoride (SDF) an alternative biological treatment modality? Use of SDF and minimally invasive techniques: A review of literature

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**Background:** The objectives of this review are to emphasize the use of minimally invasive treatment methods and to overview the use of silver diamine fluoride (SDF) as an alternative caries management agent in the treatment of deprived communities and patients with behavioural management issues.

**Literature Review:** Dental caries is still a major health problem worldwide and children experience a considerably high number of carious lesions. In some parts of the world, access to healthcare is limited, and therefore, patients may not be able to receive the dental treatments needed. In recent years, minimally invasive treatment methods that result in remineralisation and arrest of carious lesions are being promoted. These methods include the use of silver diamine fluoride (SDF), interim therapeutic restorations (ITR), atraumatic restorative treatment (ART), and Hall-style crowns. Biological caries management methods that aim to promote pulpal health and control the activity of the biofilm are becoming more popular in oral healthcare worldwide. Therefore, silver diamine fluoride (SDF) can be a good alternative option in caries management among children, who have poor access to oral healthcare and behavioral management issues.

**Conclusions:** Minimally invasive treatment options are effective tools in managing caries. Silver diamine fluoride offers a promising non-invasive method in the remineralisation and arrest of carious lesions. It is expected that SDF will be widely used for caries control to meet patient needs and the national goals of the Institute of Medicine's quality aims. However, further research is still needed to determine its efficiency and application protocols.

## 1422 | In vitro antimicrobial effect of low-fluoride toothpaste containing polyphosphate, polyols and fluoride against oral microorganisms

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**Background:** This study evaluated the antimicrobial effect of toothpaste containing 200 ppm fluoride (200F), xylitol (X, 16%), erythritol (E, 4%), and sodium trimetaphosphate (TMP, 0.25%), alone or in different associations against *Streptococcus mutans* (SM), *Candida albicans* (CA), *Lactobacillus casei* (LC) and *I Actinomyces israelii* (AI).

**Methods:** Suspensions of the microorganisms (300 µL) were added to BHI Agar medium, poured into Petri dishes, and dried for 1 h. Five wells were made in each plate to receive 80 µL of toothpaste suspensions in dilutions of 1:1, 1:2, 1:4, 1:8, and 1:16. Toothpaste containing 0 (Placebo) or 1100 ppm F (1100F) were used as controls. Areas of microbial inhibition were recorded using a digital caliper. The longest diameter at the inhibition zone's outer limit was measured (3 x).

**Results:** The data were analyzed by 2-way ANOVA and Fisher's LSD test (p 0.05). For SM, the largest halo was observed for 200F+TMP in all dilutions, followed by the experimental toothpaste (all active compounds) and toothpaste X+E. Conversely, for CA, the experimental toothpaste was consistently more effective than the other treatments, followed by 200F+X+E, and 1100F. For LC, the overall trend showed that the polyols effectively inhibited microbial growth, and the association with the other compounds enhanced such effects. Finally, for AI a less defined trend was observed.

**Conclusion:** The association of polyols and TMP in a low-fluoride toothpaste effectively inhibited the growth of some of the cariogenic microorganisms assessed, suggesting that this formulation could be an interesting alternative for children due to its reduced fluoride content.

## 999 | Carious activity in 6- and 12-year-old schoolchildren from a Romanian industrial town

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**Background:** The aim of the study is to evaluate the extent of dental caries in two groups of 6–7 and 11–12 year-old children from Slatina, an industrial town situated in the south part of Romania.

**Methods:** A clinical transversal study was performed on a sample of 200 schoolchildren of 6–7 year-old children (100 boys, average age = 7.2 ± 0.06 years) and on a sample of 200 schoolchildren of 11–12 year -old (100 boys, average age 12 ± 0.06 years). The children were clinically examined, and their dental caries was registered. The index of caries prevalence (Ip), the dmft/s, DMFT/S indices and their components, SiC30 and SiC10, were calculated for the whole group, as well as separately, on both sexes. The results were statistically processed with program SPSS, version 16.0.

**Results:** 1. For primary dentition: (a) 6–7 years: Ip = 80.5%, dmft = 3.98 ± 0.4; SiC30 = 7.29 ± 0.4; SiC10 = 9.5 ± 1.5; dmfs = 8.2 ± 1; (b) 11–12 years: Ip = 59.8%, dmft = 1.91 ± 0.4; SiC30 = 3.56 ± 0.5; SiC10 = 8.5 ± 1.1; dmfs = 4.47 ± 1. 2. For permanent dentition: (a) 6–7 years: Ip = 36.5%; DMFT = 0.78 ± 0.1; SiC30 = 2.7 ± 0.2; SiC10 = 3.35 ± 0.2; DMFS = 0.94 ± 0.2; (b) 11–12 year: Ip = 77%; DMFT = 2.8 ± 0.4; SiC30 = 5.7 ± 0.2; SiC10 = 8.6 ± 2.4; DMFS = 4.12 ± 0.2.

**Conclusions:** The main pathology in both age groups was dental decay. In both dentitions evidenced increased carious activity, which requires the implementation of special education programs for the reconstruction of a modern network of school medical consultations.

# Bioadhesive Nanoparticulate Drug Delivery System

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## Abstract

The inherent shortcomings of conventional drug delivery and the potential of nanoparticles (NPs) as drug delivery systems have offered a tremendous scope for research. The field of bioadhesion mainly focuses on the development of new devices along with intelligent polymers. Bioadhesive polymeric-based systems play an important role in delivering various bioactive molecules and APIs. A bioadhesive delivery system residing on a biological surface allows the localized therapeutic delivery by releasing bioactive molecule in the vicinity of the site of action, thus promoting bioavailability enhancement. NPs may be used for oral administration of gut-labile drugs or those with low aqueous solubility. These colloidal carriers have the ability to cross the mucosal barrier as such. In addition to the potential for enhancing drug bioavailability *via* particle uptake mechanisms, nanoparticulate oral delivery systems also have slower transit times than larger dosage forms increasing the local concentration gradient across absorptive cells, thereby enhancing local and systemic delivery of both free and bound drugs across the gut. This chapter provides a comprehensive description of the application of phenomenon of bioadhesion to nanoparticulate carrier systems and their role in efficient drug delivery.

**Keywords:** Bioadhesion, mucoadhesion, theories of mucoadhesion, mechanism of mucoadhesion, mucoadhesive polymers, mucoadhesive of nanoparticles, evaluation of mucoadhesive systems, applications

## List of Abbreviations

Alg	Alginate
AFM	Atomic force microscopy
API'S	Active pharmaceutical ingredient
CP	Carbopol
CMC	Carboxy methyl cellulose
CS	Chitosan
CLSM	Confocal Laser Scanning Microscopic

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DEAE	Dimethylaminoethyl
EC	Ethylcellulose
GIT	Gastrointestinal tract
HEC	Hydroxy ethyl cellulose
HPC,	Hydroxy propyl cellulose
HPMC	Hydroxy propyl methyl cellulose
MC	Methyl cellulose
MA	Maleic anhydride
NP	Nanoparticulate
PVA	Poly vinyl alcohol
PVP	Poly vinyl pyrrolidone
PAA	Phosphoric acid anodized
PEG	Polyethylene glycol
PC	Phosphatidylcholine
PLA	Poly(lactic acid)
PLGA	Poly(lactic-co-glycolic acid)
ROIs	Regions of interest

## 14.1 Introduction

Recent year's successful improvement in nanotechnology has resulted revolutionary enhancement in the field due to promising advancements in technology and their applicability in industry. In the context, research on bioadhesive systems has gained much attention because of their prolonged adherence to mucus, which is an integral part of each and every organ in human body which ultimately results in enhanced systemic and local bioavailability of the drug. The emergence of trouble free, non-invasive bioadhesive delivery systems along with nanotechnology has gained greater attention of researchers in developing nano-bioadhesive systems with the main aim of enhancing patient compliance and active pharmacokinetic modulation of the drug molecule. The drug molecule must reach the specific site of action in an efficient way to produce optimum drug effects. The strategy of drug delivery to specific site using advanced drug delivery system has improved the therapeutic efficacy of drug by enabling reduction in total dose of the drug administered, thus minimizing unwanted toxic effects. Due to smaller particle size, colloidal systems have a great potential for drug targeting which can be of advantage for parenteral and oral delivery of drugs to specific organ/target site.

Nanomedicine and nanodelivery systems is an emerging and rapidly growing science where materials having nanoscale range of 10–1,000 nm are used for the controlled delivery of diagnostic or therapeutic substances to specific target sites. Nanoparticles (NP) are colloidal particles of active ingredients which may be entrapped, encapsulated or adsorbed. They impart various benefits when included in formulation such as targeting drug to specific site, modulate pharmacokinetics of drug release, increase drug efficacy and safety [1, 2].

Oral administration of drug using conventional drug delivery systems is widely accepted, however due to its inherent short coming it is inefficient for effective delivery of poorly

soluble drugs and drugs undergoing enzymatic degradation. Extensive research in field of nanotechnology and potential of nanoparticles has evolved from concept to reality in effective delivery of drug which has enormous scope. Linking drugs to polymeric bioadhesive nanoparticulate systems help circumvent the problems of conventional drug delivery system. These carriers possess enhanced potential for increasing drug bioavailability which is attributed to its adhesive interactions inside the mucosa, particle uptake mechanism and slow transit time leading to increased concentration gradient (local) over absorptive cells, which ultimately improves local and systemic delivery of both bound and free drug across the gut [3, 4].

The process of bioadhesion that occurs within biological settings is called as “Bioadhesion” and at the mucosal membrane is called as “Mucoadhesion”. Both the terms have been used synonymously for the phenomenon of adhesion in body system. Polymers (natural or synthetic) which binds to the biological substrate due to presence of mucin in the physiological system namely buccal cavity, GIT, vaginal cavity, rectum, eye, ear, and nose were widely explored for the site specific delivery of therapeutic molecules in various pharmaceutical formulations [3]. The engineered systems incorporating bioadhesive coating to non-adhesive nanospheres show diversity in distribution to different tissues following uptake which suggest that surface chemistry of particles significantly influences the localization within the body thereby enhancing bioavailability *via* particle uptake mechanisms [5].

## 14.2 Mucous Membrane

The body membranes lining the gastrointestinal tract (GIT), sublingual cavities and buccal, soft and hard palates, nose, ear, eye, vagina and rectum are covered by thick jelly material referred to as mucin which contains 5% glycoproteins comprising of about 160 to 200 oligosaccharide chains in glycosylated portion while each unit of oligosaccharide contains 8 to 10 monosaccharide units. Mucin is synthesized by goblet cells and special type of endocrine cells along with mucous acini [6]. At physiological pH, the network of mucin exhibit negative charge because of presence of sialic acid and sulphate residues making the glycoprotein behave as an anionic polyelectrolyte. The composition of bioadhesive mucin thus consists of cross-linked, highly hydrated, flexible, linear and randomly coiled glycoprotein molecules with a negative charge. Mucous helps to form a linkage between the adhesive and the membrane [7].

## 14.3 Mucoadhesive Forces

The phenomenon of mucoadhesion occurs due to electromagnetic forces and electrodynamic interactions which could be of attractive or repulsive nature acting between molecules or separated portions of macromolecules. These forces have been classified into two main categories of long-range and short-range forces.

The short-range forces are generally attractive forces referred to as valence forces, however repulsive forces dominate if molecules are nonreactive and inert chemically [8].

Long-range attractive forces referred as van der forces contribute to physical phenomena of surface tension, friction, viscosity, cohesion/adhesion of solids and liquids [9]. The relationship of attractive and repulsive interactions can be expressed by Derjaguin Landau Verwey Overbeek (DLVO) theory which exists for all types of charged surfaces, such as muco-surfaces. Different theories, i.e. electronic, fracture, diffusion, adsorption and wetting have been extensively explained to understand the mucoadhesive forces [10, 11]. Complex interactions occur in the biological system due to the presence of macromolecules in aqueous media with high ionic strength. The contribution of electrostatic involvement is less in terms of force components like hydration forces, hydrophobic interactions and steric forces. Various forces involved with the mucoadhesive systems are compiled in Table 14.1 [12].

**Table 14.1** Types of forces and their attributes in mucoadhesive systems.

Sl. No.	Force	Principle	Attributes	Reference
1	London dispersion forces	Van der Waal's attraction	The attraction between temporarily induced dipoles in nonpolar molecules and interactions involve a force of about 0.5 to 1 Kcal/mol.	Whitesides <i>et al.</i> , 1991
2	Dipole-dipole interactions		Weak in nature because only partial charges are involved and have the force of 1 to 7 Kcal/mol.	Rawlins, 1984
3	Debye type forces		Interactions between permanent and induced dipoles with force of about 1 to 3 Kcal/mol.	Martin <i>et al.</i> , 1994.
4	Hydrogen bonding	Electrostatic interaction	The force is short range and highly directional and magnitude of bond energy is between 10 and 20 KJ/mol	Nylander <i>et al.</i> , 1994
5	Disulphide bridging	Strong covalent interaction	Showed the strongest mucoadhesive properties via thioldisulphide exchange reaction and an oxidation process	Leitner <i>et al.</i> , 2003

(Continued)

**Table 14.1** Types of forces and their attributes in mucoadhesive systems.

Sl. No.	Force	Principle	Attributes	Reference
6	Hydration forces	Short-range repulsive interaction	Originated from the binding of water molecules to polar surface sites and prevents contact even in the absence of charge-charge repulsion	Claesson and Christensson, 1988
7	Electrostatic double-layer forces	Attraction and repulsion	Increases adhesion to negatively charged surfaces and assigned to less repulsion between the surface and the adhering cells	Larsson and Glantz, 1981
8	Hydrophobic interactions	Attractive interactions between non-polar molecules	The hydrophobic effect can be nullified to a certain extent by lowering the temperature of the solution to near zero degrees and strength of these interactions is about 0.37 kcal/mol.	Martin <i>et al.</i> , 1994
9	Steric forces	Repulsive interaction	The maximum possible number of molecular contacts between an adhesive and its substrate may be greatly restricted by the steric aspects of molecular geometry	Glantz <i>et al.</i> , 1999

## 14.4 Theories of Mucoadhesion

The mechanism of mucoadhesion has been described by four main theories;

### 14.4.1 Electronic Theory

It refers to differences between the electronic structures of mucoadhesive and mucus which leads to transfer of electrons between mucoadhesive and mucus which ultimately results in mucoadhesion. There is a formation of double layer of electric charges of attraction due to electron transfer at the interface of mucus and mucoadhesive [13].

### 14.4.2 Adsorption Theory

It explains the mechanism of mucoadhesion due to surface interactions among mucus substrate and polymer. Primary bonds like metallic, covalent and ionic bonds develop permanent interaction between substrate and polymer. The surface interactions (temporary) arise by van der Waals forces, hydrogen bond and hydrophobic interactions which are secondary in nature are comparatively larger than electronic theory described forces [14].

### 14.4.3 Wetting Theory

The theory is suitable only for low mucoadhesive or less viscous systems. It correlates the effect of spreadability of delivery system of drug across a biological substrate on adhesion. Less interfacial tension between substrate surface and mucoadhesive system enhances the wettability and spreadability. The polymer with similar functional group as of mucus layer results in greater polymer spreadability on mucosal surface because of increased solubility [15].

### 14.4.4 Diffusion Theory

The diffusion theory emphasizes on the interpenetration to an acceptable depth and physical involvement of mucus and protein polymer chains with mucoadhesive materials, which depends on their respective molecular weight, chain length, degree of cross linking, spatial conformation and flexibility [16]. The different theories of mucoadhesion along with their mechanism are given in Table 14.2 [4].

**Table 14.2** Theories of mucoadhesion.

Theory	Mechanism
Adsorption theory	Adhesive interaction among substrate surface depends upon the intermolecular forces such as hydrogen bond, van der Waals forces, etc.
Wetting theory	Solution affinity to the substrate is inversely dependent on contact angle
Mechanical theory	Liquid adhesives diffuse into the micro-cracks and irregularities of the substrate surface which leads to formation of interlocked structure which results in adhesion.
Electronic theory	Transfer electrons among surfaces resulting in attractive forces
Cohesive theory	The intermolecular forces between the like molecules leads to bioadhesion
Diffusion theory	Diffusion of the polymer chains, present on the substrate surfaces, across the adhesive interface thereby forming a networked structure

## 14.5 Mechanism of Mucoadhesion

The proposed theories individually fail to explain the mucoadhesive mechanism. The complete process of mucoadhesion is a combination of different theories of wetting, spreading, dissolution and swelling of polymer (mucoadhesive) respectively at an interface, interdiffusion as well as interpenetration among the chains of polymer (adhesive) and the mucus or epithelial surface leading to physical cross-links and/or mechanical interlocking; polymers adsorption at the interface so the adhesive bonding beyond interface is possible and forms secondary chemical bonds among the mucin and polymer chains molecules [8]. The mechanism involved in mucoadhesion is represented in Figure 14.1.

## 14.6 Polymers Used to Prepare Mucoadhesive Nanoparticles

The phenomenon of bioadhesion leads to prolonged and close contact between the absorption site and the delivery device thereby enhancing efficiency of drug delivery, which brought an interest among researchers to develop and evaluate various bioadhesive polymeric systems. The potential advantages of using bioadhesive polymers in formulation of different drug delivery systems include:

1. Increased residence time of drug at absorption site.
2. Enhanced contact time with mucosa.
3. Localization at particular regions to increase bioavailability of drug.

The important physico-chemical characters of polymer that attribute to the potential adhesion of candidate include:

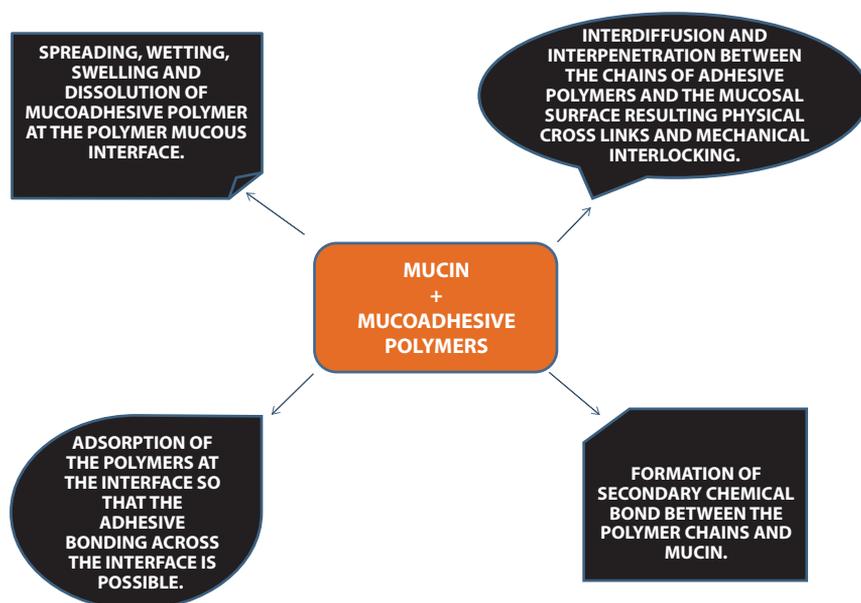


Figure 14.1 Representation of mechanism of mucoadhesion.

- Polymer with higher molecular weight (>100,000 Da) for chain entanglement as well as interpenetration.
- Molecules (hydrophilic) with higher functional groups forming hydrogen bonds with mucin.
- Anionic poly electrolytes having higher charge density of carboxyl and hydroxyl groups [17].

Studies of different polymers showed that various polymers exhibit varying mucoadhesive property with respect to their physico-chemical strength. Higher mobility of flexible polymer chain segment facilitates interpenetration of polymer chain and inter-diffusion. Similar surface characteristics to that of biological substrate provide to low interfacial free energy among adhesive and substrate. Though these properties may not be needed for bioadhesion, they are needed to increase the bioadhesive properties of the polymers [18]. For targeted drug delivery polymers with hydrophilic-functional groups like -COOH, -OH, -NH<sub>2</sub>, -SO<sub>3</sub>H are very suitable candidates for formulation. The functional groups of these polymers develop interaction with mucus via physical entanglement and chemical bonds

**Table 14.3** Classification of mucoadhesive polymers.

Criteria	Category	Examples
Source	Semi-natural/ natural	Chitosan, Agarose, Hyaluronic acid, Gelatin, Various gums (xanthan, guar, hakea, gellan, pectin, carragenan, and sodium alginate)
	Synthetic	<b>Cellulose derivatives:</b> CMC, MC, Thiolated CMC, HPC, HEC and HPMC, <b>Poly(acrylic acid)-based polymers:</b> CP, PEG, PC, PAA and copolymer of acrylic acid <b>Others:</b> PVP, PVA, Thiolated polymers
Aqueous solubility	Water-soluble	HPMC (cold water), CP, PAA, HEC, sodium alginate and sodium CMC
	Water-insoluble	Chitosan (soluble in dilute aqueous acids), PC and EC
Charge	Cation	Aminodextran, dimethylaminoethyl (DEAE)-dextran, chitosan, trimethylated chitosan
	Anion	sodium CMC, Chitosan-EDTA, CMC, CP, pectin, PC, PAA, sodium alginate and xanthan gum
	Non-ionic	Poly(ethylene oxide), Hydroxyethyl starch, PVA, scleroglucan, HPC and PVP
Potential bioadhesive forces	Covalent	Cyanoacrylate
	Hydrogen bond	Acrylates [hydroxylated methacrylate, poly(methacrylic acid)], PC, CP and PVA
	Electrostatic interaction	Chitosan

**Table 14.4** Influence of polymer properties on mucoadhesion.

Properties	Effect
Functional group	COOH, NH <sub>2</sub> , OH, SO <sub>4</sub> H groups favor mucoadhesion.
Molecular weight	Higher is the molecular weight (above 100,000), greater will be the bioadhesion.
Flexibility	Higher flexibility of polymer results in higher diffusion and hence greater mucoadhesion.
Chain length	Interpenetration increases with decrease in chain length.
Degree of hydration	Excess hydration leads to low mucoadhesion.
Degree of cross-linking	Increase in cross-linking decreases mucoadhesion.
Polymer concentration	<b>For semisolid:</b> Increase in concentration decrease mucoadhesion. <b>For solid dosage form:</b> Increase in concentration increase mucoadhesion.
Charge	Nonionic polymers possess less mucoadhesion than ionic, and cationic polymers exhibits more mucoadhesion than anionic.

leads to formation of cross linked network. Polymer chain length, degree of hydration and crosslinking, polymer concentration, charge, pH, etc. are some of other properties which can affect mucoadhesive nature of polymers. Cellulose derivatives such as Methyl cellulose, Hyroxy ethyl cellulose, Sodium Carboxy methyl cellulose, Hydroxyl propyl methyl cellulose, carbomers, chitosan, plant gums are hydrophilic in nature containing -COOH group and possess excellent mucoadhesive properties [19]. Anionic polyelectrolytes PAA has been widely used to design mucoadhesive delivery systems due to its ability to develop strong hydrogen bonding with mucin of the mucosal layer [20]. Chitosan a natural biocompatible and biodegradable cationic polymer is widely used since it undergoes electrostatic interaction with negatively charged chains of mucin, exhibiting mucoadhesive properties [21]. Nonionic polymers e.g. Poloxomer, HPMC, MC, PVA, PVP form viscous solutions and hence used as viscosity enhancing agent in ocular delivery [22]. List of mucoadhesive polymers and their effects are depicted in Tables 14.3 and 14.4 respectively [4, 23].

## 14.7 Ideal Properties of Mucoadhesive Polymers

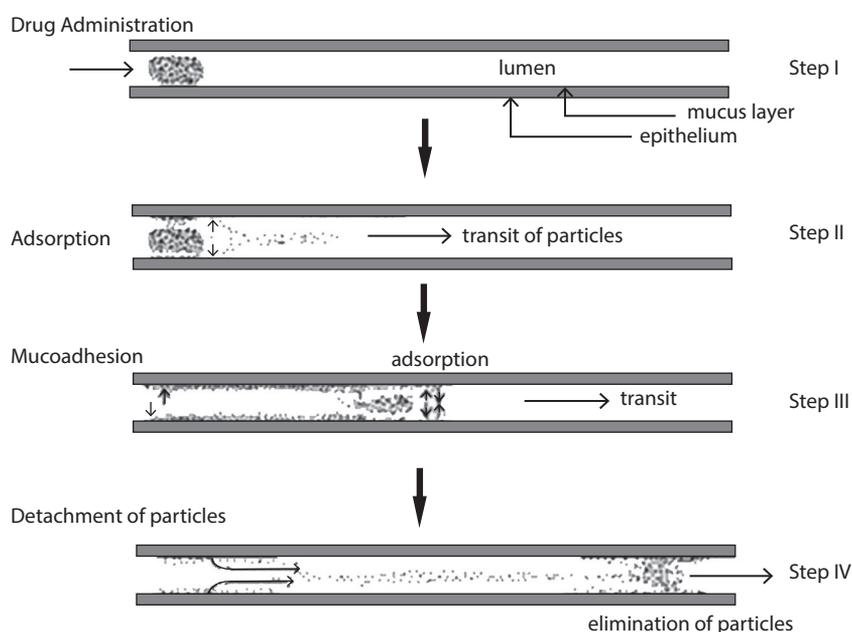
- Should rapidly adhere to mucosa.
- Should develop stronger interaction with epithelial tissue of mucin.
- Should possess spreadability, solubility, wetting, swelling and biodegradability properties.
- Should remain unaltered by the fluid dynamic conditions, pH changes and food.

- Must be feasible to incorporate in different dosage forms.
- Should possess adequate bioadhesive properties i.e. peel, tensile and shear strengths.
- Should be bioadhesive in both dry as well as liquid state.
- Should exhibit local penetration enhancement and enzyme inhibition properties.
- Exhibit acceptable duration of shelf-life.
- Should possess sufficient molecular weight.
- Should hold active groups of adhesive nature.
- Must sufficiently cross-link but not to the extent as to suppress groups forming bonds.
- Should have sufficient viscoelastic properties and should not breakdown at the mucosa [24].

## 14.8 Mucoadhesion of Nanoparticles

A description of the series of steps involved in bioadhesion of nanoparticles when administered orally in form of suspension is depicted in Figure 14.2.

1. A suspension of particles when orally administered immediately enters and reaches the mucosal portion of oral cavity.
2. The rapid and irreversible adsorption takes place at mucus layer where concentrated particle suspension acts as reservoir.



**Figure 14.2** Mucoadhesive behavior of colloidal particulate systems following oral administration.

3. The particle suspension at lumen perfused via intestine and extends continuously all parts of mucosa. The concurrent process of adsorption leads to covering whole of intestinal mucosa by particles (adherent).
4. At the proximal region separation of particles from mucosa commences and extends to distal region [25].

## 14.9 Preparation Methods of Mucoadhesive Polymeric Nanoparticles

### 14.9.1 Solvent Displacement Method

Solvent displacement method is also called as nanoprecipitation method. In the method preformed polymer gets precipitated from organic solvent which is diffused in to aqueous medium either in the absence or presence of surfactant [26–29]. In first step generally PLA polymer gets dissolved in solvent (water-miscible) with intermediate polarity, which leads to precipitation of nanoparticles. In the second step, this solution is injected in to the stabilizer (surfactant) containing aqueous solution with continuous stirring. Due to fast diffusion of solvent, there is a polymer deposition at the interface of organic solvent and water, leading to instantaneous formation of colloidal solution [30]. At the first stage of procedure, the phase separation was achieved by using miscible solvent which is also non-solvent for the polymer to facilitate the preparation of colloidal polymeric particles [31]. The method is depicted in Figure 14.3.

This is a simple technique of nanoformulations, applications limited only to water miscible solvents where the diffusion rate is sufficient to produce spontaneous emulsification. Generally the method well suited for lipophilic drugs due to the miscibility of the solvent in aqueous phase but inefficient in encapsulation of water soluble drugs.

This method was well adopted for the formulation of bioadhesive nanoparticles. Weiwei *et al.*, prepared bioadhesive PLGA-carbopol nanoparticles for local delivery of Rapamycin. PLGA is a well-known polymer to protect and control the release of drug molecule. Carbopol is a promising stabilizer as well as great bioadhesive material which possess good bioadhesive property, thus prolonging retention both *in vitro* and *in vivo* [32–34]. Juan, prepared the copolymeric nanoparticles of methyl vinyl ether with maleic anhydride (PVM/MA), which is commercialized as Gantrez from ISP, USA by using

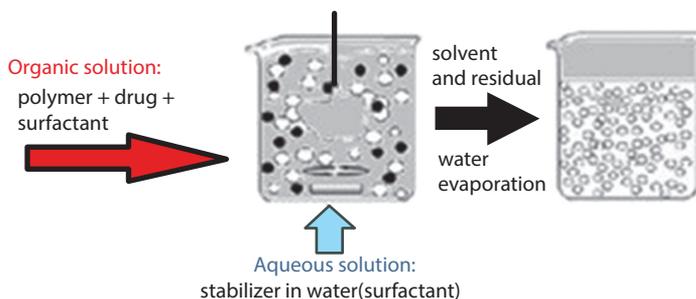


Figure 14.3 Nanoprecipitation method for nanoparticle preparation.

solvent displacement method. As PVM/MA co-polymer reacts with amino residues of molecule, this property was utilized for coating the nanoparticles. For coating prepared nanoparticles were incubated with gelatin or bovine serum albumin for 2 h; purified by centrifugation and lyophilization [35].

### 14.9.2 Surface Modification of Nanoparticles With Mucoadhesive Polymers

Addition or conjugation of excipients having mucoadhesive property, chemical alteration by co-mixing or charge induction, copolymerization and coating are the few evaluated techniques for improving the polymer strength of mucoadhesion. These modified polymers are then used for coating of drug carrying nanoparticles. Some polymers modified to enhance mucoadhesive property are loaded in Table 14.5 [36].

Wang *et al.* [37] formulated microspheres by using aminated gelatin. Due to enhanced chain flexibility and increased amino group content, these microspheres showed greater

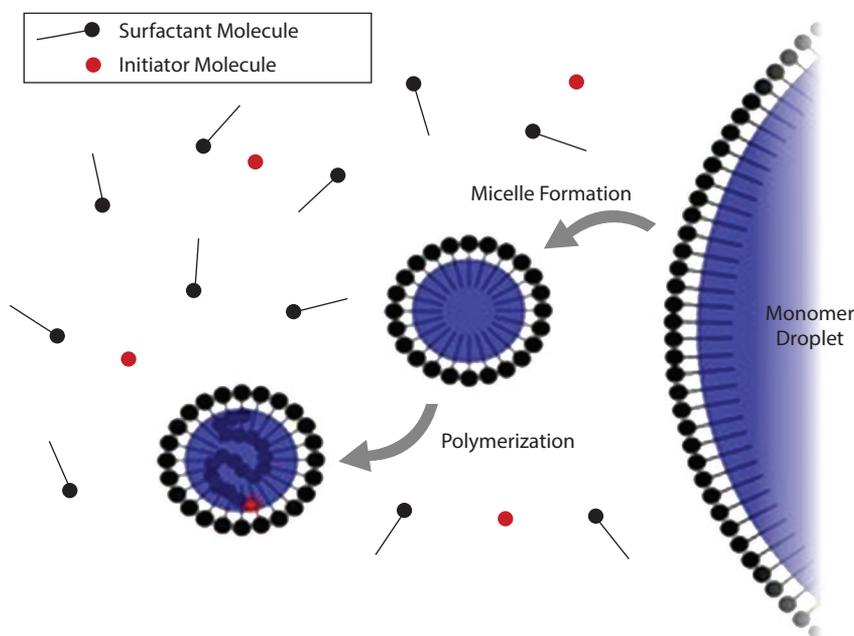
**Table 14.5** Modified mucoadhesive polymers.

Modified mucoadhesive polymer	Drug delivery system
Acrylated poly(ethyleneglycol)-alginate conjugate	–
Concanavalin-A ethylcellulose conjugate	Microspheres
Chitosan coated poly(lactide-co-glycolide)	Microparticles
Bioadhesive polymers: sodium carboxymethyl cellulose, Carbopol 974P and polycarbophil	–
Chitosan, sodium carboxymethyl cellulose and poloxamers (Lutrol® F68 and F127) containing Precirol® ATO 5 and Gelucire® 53/10 microparticles	Microspheres
Carbopol 934 and poly(vinyl pyrrolidone) (PVP) K30 were incorporated into the Eudragit patches	Transdermal patch
Aminated gelatin	Microspheres
N-trimethyl chitosan	Nanoparticles
Hydroxypropyl methylcellulose (HPMC), chitosan	Tablets
Carrageenan as mucoadhesive polymer and Eudragit RL PO CR polymer	Tablets
Amine-terminated poly(methyl methacrylate)	–
3,4-dihydroxyphenyl-L-alanine (DOPA) functionalized PEG polymers	–
Mucinated MCC	–
Film forming polymers: hydroxypropyl methyl cellulose, hydroxyethyl cellulose, chitosan, Eudragit and sodium alginate	Buccal films
Ethylcellulose as matrix and Carbopol 974P NF as mucoadhesive polymer	Microsphere

gastric mucoadhesion when compared to simple gelatin microspheres. Concomitant administration of mucoadhesive polymers like carrageenan, Carbopol 934, sodium carboxymethyl cellulose, polycarbophil were found to improve mucoadhesive strength of developed drug delivery systems. Albertini *et al.* [38] utilized mucoadhesive polymers sodium carboxymethylcellulose, polaxomers (F127 and Lutrol F68) and chitosan for the preparation of mucoadhesive Econazole nitrate microparticles for localized vaginal delivery. From all these polymers, polaxomers showed significant improvement in mucoadhesive strength and bioavailability of drug molecule. Manca *et al.* [39] prepared chitosan coated PLGA microparticles which exhibited enhanced drug loading efficiency, nebulization efficiency, mucoadhesive property and stability. Also chitosan coating controls the release of drug from particles.

### 14.9.3 Emulsion Polymerization

Emulsion polymerization is a prevalent commercial method for polymerization of various copolymers like chloroprene, vinyl acetate, and various acrylate co-polymers. The method is depicted in Figure 14.4. In this method, surfactant is first dissolved in water which is used as continuous phase until critical micelle concentration (CMC) is reached. The micelle interior provides site needed for polymerization. The oil phase a monomer which is insoluble in continuous phase is then added and stirred continuously to make an emulsion. The decomposition of an initiator forms radicals which emigrate in to micelle to react with monomer molecule which initiates polymerization process. Also to develop polymer chain between two monomer units, the radicals of monomer extends in the presence of another monomer. The process continues until full length (sum of monomer one and monomer two) of polymer chain is achieved [40].



**Figure 14.4** Scheme of emulsion polymerization.

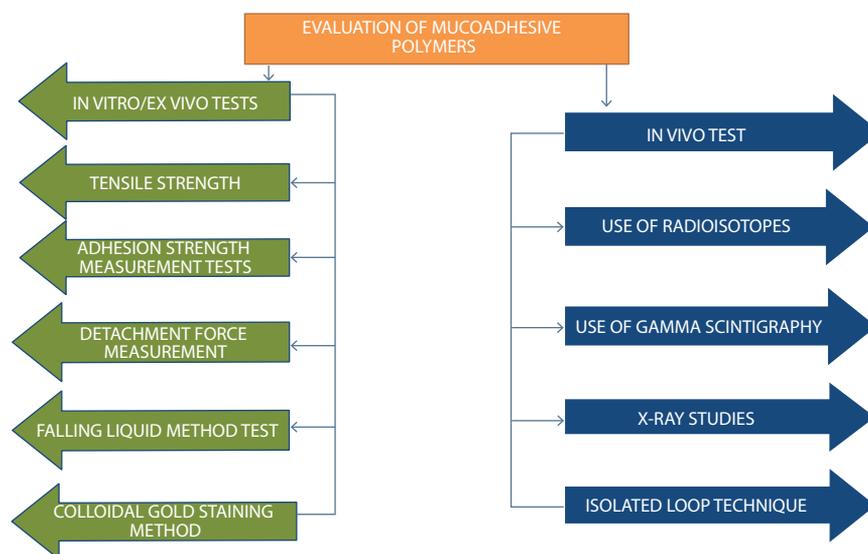
Fuying *et al.*, developed mucoadhesive NPs using Chitosan, poly(acrylic acid) and different grades of Carbopol (934PNF, 974PNF, 934PNF) as a mucoadhesive polymers by polymerizing methyl methacrylate using emulsion polymerization method. The NPs were suitable hydrophilic carriers for protein or peptide drugs [41]. Tapas *et al.*, prepared polyacrylic acid bioadhesive NPs by using reverse microemulsion polymerization method. By this method monodispersible, bioadhesive NPs were achieved for mucosal drug delivery [42]. Peptides and protein drugs can degrade before reaching the blood stream and thus they are not able to cross mucosal barrier this problem can be overcome by mucoadhesive drug delivery systems. Towards this effort, researcher prepared a polysaccharide chitosan (mucoadhesive polymer) coated methyl methacrylate NPs for proteins and peptides which were found to improve mucoadhesion by interacting with mucus glycoproteins [43].

## 14.10 Evaluation of Mucoadhesive Systems

Adhesion strength measurement is the main evaluation parameter for mucoadhesive delivery systems. Different *in vitro* and *in vivo* tests employed to measure the strength of adhesion of mucoadhesive polymers is enlisted in Figure 14.5.

### 14.10.1 *In Vitro* and *Ex Vivo* Tests

*In vitro* and *ex vivo* studies significantly contribute in successful development of bioadhesive systems with controlled release pattern as they demonstrate permeation, drug release, stability, compatibility and interactions among developed system & mucous membrane along with bioadhesive bond strength. Studies can facilitate simulation for different routes of drug administration like oral, nasal, buccal, gastrointestinal, vaginal, etc. Some of the *in vitro* as well as *ex vivo* tests which are highly accepted are discussed as below.



**Figure 14.5** Methods used for the evaluation of different properties of mucoadhesive systems.

### 14.10.2 Measurement of Tensile Strength

Texture analyzer, an analytical instrument that measures the tensile strength by measuring the total force needed to remove the test sample (formulation) from the membrane model. The test is performed by immersing filter paper in the mucin dispersion (8%). Then, the filter paper coated with mucin is brought in touch with hydrated samples of polymers in physiological solutions for a specified time period. Thereafter, the maximum force which is required to separate the filter paper from the polymer surface after mucoadhesive-bonding is determined [44].

### 14.10.3 Measurement of Detachment Force

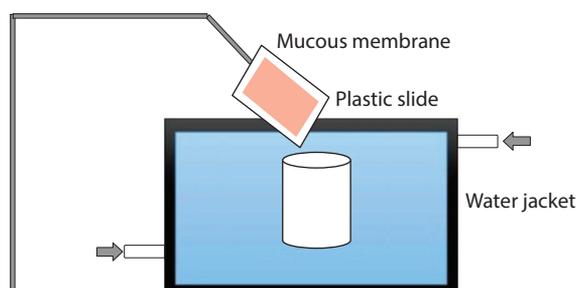
The force of mucoadhesion is measured as shear strength. In this method, the force needed to separate two glass slides placed parallel to each other, coated with mucus film and polymer respectively is measured. With the help of microforce balance, the glass plate is dipped in a sample of mucus under controlled and specified temperature conditions. Then the force applied to pull out the plate from sample is also measured under specified conditions [45, 46].

### 14.10.4 Falling Liquid Film Method

It is an *in-situ* quantitative method. In this method quantity of particles detained on the mucosal tissue is measured. Briefly, a nanosuspension or microsuspension is allowed to flow down along plastic slide in an inclined position of  $45^\circ$  relative to horizontal plane. The same is depicted in Figure 14.6. The quantity of adhered particles is calculated by noting the difference in weight of applied and flowed particles. Here the ratio of adhered micro or nano particles was calculated as percent mucoadhesion [47]. Coulter current method is also used for quantification [48].

### 14.10.5 Colloidal Gold Staining Method

In this method conjugate of mucin–gold interacts with hydrogel surface which results in a red coloration. The method came in to existence to compare mucoadhesive properties of different hydrogels quantitatively by measurement of color intensity developed. The optimum environment for mucin gold staining was fixed by examining pH-dependent stability of gold conjugates and mucin.



**Figure 14.6** Falling liquid film method to measure mucoadhesion.

Many other *in vitro* tests are used to determine the mucoadhesion strength. The effect of different polymers and mucin can be determined by using fluorescent probes. In this method lipid-bilayer of cultured human conjunctiva is labeled with pyrene (fluorescent probe). The change in intensity of fluorescence is proportional with polymer binding [49].

#### 14.10.6 Biacore System

This instrument is based on Surface Plasmon Resonance (SPR), a principle of optical phenomenon. The variation in refractive index with respect to solute concentration of a solution (which contacts sensor chip) SPR response is measured. If a known molecule is adhered to sensor chip surface or if analyte binds with the known molecule, the content of solute above the surface of sensor chip raises, resulting in SPR response [50]. While measuring the mucoadhesiveness of various polymers with BIACORE, each and every polymer is immobilized on sensor chip (CM5) surface and the mucin suspension was allowed to pass through sensor chip. If the particles of mucin bind to ligand molecules of polymer on the surface of sensor chip, the refractive index (RI) and solute concentration on the surface changes, which enhances the resonance unit (RU) response and when they dissociate, it leads to fall in the RU response [51].

#### 14.10.7 Confocal Laser Scanning Microscopic (CLSM) Method

The CLSM technique utilizes optical images with high-resolution and depth selectivity. CLSM design is a combination of two methods i.e., laser scanning and 3-D detection of fluorescent marker labeled biological objects. To measure the mucoadhesive strength of nanoparticles, fluorescent marker 1,1'-dioctadecyl-3,3,3',3'-tetramethylindole carbocyanine perchlorate is utilized. CLSM observation is considered to be the promising method in characterization of mucoadhesive properties of nanoparticulate drug carrier systems for oral drug administration [52].

#### 14.10.8 *In Vivo* Methods

##### 14.10.8.1 *Gamma Scintigraphy*

It is an excellent method to understand the clear pattern of *in vivo* distribution of different dosage forms. The method is mainly based on utilization of radioactive tracers incorporated into the drug, selected so that it permit gamma ray camera for its optimum detection. The selection of convenient label allows an *in vivo* identification of target site of formulations administered through various routes [53]. For the identification of formulation activities between the regions of interest (ROIs) scintigrams are used. ROIs which relate to target site of mucoadhesion are drawn on images of gamma at each point of time and ROIs relating counts are determined with the help of xeleris software [54].

##### 14.10.8.2 *X-Ray (GI Transit Time) Studies*

The GI transit time is determined by using barium sulphate as a radio opaque marker, which is coated on bioadhesive dosage forms to determine the GI transit time through

X-ray examination. The study conducted on mucoadhesive sustained release theophylline tablets, in which the barium sulphate-loaded tablets were taken to assess *in vivo* mucoadhesion. Rabbits (two) weighing 2.5 kg were chosen. Barium sulphate-loaded tablet was administered orally and X-ray photographs were taken at various time intervals [55].

#### 14.10.8.3 Isolated Loop Technique

To determine the GI transit time of microspheres, isolated ileal loop model in rats can be used. Bioadhesive property can be determined by measuring the average residence time of microparticles after injecting into the *in situ* perfused gut segment [56].

### 14.11 Evaluation Tests of Mucoadhesive Nanoparticulate Systems

Various methods have been introduced for evaluation of mucoadhesive properties of polymers tablets, however, a special method may be required for the evaluation of mucoadhesive properties of nanoparticle systems which are discussed below.

#### 14.11.1 Adhesion Test

The particulate systems are prepared by coating glass beads of size range 0.45–0.5mm or acetyl salicylic acid crystals with more than 630  $\mu\text{m}$  size with polymers (hydrophilic) such as Sodium carboxymethyl cellulose, Polycarbophil, Methyl cellulose, Hydroxypropylmethyl cellulose, etc. *In vitro* adhesion test is done by placing coated particles on stomach or rat jejunum in humid environment. The index of bioadhesion is the measurement of the percentage of particles retained on the tissues. *In situ* perfused ileal loop in rat can be used to demonstrate the mucoadhesiveness of multiple unit bioadhesive dosage forms [5]. Ensign *et al.* evaluated polymer-coated microspheres perfused with isotonic saline. Mean retention time was calculated by counting the number of particles collected with the help of residence curves of particles. The polymer coated particles possess greater mucoadhesive properties. For intestinal absorption study the authors also suggested an *in vitro* model of testing using rat intestine for adhesion studies [57].

#### 14.11.2 Atomic Force Microscopy

The bioadhesion studies of nanoscale systems can be performed by utilizing atomic force microscopy (AFM) which provides surface images of particles with high resolution. AFM can also measure forces due to single molecule interactions in pico to nano-newton range [58–60].

In this, the contact of the sample surface and probe produce force–distance curves represented by two segments, one is advancing curve corresponding to AFM piezo extension that reveals the mechanism of how the probe reaches the surface and another one is retracting curve that depicts how the probe separates from the surface. A different snap-off point is seen in the retracting force curve, which represents the force necessary to detach tip from sample surface which is the measured adhesive force. An illustrative force–distance curve is depicted in Figure 14.7.

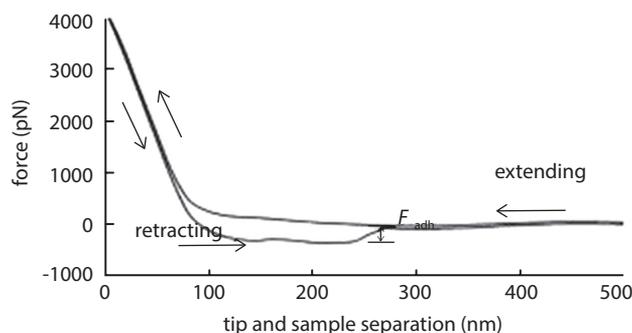


Figure 14.7 Atomic force microscopy force–distance curve.

### 14.11.3 Fluorophotometric Evaluation

Mucoadhesive property of surface modified polymeric nanoparticulate system can be measured by using isolated rat intestine sac [61]. Counting of submicron sized particles from nanosuspension is very difficult therefore, the total amount of nanoparticles adhered is measured with the help of fluorophotometer. For this nanoparticles needs to be labeled with fluorescence. In the test inverted rat intestinal sac is suspended in fluorescence labeled particles and gently stirred for 15–20 min. The quantity of nanoparticles adhered to the sac is measured fluorophotometrically after extraction with acetone.

## 14.12 Applications

The phenomenon of bioadhesion has an excellent research insights and it generally focuses on designing new devices with smart polymer for many APIs where the drug can be delivered in targeted as well as controlled manner. Considering different properties of polymer and environmental conditions, an optimum bioadhesive polymer may be engineered to fulfill the expectations of drug delivery system.

Nanomedicine is the science of nanotechnology for diagnosis and treatment of various diseases by utilizing nano-scale materials like biocompatible polymeric NPs for various purposes [62], delivery [63], diagnosis [64], sensory [65] and for actuation in living organisms [66]. The drugs with low aqueous solubility relate to biopharmaceutical issues which relate to low bioavailability on oral administration, low diffusion through membrane, need of more amount for IV administration, adverse effects preceding vaccination process.

In contrast, all above mentioned limitations can be conquered by utilizing nanotechnology concepts in the mechanism of drug delivery. Nanotechnology and mucoadhesive concepts are brought together to develop dosage forms for low soluble drugs, chemotherapeutic and immunotherapeutic agents, peptides etc. to treat various diseases at target site like oral, GI tract, ocular, nasal, rectal and vaginal [67]. Extensive research has been carried in areas of bioadhesive nanoparticulate carrier systems for drug delivery of which a few literature reviews are enlisted.

The pharmacokinetics of many drugs administration orally has been improved via of NPs. Vincamine bioavailability was about 25% in rabbits after administering in aqueous solution form, while it was increased up to 40% when drug adsorbed on poly (hexyl cyanoacrylate)

nanoparticles was administered. This is attributed to adhesion of nanoparticles to mucosa for longer period of time [68].

Costa *et al.* reported studies performed on chitosan (CS) coated alginate (Alg) NPs for permeation enhancement of daptomycin in ocular epithelium to provide an efficient antibacterial action. Epithelial (ocular) cell culture model was used for *in vitro* permeability test which results in potential increment in antimicrobial effect of nanoencapsulated drug. In ocular permeability study it was found that drug encapsulated with CS/Alg NPs was able to cross ARPE-19 and HCE cells. The study concludes that, the developed system leads to enhanced drug residence time in ocular epithelium [69].

Extensive research has been reported on chitosan-based nanomaterials for targeted and controlled delivery systems of drugs for different types of epithelia, including buccal [70], intestinal [71], nasal [72], eye [73] and pulmonary [74]. In one of the study, efficacy of isotonic solution (0.75% w/w) of HPMC containing CS/hyaluronic acid/sodium triphosphate was evaluated as well as NPs for ocular delivery of ceftazidime. The nanoparticles exhibited enhanced contact time of drug with ocular mucosa due to mucoadhesion leading to prolonged release of drug. The nanoparticles were nontoxic to HEK 239T & ARPE-19 tested cell lines. The NPs also preserved the antibacterial activity, thus making the formulation promising for the administration of ocular drugs with improved mucoadhesive properties [75]. Patil and Devarajan prepared Alg-NPs containing insulin using nicotinamide as permeation agent to reduce the glucose level in serum and increase the serum insulin level in diabetic rats. NPs administration in presence of nicotinamide sublingually (5 IU/kg) showed greater bioavailability. Thus the developed NPs were proved to be promising insulin carriers for sublingual route [76].

### 14.13 Conclusion

The existence of nano-based drug delivery systems approved by FDA (since 1990) and their clinical trials has attained steadily growing potential in recent years. The large-scale pharmaceutical research on bioadhesive nanoparticles has moved from evolution of newer chemical molecules to the development of advanced drug delivery systems for existing entities for enhancement with respect to therapeutic effect, patient safety and patient compliance. The prospective of bioadhesive nanoparticles in therapeutics have modernized the ability to diagnose disease and combine with treatment of disease. However, regulatory mechanisms for safety and toxicity assessments are the needs of further development in the future.

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# Mono and Multi-Stimuli Responsive Polymers: Application as Intelligent Nano-Drug Delivery Systems

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## **Abstract**

Stimuli-responsive polymers are one, which exerts a sharp and reversible transition in physical/chemical properties in response to tiny variations in environmental conditions. This type of polymer response is affected by different stimuli which were classified as internal stimulus (e.g. pH, redox potential, lysosomal enzymes and glucose) and external stimulus (e.g. light, magnetic field, temperature and ultrasound). The mono, dual or multi stimuli responsive polymers respond to a single, addition of two or more than two stimuli respectively. In this ambience, different “intelligent” polymeric nanoparticles which swell, dissolve and/or disintegrate as a response to external or internal stimulus have been actively developed to achieve enhanced release of drug at the target site. With the aim to further enhance release performances of intelligent nanoparticles, novel dual as well as multi-stimuli responsive nanoparticles which respond to a combination of two or more signals such as pH/redox, pH/temperature, pH/magnetic field, temperature/pH/redox, temperature/pH/magnetic, pH/redox/magnetic etc. have gathered much attention in the fields of drug delivery. In this chapter we highlight recent exciting developments in dual and multi-stimuli responsive polymers and their applications in nono-based delivery systems with a main focus on the release profile and therapeutic benefits in different disease conditions.

**Keywords:** Stimuli responsive polymers, dual responsive polymers, multi-responsive polymers, pH responsive, temperature responsive, light responsive, magnetically responsive, stimulus

## **List of Abbreviations**

BCS	Biopharmaceutical Classification System
DDS	Drug Delivery Systems
GIT	Gastrointestinal Tract
CST	Critical Solution Temperature

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UCST	Upper Critical Solution Temperature
PNIPAM	Poly (N-isopropylacrylamide)
PEGMA	Poly Ethylene Glycol Methacrylate
MSN	Mesoporous Silica Nanosphere
PLGA	Poly(D,L-lactide-co-glycolide)
AuNPs	Gold Nanoparticles
CCK8	Cell Counting Kit 8
MF	Magnetic Field
MDDS	Magnetic Drug Delivery System
EVAc	Ethylene Vinyl Acetate Copolymer
SCM	Single Constant Magnet
VMFS	Varying Magnet Field Systems
MRI	Magnetic Resonance Imaging
PLA	Poly lactide
PCL	Poly ( $\epsilon$ -caprolactone)
GSH	Glutathione
CS	Chitosan
MBA	N,N-methylenebisacrylamide
CS-g-PNIPAM	Chitosan-graft-Poly (N-isopropylacrylamide)
DMA-st-MAABO	N-dimethylacrylamide -st- 5-Methacrylamido-1,2-benzoxaborole
ICG	Indocyanine Green
DOX	Doxorubicin
NIR	Near Infrared Radiation
TDN	Triple-responsive Nanocages
LCST	Lower Critical Solution Temperature

## 11.1 Introduction

Smart or intelligent materials are those which possess the intrinsic ability to respond for the stimuli, thus these are also called as stimuli-responsive materials. These constitute one of the widely emerging and appealing classes of materials. Most leading category of intelligent materials is polymeric materials, because polymers are cheaply available and can be tailored easily than that of ceramics or metals [1]. The polymeric smart materials are those which exhibit a sharp and reversible variation (transitions) in their physical or chemical properties as a response to small changes in its environmental conditions [2]. The polymer is affected by various stimuli which are mainly classified in to two types.

**Internal stimuli**—In this any biological factor acts as stimuli to which polymer responds automatically. Ex.—Temperature, pH, redox potential, glucose concentration, antibody concentration, lysosomal enzymes, etc.

**External stimuli**—In this, polymers will not respond automatically to initiate their responsiveness. External application of stimuli is needed to change environment. Ex.—Temperature, magnetic field, electric field, ultrasound, light, etc. [3].

The response of polymer to stimuli is established in many ways: chain (individual) dimensions, size, secondary structures, solubility, surface characteristics and also the level of intermolecular association. These unique potentialities have been extensively applied for controlled drug delivery [4–6], biological coating technologies [7, 8], diagnostics [9, 10], biosensors [11, 12], chromatographic separations [13, 14], tissue engineering [15, 16], etc.

Nanoparticles are particles within the size range of 1 to 100 nm and some define them up to 1  $\mu\text{m}$ . These nano-structured carriers have tremendous potential to establish effective drug delivery systems which afford many advantages over conventional system of drug delivery by controlling drug release from nanoformulations, enhancing the bioavailability of BCS (Biopharmaceutical Classification System) class-II drugs, targeted delivery of drugs, prolonged circulation time of nanoparticles, reduced dose frequency and side effects of drugs [17]. Conventional drug carriers (delivery systems) physically encapsulate the drug molecules in the polymer matrix. The drug release mechanisms are either diffusion or degradation of polymer network which cause quick peak plasma concentration of drug, then steady state level is maintained followed by linear drug release pattern. These systems are far away from ideal drug delivery systems because in these systems site of drug delivery as well as site specific drug delivery cannot be precisely controlled. Various polymers with specific properties can be used to control the drug release. Such controlled/sustained drug delivery systems (DDS) keep the drug concentration in the therapeutic range, for a longer period of time. Despite the fact that, these controlled and sustained drug delivery systems are superior over conventional delivery systems, they remain insensitive for the varying metabolic phases of the body and are unfit to modify drug release as well targeting the drug to specific site or tissues. Delivery systems effective in responding to the physiological changes needs to be set up to adjust the release profiles of drug with varying physiological changes [18]. An excellent delivery system for drug is the one, which must respond to the various physiological needs, sense variations and modify the release pattern of drug respectively. As vehicles, ideal nanoparticles are pledged for possessing higher levels of drug loading and delivery of it to the particular therapeutic site or target cells (tissues) without any loss of drug on its path, while quickly release the drug at required (target) site of action.

At this point, various “smart or responsive” polymeric nanoparticles came in to existence. The response of these nanoparticles can be multifold: dissolve, collapse or swell, precipitate or dissolve, polymer degradation, variation in hydration phase, hydrophilic or hydrophobic surfaces of systems, conformational changes etc. Recently, nanoparticulate systems responding to an internal or external stimulus have actively been developed to achieve enhanced delivery of drug at the accurate time (temporal control) and/or at the target site (spatial control). Such bioresponsive systems are capable of distinguishing between healthy and diseased tissues and have resulted in better and upgraded *in vitro* and *in vivo* release profiles of drug. With the aim to further enhance release profiles of intelligent nanoparticles, novel dual as well as multi-stimuli responsive nanocarriers have achieved much recognition in the areas of drug delivery. By tuning the formulations with smart polymers or polymers chemical moieties, the responsiveness to the particular stimuli can be controlled precisely. In this chapter we highlight current inspiring evolutions in dual as well as multi-stimuli responsive polymers and their utilization in nano-based delivery systems with a main focus on the release profile and therapeutic benefits in different disease conditions.

## 11.2 Smart or Stimuli-Responsive Polymers for Drug Delivery

The stimuli-responsive polymers are classified in to three major categories.

### 11.2.1 Mono-Stimuli Responsive Polymers

Mono-stimuli responsive polymers are one which responds to only a single stimuli. Ex.—temperature, pH, redox potential, magnetic field, electric field, etc.

### 11.2.2 Dual-Stimuli Responsive Polymers

These are those which respond to a blend of two triggers (stimuli). Ex.—pH and temperature, pH and redox potential, magnetic field and temperature, light and temperature, pH and magnetic field, dual pH, etc.

### 11.2.3 Multi-Responsive Polymers

These are those which respond to a combination of more than two triggers. Ex.—pH, temperature and redox potential; pH, temperature and magnetic field; redox, pH and magnetic field; redox, temperature and guest molecules, etc.

In this chapter, extensively studied and important mono, dual as well as multi-responsive polymers and their relative applications in the field of drug delivery systems are discussed in brief.

### 11.2.4 pH Responsive Polymers and Delivery Systems

To evolve pH-responsive drug delivery systems, one should understand the changing physiological conditions of the body. For instance, pH variations occur throughout the GI tract, however many precise pH changes can be observed in different body tissues and the same are enlisted in Table 11.1 [19, 20]. Since pH variations occur inside the body, this stimuli was

**Table 11.1** pH variations in several tissues and cellular regions.

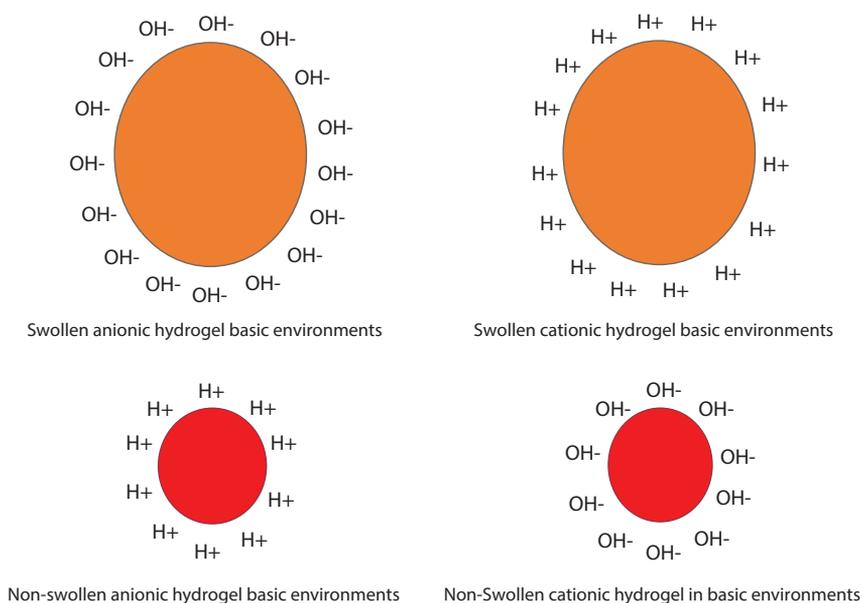
Body tissue or cellular regions		pH Range
GIT	Stomach	1.5–2.0
	Small intestine	5.5–6.8
	Colon	6.4–7.5
Blood		7.35–7.45
Extracellular tumor		6.0–7.0
Chronic wounds		5.4–7.4
Endosomes		5.0–6.5
Lysosomes		4.5–5.0

exploited to provide a response to some tissues or cellular compartments. Further, pH can be changed locally with particular substrates and this concept can be utilized for altering release pattern of drug.

Another important application of pH responsive polymers is modeling carrier for the delivery of insulin to treat diabetic patients. Compared to other drugs, delivery of insulin to patients differs, as insulin needs to be delivered with exact dose at the right time when it is required for the body. Various types of devices were explored to meet this purpose. All these devices were fitted with a glucose sensor system in it. Glucose oxidase catalyses glucose into gluconic acid in blood stream (glucose rich environment) after food, which reduces pH approximately to 5.8. The enzyme glucose oxidase is extensively utilized for glucose sensing and thus it is possible to apply various types of pH responsive polymeric systems for modulating insulin delivery.

Polymers with pH responsive nature are generally polyelectrolytes bearing pendant weak basic or acidic groups which either release or accept protons as a respond to its surrounding pH changes. This is a result of ionization of these groups. If the polymer structure is linked with ionizable groups, the pH variations lead to conformational changes in the soluble polymers that ultimately change the swelling property of polymer hydrogels. The swelling and deswelling behavior of pH-sensitive hydrogels is attributed to the ionization degree (protonation or deprotonation) of polymer groups. Upon exposing polymer hydrogels to solutions (aqueous) with sufficient pH & ionic strength, acid or basic groups undergo ionization and establish uniform changes on the network of polymer, leading to electrostatic repulsive forces which are mainly responsible for the swelling or deswelling (pH-dependent) of the polymer hydrogels, that ultimately modulate the release of drug from hydrogel [21].

Polyacidic pH-responsive polymers don't swell at low pH values, as their acidic groups will protonate and unionize. But by increasing pH value the negatively charged polymer



**Figure 11.1** The pH-responsive swelling behavior of anionic and cationic hydrogels.

undergo swelling. The visa-versa swelling behavior is observed in polybasic pH responsive polymers, since here basic groups undergo ionization at low pH values. The same is represented in Figure 11.1 and in Table 11.2 different types of pH responsive polymers, their nanoformulations, loaded drug and target site are enlisted.

**Table 11.2** Types of pH responsive polymers and their applications in drug delivery.

Polymer type	Example of polymeric systems	Drug	Target site or controlled release	Reference	
<b>I. Polymers bearing anionic groups</b>	Salecan- <i>g</i> -PAA hydrogel	Doxorubicin	Controlled release	22	
	1. Poly(acrylic acid) (PAA)	(PAA-co-vinylamine) hydrogel	Doxorubicin	Controlled release	23
		(PAA- <i>b</i> -PCL)-poly (acrylic acid)- <i>b</i> -polycaprolactone	Gambogenic acid	Controlled release	24
		Carboxymethyl Chitosan-Grafted-Poly (Acrylic Acid)	5-Fluorouracil	Colon targeted	25
2. Poly(methacrylic acid) (PMAA)	PMAA (polymethacrylic acid) template and N-vinyl pyrrolidone (N-VP) monomer	Rifampicin and Doxorubicin	Controlled release	26	
	polymethacrylic acid-chitosan-polyethylene glycol (PCP) nanoparticles	Insulin and bovine serum albumin	Oral peptide delivery	27	
	methacrylic acid and 2-ethyl hexyl acrylate (co-polymer) nanogel	5-Fluorouracil	Colon targeting	28	
3. Polysulfonamides	poly(L-cystine bisamide- <i>g</i> -sulfadiazine)- <i>b</i> -PEG (PCBS- <i>b</i> -PEG)	Doxorubicin	Tumor targeting	29	
<b>II. Polymers bearing cationic groups</b>					
1. Poly(N,N-dimethylaminoethyl methacrylate)	(3-Aminopropyl) triethoxysilane (APTES), alpha-bromoisobutyryl bromide (BiBB), and poly (N,N-dimethylaminoethyl methacrylate)	Diphenhydramine	Controlled release.	30	

(Continued)

**Table 11.2** Types of pH responsive polymers and their applications in drug delivery. (*Continued*)

Polymer type	Example of polymeric systems	Drug	Target site or controlled release	Reference
(PDMAEMA)	(PDMAEMA) chain. (halloysite nanotube)			
2. Poly(2-diethylaminoethyl methacrylate) (PDEAEMA)	poly( $\epsilon$ -caprolactone)-b-poly(2-(diethylamino) ethyl methacrylate)-b-poly(poly(ethylene glycol) methyl ether methacrylate) (4/6AS-PCL-b-PDEAEMA-b-PPEGMA) micelles	Doxorubicin	Controlled drug delivery	31
3. Poly(2-vinylpyridine) (PVP)	poly(2-vinylpyridine)	Folic acid	Intracellular targeting	32
4. Poly(vinylamine) (PVAm)	Poly(L-glutamic acid) dendrimers with a polyhedral oligomeric silsesquioxane (POSS) nanocubic core.	Doxorubicin	Tumor targeting	33
<b>III. Natural polymers</b>				
1. Chitosan	chitosan-coated mesoporous silica nanospheres.	Ibuprofen	Controlled release	34
	Chitosan microparticles	dexamethasone	Tamoxifen	35
2. Albumin	Albumin nanoparticles	Doxorubicin and Curcumin	Cytosol	36
3. Gelatin	gelatin-based nanospheres	Diclofenac sodium	Controlled release	37
	Gelatin based pH-sensitive hydrogels	Ketoprofen	Colon-specific	38

*(Continued)*

**Table 11.2** Types of pH responsive polymers and their applications in drug delivery. (*Continued*)

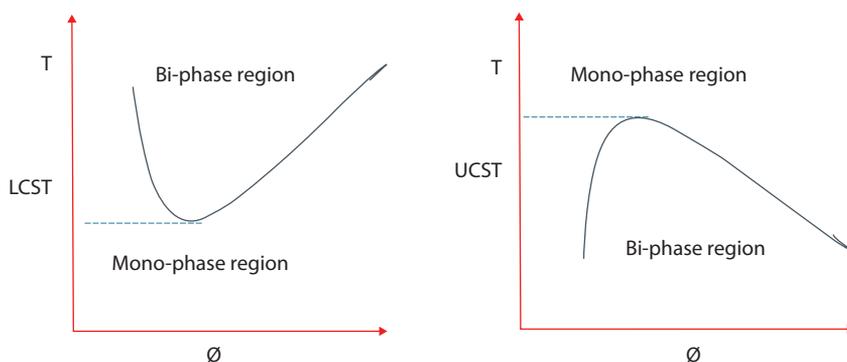
Polymer type	Example of polymeric systems	Drug	Target site or controlled release	Reference
Marketed pH responsive polymers				
Eudragit® L100-55	Composed poly(methacrylic acid) and polyethylacrylate	Paclitaxel	Duodenal drug release	39
Eudragit® S100	Composed poly(methacrylic acid) and polyethylacrylate	Insulin	Jejunum and Ileal release	40
Cervidil®	Composed of polyoxyethylene and urethane	Dinoprostone	Veginal delivery	41

### 11.2.5 Temperature Responsive Polymers in Drug Delivery

Temperature responsive hydrogels are most extensively studied category of stimuli responsive polymeric systems for delivery of drug. These hydrogels are very useful biomaterials which show sol to gel transformation upon increasing the temperature. The physiologic and ambient temperatures are considered to be an optimum and critical temperature range for hydrogel systems. Initially hydrogels will be in sol form and as soon they are exposed to temperature they get transformed in to gel form. This sol-to-gel transformation process is called as curing. This process includes the covalent cross links formation among polymer chains to create macromolecular network [42]. The development of thermo responsive device into clinically efficient systems, lack in modifying the device (implanted) temperature. However, the changes in temperature must be quick to control structural modifications in the polymeric systems. To eschew damage to surrounded normal tissue the temperature changes should be restricted to the carrier. Certain methods for temperature changing includes heating pads, exothermic chemical reactions and non-targeted light are being investigated [43].

Temperature responsive polymers are mainly categorized in to two types based on the systems exhibiting critical solution temperature (CST) at which there is a change in polymer and solution phase with respect to their composition. The systems which exerts single phase above specific temperature and separation of phase (two-phase) below it will exhibit UCST (upper critical solution temperature). While, the system of polymer solution which exhibit two phase above particular temperature and emerge as single phase below it will possess LCST(lower critical solution temperature) as shown in Figure 11.2 [1].

To develop drug delivery systems mainly polymers exhibiting LCST (approximately 20–40 °C) are generally used thus, will focus on polymers with LCST. Generally, polymers solubilizes with increasing temperature but in case of thermo-sensitive polymers exhibiting LCST, the polymer begin to insoluble at higher temperature and thus hydrogels of such polymers shrinks with respect to temperature rise above LCST. This swelling behavior is called as inverse temperature dependency which occurs because of dominating hydrophobic



**Figure 11.2** Representation of LCST and UCST concepts of temperature responsive polymers.

interactions. Polymer chains of these hydrogels are consisted of either hydrophobic groups or hydrophilic and hydrophobic segments. Hydrogen bonding among hydrophilic segments of polymer and water results an increased dissolution below LCST and as temperature rises above LCST, the hydrophobic segments will strengthen leading to shrinkage of hydrogels due to association of inter polymer chains [44, 45]. Raise in temperature is associated with several disease conditions, especially in cancerous tissues where the temperature will be 1 to 1.5 °C more than normal temperature of human body and at wound sites (chronic and surgical wounds) temperature will also be always more than normal body temperature depending upon the severity of infection [46]. Temperature responsive polymeric carriers have been hired to perform drug release in environments having temperature higher than physiological temperature. Temperature changes that trigger drug delivery are either because of enhanced body temperature in disease conditions or triggering drug release by external application of heat. Temperature responsive polymers may be used alone or in combination with other polymers (monomers) to achieve controlled or site specific drug delivery.

Poly (N-isopropylacrylamide) (PNIPAM) is the most hugely utilized thermo-responsive polymer with LCST of 32 °C which can be adjusted by co-polymerization of PNIPAM either with hydrophobic monomer to decrease LCST or with hydrophilic monomer to increase the LCST. Nevertheless it should be known that LCST modulation thermo-responsive polymers also depends on the solvent quality and salt concentration, architecture and molecular weight of polymer as well as size and chain length of side groups [47–50]. For instance, PEGMA (PEG-methacrylate) polymers possessing PEG side chain (consisting of 2 to 10 ethylene-oxide units) and its LCST differs with length of ethylene oxide side chain [51]. Obviously, optimization of temperature responsiveness (LCST) is must for intended application. Among all stimuli-responsive systems, temperature responsive DDS's afford greatest potential over other stimuli-responsive systems due to versatile design, ability of targeting passively, phase transition tenability and *in-situ* phase transition. Some of the temperature responsive polymeric carriers and their applications in DDS are enlisted in Table 11.3.

### 11.2.6 Light Responsive Drug Delivery Systems

Light is an external stimuli which is cheap and can be applied and altered instantaneously. Light (visible or ultraviolet) responsive carriers for drug delivery have been built by

**Table 11.3** List of temperature responsive polymeric nano-formulations.

Temperature responsive polymeric nano-formulation	Drug release mechanism	References
(PNIPAAm-co-oleic acid)-g-chitosan nanoparticles	Thermo-responsive release of erlotinib at LCST of about 36 °C.	52
folate-conjugated PNIPAm-N,N-dimethylacrylamide micells	Thermo-responsive release of paclitaxel at tumor site	53
(PNIPAAm-co-N,N dimethylacrylamide)-b-poly(D,L-lactide-co-glycolide) micelles	Thermo-responsive and controlled release of paclitaxel at 39.5 °C temperature than at 37 °C in breast carcinoma cells	54
(PNIPAAm-co-((2-dimethylamino) ethyl methacrylate))-based nanoparticles	camptothecin release rate at 42 °C was higher as compared to release rate at 37 °C.	55
poly(N,N-diethylacrylamide)-N-vinyl-2-pyrrolidone hydrogels	Thermo-responsive deswelling at pH 1.4 and pH 6.8 leads to release of Aminophylline and increased crosslinker amount provides lag time prior to drug release which results in specific and delayed drug release in the intestine.	56
Folate-Conjugated Poly(N vinylcaprolactam)-block-Poly(ethylene glycol) micelles	5-Flurouracil release was slow at 25 °C and at 37 °C the release was in controlled manner.	57
(PNIPAAm-co-((2-dimethylamino)ethylmethacrylate)) nanoparticles	camptothecin (SN-38) release rate at above LCST (42 °C) was greater than that at below LCST (37 °C). Thus by applying heat the drug release could be controlled	58
chitosan-g-poly (N-vinylcaprolactam) nanoparticles	The <i>in vitro</i> drug release was higher at above LCST as compared to release at below LCST	59
Pluronic F127-Chitosan nanocapsules	Tiny molecule release can be achieved with cryotherapy (heating and cooling between 37 °C & at hypothermic temperature)	60
poly(methyl vinyl ether-co-maleic anhydride)—Pluronic® F127	Thermo-responsive controlled release of bovine serum albumin and Leishmania	61

polymers composed of photoreceptor (photochromic chromophore), functional group and light sensitizers like triphenylmethane, stilbene and azobenzene [62–64]. These systems when triggered by light results in macroscopic changes within the system leading to controlled drug release with respect to exact quantity, exact time and at exact site. Polymers with light responsiveness are widely applicable in the development of ophthalmic DDSs, optical switches and display units because of rapid sol-gel delivery system. The release of payload from light responsive systems occurs only when it is irradiated by light source externally. One of the main drawbacks of such system is if patients are exposed to sunlight, the system activates and starts releasing drug. To avoid early release of drug patient has to stay in dark for some period of time which is known as “dark toxicity” which is also a disadvantage of photodynamic therapy. Examples for photosensitive polymers are leucoderivative molecule Bis(4dimethylamino) phenylmethyl leucocyanide and Triphenylmethane which possess UV light responsiveness. These polymers swell in response to light and release the drug. Upon removing the light they again undergo shrinkage and stop drug release from the system.

Juan *et al.* developed photoresponsive-Au-nanoparticles capped-mesoporous silica nanosphere (PR-AuNPs-MSN) for paclitaxel. Here the MSNs were capped efficiently with PR-AuNPs and there was zero premature drug release. To regulate the release of drug low power (10 min at 0.49 mW/cm<sup>2</sup>) light irradiation in biocompatible conditions was demonstrated in this study. Thus it was concluded that it is an efficient carrier material for intracellular delivery of toxic agents [65]. Cabane and co-workers developed an amphiphilic poly (methyl caprolactone)-O-nitrobenzyl-poly(acrylic acid) copolymeric polymersomes. Here O-nitrobenzyl is light sensitive linker attached between two polymers which acts as an initiator to grow polymer segments. Also the synthesized polymerosomes (self-assembled) get activated upon irradiation by UV rays, alter the morphology as well as size, yield tiny micellar like structures and ultimately release the payload. The system versatility was checked with low molecular weight substances like ATTO655 dye and fluorescein and also with fluorescent protein. By altering the intensity of UV light, the controlled payload release was achieved thus the system has a suitable applicability for different types of molecules and DNA [66]. Yao *et al.* developed hybrid lipid-polymers combined of PLGA (poly(D,L-lactide-co-glycolide)) core used to load anti-cancer drug doxorubicin, soybean lecithin monolayer between core & cell and anti-biofouling polymeric shell (photoresponsive). This shell maintains the stability of nanoparticles. Upon irradiation by light polymeric shell detaches from nanoparticles and thus nanoparticles stability decreases which triggers release of doxorubicin from nanoparticles. Release studies demonstrated excellent light responsive controlled drug release up to 76% in the presence of light and only 10% drug release in the absence of light irradiation. Further, CCK8 assay confirms efficient killing of cancer cells upon light irradiation [67]. Sreejivungsa *et al.* investigated monolayer-gold nanoparticles (AuNPs) presenting light sensitive ligands, as potential carrier for drug where drug release was initiated by using UV light. Upon irradiation with UV light cleavage of dinitrobenzyl linker takes place, thus the hydrophobic molecules (*Goniiothalamus elegans*) entrapped in monolayer compartments release. *In vitro* release studies demonstrated excellent light responsive controlled drug release up to 83% in the light and only 19% release in the absence of light irradiation. This concluded an alternative way to encapsulate drugs noncovalently followed by their controlled release by UV irradiation [68].

### 11.2.7 Magnetically Responsive Polymeric Drug Delivery Systems

Magnetic based nano-carrier delivery is most potential technique to deliver drugs to a local target site. While designing such systems due consideration should be given to some factors like magnetic properties of nano-carriers, field geometry, binding capacity of drug, magnetic field (MF) along with some physiologic parameters like blood flow rate, local vascular supply and body weight [69]. Targeting by magnetic field involves attraction of magnetic nano and micro-particles towards the source of external magnetic field. Due to gradient of magnetic field, translation force exhibited on the drug-complex which traps and pulls the complex in magnetic field at target site [70, 71]. There are three important advantages of magnetic drug delivery system (MDDS): It views the delivery vehicle, [72] drug release and tissue ablation can be modulated by thermal heating [73], it guides the carrier movement via magnetic field. Different magnetic drug carriers such as maghemite, carbonyl iron, magnetite and cobalt ferrite are non-toxic, biocompatible and non-immunogenic [74]. Radiological and chemotherapeutic drugs can be delivered at target site (tumor) without any adverse or toxic effects on body and surrounding normal tissues. In this system elastic polymers (usually ethylene vinyl acetate polymer) are incorporated with magnetic beads. Application of MF (oscillating) leads to polymer swelling that modulates release of drug by polymer matrix. The MDDS is administered (blood stream) to patients and it is stopped at target site with the help of magnetic field. The drug is then released slowly from the carrier under MF. Another application of MDDS is slowing down the delivery of oral drugs in GI tract. This is done by filling capsules and tablets with magnetic substances. The bioactives like insulin & many macromolecules can be released continuously by incorporating them in magnetic carrier (ethylene vinyl acetate copolymer—EVAc). One more system consisted of EVAc–protein matrix having magnetic beads results in higher amount of drug release when exposed to oscillating-MF [75, 76]. The MDDS were mainly categorized in to two main categories: varying field systems and constant field systems.

#### 11.2.7.1 Static (Constant) Field Systems

System of static magnetic field is one where the magnetic field stays constant during the period considered. Based on source of MF obtained, static field systems can again be categorized into permanent and electromagnet systems. Single constant magnet (SCM) is generally used in clinical trials on animals, in which magnet is placed near lesion site. Attractive forces generated by magnet captures drug carrier in to magnet region to release the payload. Targeting activity of these systems is dependent on size and shape of magnet and compared to electromagnets, single magnet possess diverse shapes. Depalo *et al.* studied and compared the nanoparticles uptake by cells in ring shaped as well as square shaped magnets kept inside the cell culture by using similar magnetic induction. The results demonstrated that ring shaped magnet was significantly effective than square shaped one. One other researcher mentioned cylindrical shaped magnet effective than rectangular shaped magnet [77, 78].

Though single constant magnet is easy to apply, in drug targeting process properly designed MF distribution with enhanced MF and more precise field distribution is highly suitable for drug targeting. SCM may reach up to 1.5 T and to increase field intensity more

number of constant magnets needs to be used. Among all designs Halbach array considered to be the best one. In this design MF is “squeezed” in one direction thus, there develops MF gradient between each side of array. By Halbach array MF can be reached up to 4–5T [79–81].

In another study a disc shaped (annular) assembly of constant magnets comprising of eight sphenoid block constant magnets with similar size, shape and the magnetization directions for contiguous two constant magnets were 135 °, which reproduced capturing process and ended with results showing larger particles are easy to capture [82]. Riegler *et al.*, compared the four types of magnets and different magnetization processes in drug targeting. The results concluded that efficient magnet design was annular Halbach array with twelve constant magnets. The magnetization of four constant magnets was done along axial position (direction) of the assembly and inducted at the edges of assembly. Numerical simulations estimate (predict) that posterior tibial artery cells can be targeted by this magnet structure with targeting efficiency up to 6.25% [83].

#### 11.2.7.2 Varying Magnet Field Systems (VMFS)

In this system magnetic field varies along with time and based on MF source, these systems are again classified in to two categories: which are moving constant magnet system & varying field electromagnet system. To produce changing MF from constant magnet, the magnet must be moved constantly along the sample & movement (motion) may be rotational, translational or combination of both the movements. Another researcher utilized constant magnet which has rotational and translational movements simultaneously to direct magnetic particles movement linearly. The device developed was utilized to check the motion of magnetic particles [84]. Varying MF can be perceived by mechanical motion and current control. Practically, the mechanical motion of greater electromagnets is not convenient. This mechanical motion is replaced with the motion, thus the magnet exhibit relative motion [85–87]. But in many cases to attain field variation (supplemented by mechanical motion) it's preferred to change electric current. On the basis of superconducting coils, the systems of magnet chiefly utilize MRI facilities, which are generally constructed by superconducting coil, magnets (permanent) and/or many other supplementary devices to achieve delivery of drug. The other magnet systems used for targeting drug are based on Helmholtz/Maxwell coils and conventional coils.

#### 11.2.8 Other Stimuli Responsive Polymeric Nanoparticles

There are many other stimuli-responsive delivery systems which were studied by researchers like ultrasonically responsive, electrical field responsive, protein responsive, enzyme responsive, redox potential responsive, etc. Internal stimuli responsive DDS have acquired much attraction than that of external stimuli because of their suitability in therapeutic application, cost consideration and scale up of product. An overview of these stimuli responsive DDS are explained (using one or two examples) in Table 11.4 with formulation type and their mechanisms of drug release.

**Table 11.4** The different stimuli-responsive polymeric systems and their drug release mechanisms.

Stimulus	Formulation types	Mechanism of drug release	Reference
Enzyme	Nano-capsules, Hydrogels coupled with biocatalyst (glucose catalase) or enzymes (glucose oxidase)	Environmental changes (conversion of glucose to glucuronic acid in blood stream) results conformational changes in polymer that affects the enzyme activity as well as substrate access the pH decrease leading to insulin release.	20
	Lipophilic prodrug Retinoid attached liposomes	Drug release was triggered by secreting the enzyme phospholipase A2 (sPLA2) IIA as the lipid backbone of prodrug is degradable by these enzymes.	88
Inflammation	Hydrogels loaded with specific enzyme cleavage peptide generally human neutrophil elastase (HNE).	HNE (serine protease) is secreted by neutrophils at the inflammation site. HNE-sensitive peptides release from hydrogels occurs in the presence of HNE	18
Ultrasound	Doxorubicin loaded polymeric micelles	Upon applying low frequency ultrasound at tumor site trigger drug release by increasing the local temperature or causing cavitation. This also increases permeability through cell membranes.	89
	Fluoride anion modified nanogel of gelatin loaded with Adriamycin	Ultrasound frequency of 20 kHz triggers efficient drug release from the system	90
Electrical field	Nanoscale thin film incorporated with +vely charged gentamycin and -vely charged Prussian blue nanoparticles	Drug release is triggered and controlled by applying various anodic electric potential profile (at least +0.5)	91
	Polyelectrolyte polymeric hydrogels	Ionizable polymer groups make it pH & electrical field responsive. Hydrogel shrinks under the influence of electrical field leading to drug release.	20

(Continued)

**Table 11.4** The different stimuli-responsive polymeric systems and their drug release mechanisms. (Continued)

Stimulus	Formulation types	Mechanism of drug release	Reference
Redox potential	Disulfide bond bridged polymeric nanoparticles loaded with doxorubicin	The redox potential difference in intracellular (reductive) & extracellular (oxidative) regions acts as a trigger to drug release. At intracellular regions the polymers degrade resulting in drug release.	92

### 11.3 Dual and Multi-Stimuli Responsive Drug Delivery Systems

Significant benefits have been attained from mono-stimuli responsive polymeric nano-carriers in both *in vitro* and *in vivo* performances. Despite the accomplishment of many advancements, the area of mono-stimuli responsive biomaterials still possess many drawbacks which are as follows;

- They focus only on single stimulus but many disease conditions may explore two or more than two triggers for biomedical application of the systems. For ex-tumor tissues/cells provide varying intra and extracellular pH gradient compared to normal tissues, temperature differences between normal and cancerous tissues.
- Behavioral change in macromolecule (proteins and nucleic acids) many times is a result of its response not to a one of the factor, but to a mixture of environmental changes, thus mono-responsive system may not work efficiently for them.
- External application of stimulus like temperature, light or magnetic field may not reach the deep organs or tissues to be targeted.
- Internal stimuli responsive systems may need greater difference between normal and disease conditions to deliver significant amount of drug at target site. Ex.—pH responsive systems require large pH gradient to dissolve under acidic environment.
- Difficult to fine tune the responsiveness as some polymers poly( $\epsilon$ -caprolactone) (PCL), (polylactide (PLA)), PLGA, etc. degrade slowly at the target site and thus cannot readily release drug from nanoparticles.

With an aim to further enhance the release behavior and augment therapeutic efficacy of intelligent delivery systems for drug, dual and multi-stimuli responsive systems have gathered much attention aggressively in the area of drug delivery. Thus, engineering smart systems with dual or multi-responsiveness properties are highly potential to obtain precise, systematic and site specific drug delivery. Though these systems are challenging synthetically, are systems of emerging attention and interest. Moreover, dual and multi-responsiveness could highly enhance the versatile applicability of these systems by combining the drug

delivery with desirables like imaging, detection or feedback. These systems also furnish a unique opportunity optimize their response to every stimuli independently, so that release of drug can be regulated precisely under the merged effect of different stimuli. In these systems two or more stimuli are merged to: (i) facilitate nano-formulation in mild environment by applying external stimuli like temperature, pH, etc, as in these systems one of the stimuli can be used to load drug in carrier and other/s is/are to trigger the drug release; (ii) trigger drug release under stimuli (external) like magnetic field, temperature, light and ultrasonic; (iii) drug release is also triggered at target site and reversible deshielding of nanoparticles in biological environment. Due to versatile tumor micro-environment such as oxygenation, perfusion, vascular abnormalities, and other metabolic states these stimuli-responsive systems were exclusively developed for anti-cancer drug delivery [3].

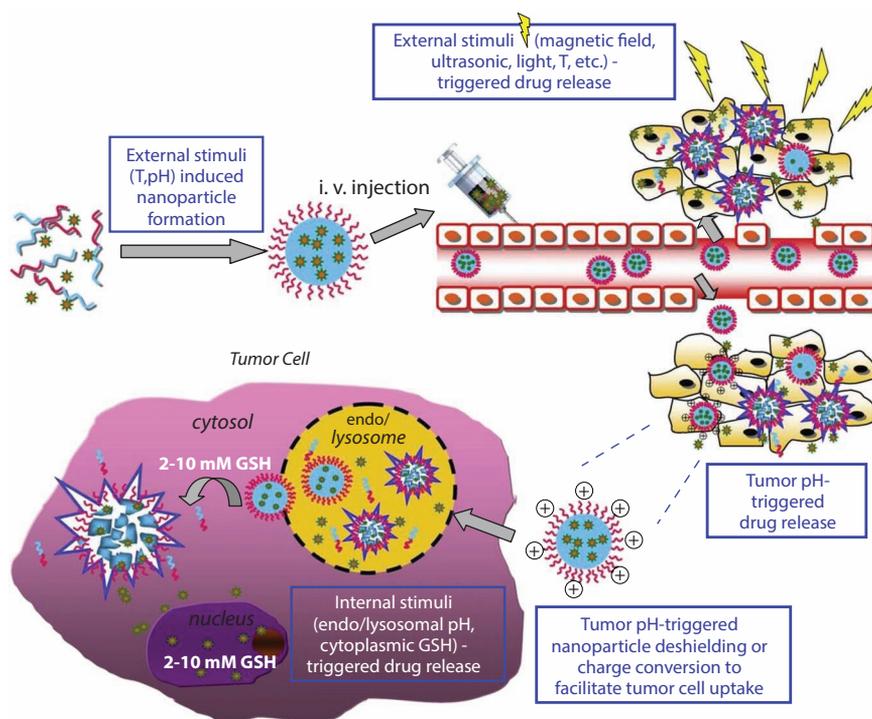
Rapid growth rate of the cancerous cells results in temperature increase and pH decrease in tumor tissues. The higher redox potential of cytosol & cell nuclei containing 100 and 1,000-fold greater amount of glutathione (GSH) tri-peptide than blood and extracellular milieu ( $0.5e-10$  mM *versus*  $2e-20$  mM GSH) were exploited for intracellular drug release [93]. Further, tumor tissues are extremely hypoxic and possess 4-times high GSH quantity compared to normal tissues. The systems designed based on such internal stimuli are advantageous for self-regulated drug release and can be easily employed in clinical settings with greater patient compliance. On the other hand, external stimuli-responsive carriers offer demonstrable merits of temporal, precision spatial and dose control over a period of release via remote device, in which release of drug might be switched on and off as and when needed [94].

Group of numerous enzymes, like glucuronidase, carboxylesterases or proteases which are differentially expressed by normal (intra- or extracellular) and cancerous cells can also be utilized as biochemical trigger. To develop an enzyme-responsive carrier, protease cathepsin (especially cathepsin B) which degrades lysosomal proteins is extensively studied. Extracellularly expressed proteases like matrix metalloproteases are very particular biomarkers of cancerous tissues which cause proteolysis of the basement membranes and extracellular matrix and are also responsible for embryo morphogenesis, angiogenesis, parasitic or bacterial invasion and tissue remodeling [95–98]. Such biochemical signals act as a trigger when specific site oriented release of drug is needed by the system. Which can be achieved either by incorporating particular enzyme substrate sequence to linker segment, which connects drug to nanocarriers or to nanocarrier matrix.

In dual and multi-responsive systems, responses appear either at the same site simultaneously or in subsequent pattern in various compartments and/or settings. These systems in nano form provide remarkable control of drug release, resulting in superior *in vitro* and/or *in vivo* anti-cancer potency.

An overview of how the external stimuli are utilized in nanoparticle preparation as well as how the internal and external stimuli together trigger precision spatial, dose controlled and temporal release of drug with shielding and de-shielding mechanisms at tumor site are represented in Figure 11.3.

Polymers responsive to more than one stimuli are often synthesized by combining more than one monomers responsive to different stimuli based on their applicability. In one of our studies, temperature and pH responsive co-polymer was synthesized by the combination of biodegradable and biocompatible chitosan (CS) as pH responsive polymer and

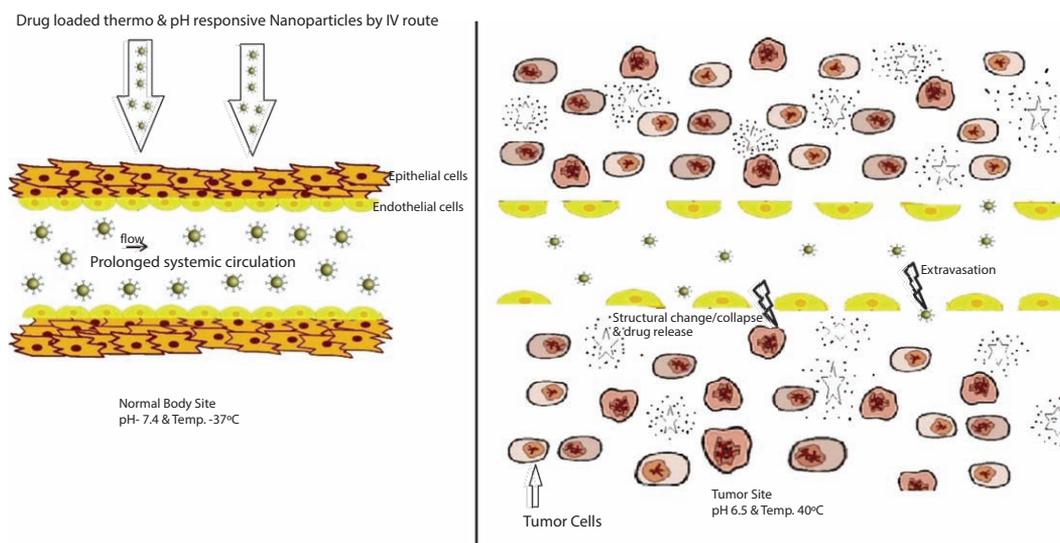


**Figure 11.3** Representation of role of dual and multi-responsive polymeric nanoparticles, tumor microenvironment and external stimuli in precision and dose controlled release of drug at target site [3].

PNIPAM as a reversible thermoresponsive polymer. In preliminary study, the effect of N,N-methylenebisacrylamide (MBA)-cross linking agent and chitosan concentrations on the responsiveness of CS-g-PNIPAM co-polymer and other properties were investigated and based the preliminary findings the responsiveness of CS-g-PNIPAM co-polymer was fine tuned to tumor microenvironment. The co-polymer was then loaded with an anti-cancer drug Oxaliplatin and evaluated for its targeted delivery of drug at tumor microenvironment temperature and pH. The same is represented in Figure 11.4 [99, 100]. Many of such co-polymers with multi-responsive properties and their applications with respect to delivery of drug are enlisted in Table 11.5 and some very recent findings are discussed below:

Chen, developed multi-responsive co-polymeric (poly(DMA-st-MAABO)) hydrogel with self-healing property which was responding towards temperature, pH, hydrogen peroxide, adenosine triphosphate and sugar. The study demonstrated potential biomedical application of the system with respect to controlled drug delivery and tissue engineering [101].

Zhang *et al.* designed folate conjugated pH/reduction dual responsive micelles as theranostic carrier for indocyanine green (ICG) and doxorubicin (DOX) to achieve targeted NIR imaging as well as combined chemo-photothermal therapy. Here they prepared copolymers composed of PEG and PCL with disulphide and acetal linkages ((PCL-ss-PEG-ss-PCL) and (PCL-acetal-PEG)), the combination of which results in dual responsive micelles. For thermal therapy ICG was sensitized with NIR light. Micelles exhibited greater *in vivo*



**Figure 11.4** An overview of site specific drug delivery from thermo and pH dual responsive polymeric nanoparticles.

**Table 11.5** List of dual and multi responsive polymeric systems.

Sl. No.	Responsiveness	Name of polymer	Drug	References
<b>Dual responsive polymeric systems for drug delivery</b>				
1	Temperature and pH	-PNIPAm-co-MA	Proteins and peptides	105
		-PNIPAm-AM-VP	Naltrexone	106
		-PNIPAM/CMCS/MWCNTs	Dox	107
		-CTS-g-PNIPAAm	10-hydroxycampothecin	108
2	Magnetic and pH	-PEGylated Fe <sub>3</sub> O <sub>4</sub> (Fe <sub>3</sub> O <sub>4</sub> -NH <sub>2</sub> )	Dox	109
		-MPEG- <i>b</i> -PMAA- <i>b</i> -PGMA-Fe <sub>3</sub> O <sub>4</sub>	Adriamycin	110
		-(Ac-β-CD) & Fe <sub>3</sub> O <sub>4</sub> Composit	Camptothecin	111
		- Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> , poly(L-Asparagine) and mPEG	Dox	112
		-DOX-tethered Fe <sub>3</sub> O <sub>4</sub> conjugates nanoparticles	Dox	113

(Continued)

**Table 11.5** List of dual and multi responsive polymeric systems. (Continued)

Sl. No.	Responsiveness	Name of polymer	Drug	References
3	Magnetic and temperature	-PNIPAM–chitosan	Curcumin	114
		-PNIPAM-co-AA-MnFe <sub>2</sub> O <sub>4</sub>	Dox	115
		-Pluronic with Fe <sub>3</sub> O <sub>4</sub> nanoparticles	Dox	116
4	pH and redox	-PEG-SS-PDEA	FITC-BSA/CC	117
		-PCL-b-P(OEGMA-co-MAEBA) micelles	CPT and Dox	118
		-PDS-g-PEG/cRGD nanoparticles	Dox	119
		-Poly(b-amino ester)s-PEG micelles	Dox	120
		-DOX-conjugated PDSM-b-PHPMA micelles	Dox	121
5	Temperature and redox	-PEO-PAA-PNIPAAm polymersomes.	Proteins	122
		-poly(ether urethane)	Dox	123
6	Double pH	-Poly-b-amino ester ketal nanoparticles	BSA-Alexa flour	124
		-PPC-Hyd-DOX-DA nanoparticles	DOX	125
		-Poly(L-lysine)- <i>block</i> -poly(L-leucine) micelles	Nuclear	126
7	Temperature and enzyme	-DNA-capped MSNs	Floxuridine	127
		-CuS@Gel-DOX nanoparticles	Dox	128
<b>Multi responsive polymeric systems for drug delivery</b>				
8	Light, temperature and pH	-N-isopropylacrylamide and 4-[(4-(acryloyloxy)ethoxy)phenylazo] benzoic acid(hydrogel) (PNIPAM-AEPAZA)	Dox Nile Red	129 130
		-P(DMAEMA-co-NBM)		

(Continued)

**Table 11.5** List of dual and multi responsive polymeric systems. (Continued)

Sl. No.	Responsiveness	Name of polymer	Drug	References
9	Temperature, pH and guest molecule	-Methylviologene functionalized PNIPAAm Naphthalene terminated PDMAEMA	Dox	131
		-cucurbit[7]uril (a macrocyclic cavit and comprising seven glycoluril units) hydrogel	-	132
10	Temperature, pH and magnetic	-AT-Fe <sub>3</sub> O <sub>4</sub> /PMOA nanocomposite microgels	-	133
		-VCL-AAEM-VIm microgels	-	134
11	pH, redox and magnetic	-amphiphilic PCL-SS-PDMAEMA	Dox	135
		-Fe(II) loaded PMAA microcontainers crosslinked by N,N-methylene-bisacrylamide and N,N-bis(acryloyl)-cystamine	Daunorubicin	136
		-PMAA@P(MAA-co-PEGMA-co-MBAAm-co-BAC) (PMAA@PMAAS-S	Daunorubicin	137
12	Temperature, redox and guest molecule.	-p-sulfonatocalix[4]arene (C4AS) and 1-methyl-1'-dodecyl-4,4'-bipyridinium (MVC12)	Dox	138
13	Temperature/pH and redox	-THP-protected HEMA monomer and NIPAM Amphiphilic Block Copolymer	-Nile red	139
		-P(MAA-co-BAC)/P(NIPAAm-co-BAC)-FA microspheres	-Dox	140

efficacy due to combined effect of chemotherapeutic drug and thermal therapy with ICG-photosensitizer. The system exhibited immense potential in chemo-photothermal therapy guided by imaging as theranostic carriers [102].

You *et al.* synthesized glutathione and NIR light dual responsive system for targeted cis-platin & ICG delivery. Drug release profile demonstrated higher percentage of drug release

in acidic conditions especially on exposure to GSH and NIR irradiation (99.35%) in comparison to glutathione alone (58.45%) or NIR light alone (73.46%) or without both the stimulus (12.35%) at a pH of 7.4 after 72 h. However, these findings were not significant under pH 5.5. In cytotoxicity assay, cells viability was reduced to 1.95% (SGC-7901) upon exposure to NIR light and it was reduced to 1.25% in MCF-7 cells [103].

Zhong *et al.* reported biocompatible, (acid pH, temperature and reducing agent) triple-responsive nanocages (TDN). These nanocages show significantly improved drug release pharmacokinetics and biodistribution of anti-cancer drugs under triple stimuli, which confirms the potent *in vivo* therapeutic effect with reduced side effects [104].

## 11.4 Conclusion

Several years of hasty improvement in the development of mono, dual as well as multi-responsive polymeric nanoparticulate systems with designed targeted delivery of drug are unlimited in their design and chemical composition. Each mono-responsive or combined responsive system represents their own merits and demerits. These systems obviously addressed the challenges of current nano-systems with respect to *in vivo* stability, intracellular drug delivery, shielding and deshielding of systems, unprecedented self-regulated controlled release and many more. Ability to modulate drug biodistribution by altering drug release via the utilization of intelligent polymers could translate delivery from passive to active stimuli-controlled drug delivery. This ultimately reduces the toxic and adverse effects while enhance the therapeutic outcome through programmed site-specific drug delivery.

Despite of several advancements, there are still many challenges exist to transform stimuli-responsive polymeric drug delivery systems for clinical application. The need of the hour is to develop polymeric systems with greater sensitivity, biocompatibility, non-toxicity and multiple-responsive properties. During the review of research we found that the methods of stimuli-responsive polymer synthesis are complex. Therefore, along with engineering of smart polymeric systems, development of simple synthetic methods of copolymer preparation needs to be designed. Many of multi-responsive polymer systems are just evidence for concept studies which are evaluated only *in vitro*. Thus, extensive *in vivo* performance of multi-stimuli responsive systems needs to be evaluated. We expect the continuous development of new responsive polymeric nano-systems, with extensively elaborated and adoptable drug carriers to be offered in the future.

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# NANOBIOTECHNOLOGY

MICROBES AND PLANT ASSISTED SYNTHESIS  
OF NANOPARTICLES, MECHANISMS  
AND APPLICATIONS

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# Nanobiotechnology for E-waste management

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## Abbreviations

**BFRts** brominated flame retardants  
**CPCB** Central Pollution Control Board  
**EEE** electrical and electronic equipment  
**E-waste** electronic waste  
**NPs** nanoparticles  
**PCB** printed circuit boards  
**PROs** Producer responsibility organizations  
**PVC** Polyvinyl chloride  
**UNEP** United Nations Environmental Program  
**WEEE** waste electrical and electronic equipment

## 17.1 Introduction

"E-waste can be classified as an electrically powered appliance that has reached its end-of-life" (Deepali et al., 2005). E-waste generated from electrical and electronic equipment (EEE) may add to and exacerbate the existing pollution problem. These types of equipment release many hazardous substances to the environment, which causes pollution (Rajarao et al., 2014; Widmer et al., 2005). The E-waste generated from all sources of electronic goods should be recovered, but is something we presently lack in terms of the technology required (Jujun et al., 2014). E-waste recycling from electronic equipment and goods may yield valuable metals in higher concentrations as in ores (Cayumil et al., 2016) and this may add appreciable strength to the economy.

E-waste and its accessory components like computer systems, printers, and television sets contain toxic metals like lead. The recycled products that contain such toxic metals are sold in the market for public use, which may pose health risks that are normally overlooked. Scruggs et al. (2016) suggested sanctioning laws and regulations to protect the public health and environment that will monitor the use of chemicals in EEE.

## 17.2 The lifecycle of electronic goods

EEE may be prepared and gathered in India and maybe a form of imported material from foreign countries, like those in Europe, Korea, and China. The manufactured goods reach the costumers via distributors and retailers, who

are referred to as “Associated Elements” in the generation of EEE, but not in waste electrical and electronic equipment (WEEE) generation. In the Indian market, electronic goods are easily accessible in the assembled form, wherein the contractor gathers all the things and directly delivers to the consumers at lower prices. Whereas branded personal computers are costly due to various norms, regulations of taxes and licensing contribute to the higher prices. The responsibility of the extended producer is not always followed and the monitoring of a middleman (like assemblers) often fails. In the present scenario, the handling of the black market is very important, because much illegal, unlawful, and irregularities are found in this market.

Electronic goods/gadgets are classified under three major classes:

- *White goods: Household appliances*
- *Brown goods: TVs, camcorders, cameras*
- *Gray goods: Computers, printers, fax machines, scanners, etc.*

### 17.3 Global effects of E-waste

The generation of WEEE has exponentially increased because of developed research and innovations in the electrical and electronics field. Increasing demand for this equipment in developing countries and their short lifespan has added to the excess generation of such wastes (Gusseme et al., 2010; Hussein et al., 2004). Other contributing factors include international legislative consensus and failures in the management of WEEE (Friege, 2012) as well as affordability. For large EEE and mobile phones, a decrease lifespan with an average of 10–2 years and 24–9 months was observed, respectively (Gusseme et al., 2010; Kasper et al., 2011; Ongondo et al., 2015). It is assumed that in the coming few years, large populations and rapid economic growth regions are expected to produce huge amounts of WEEE. An overview of the total expected of the waste generation million tons (Arda et al., 2019) in 2020 is shown in Fig. 17.1.

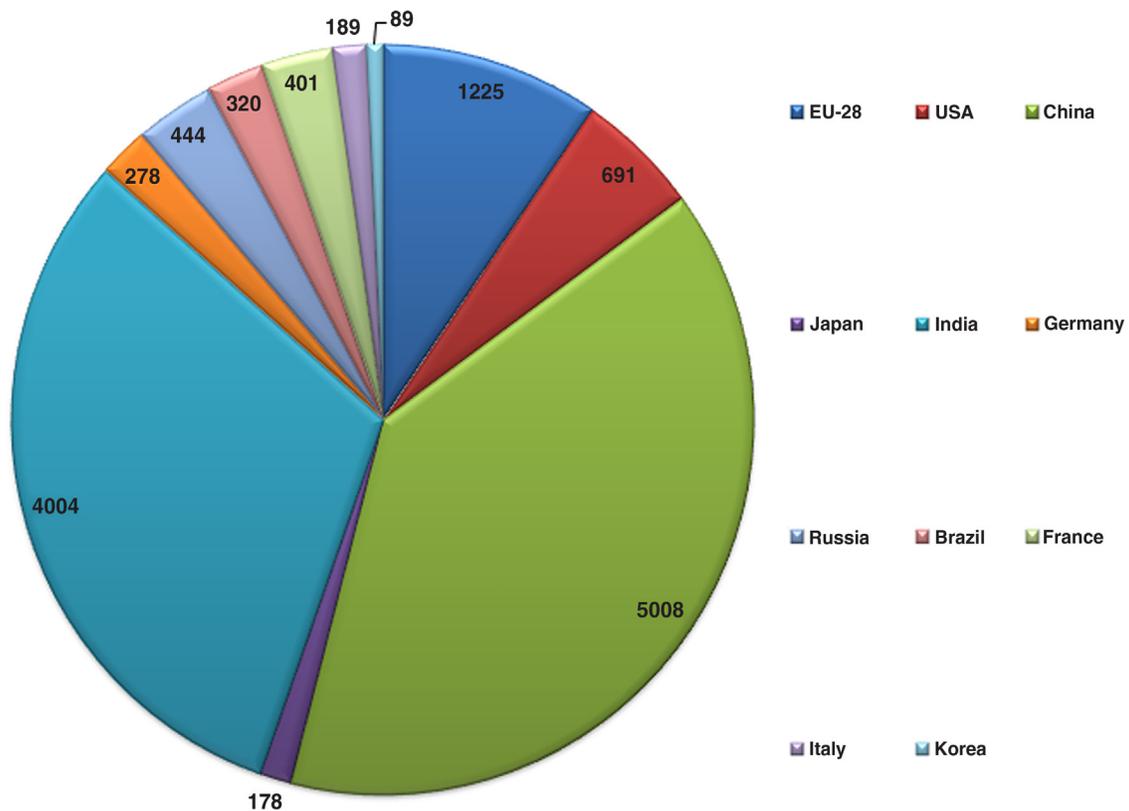


FIGURE 17.1 Predicted annual electronic waste generation in million tons.

## 17.4 E-waste hazards

The incineration process of waste electrical goods like electrical wires, circuit panels, metal-holding acidic solutions (Borthakur and Singh, 2017), polychlorinated biphenyls, polybrominated diphenyl ethers, and polychlorinated dibenzo-p-dioxins increase in the environment and may enter the food chain and may result in adverse impacts on human health (Luo et al., 2011; Tue et al., 2014). The most common materials in e-waste are lead, iron, copper, nickel, cobalt, chromium, silver, palladium, and gold. Plastics and ceramics used in making electrical goods alter their composition during manufacturing (Robinson, 2009). Borthakur and Singh, (2017) as well as Williams (2011) have reported the harmful action of such e-wastes and showed its presence in air and soil during recycling. Many countries including India, Ghana, China, Thailand, Pakistan, Indonesia, Vietnam, and Bangladesh are involved in illegal practices of recycling electronic and electrical goods.

## 17.5 Health and environmental impacts of E-waste

The chemicals present in electronic goods are potential threats to life on earth because they contain/possess harmful or fatal toxicants; in addition, the electronic goods possess a complex mixture of thousands of micro and macro elements of lethal nature. Most of the constituents in electronic devices comprise (Fig. 17.2) lead, mercury, chromium, cadmium, beryllium, polyvinyl chloride (PVC), and brominated flame retardants (BFRts). Furthermore, devices like TVs, computers, and related components possess lead, which has neurological effects (such as the CNS or central nervous system) and is further explained in Fig. 17.2. The e-waste if disposed of without proper treatment and any controls may contaminate the soil, water, and air.

## 17.6 The need for e-waste management

In developing countries, unsanitary modes of landfill disposing and recycling have been reported. Like discussed in the previous section, improper recycling practices of Copper (Cu) and plastic, by burning the wires in open spaces and recovery of metals from polychlorinated biphenyls using acid extraction techniques are followed. These processes result in environmental pollution and may contaminate natural resources (Ikhlayel, 2018).

Metal /materials	Source	Effects
Lead	Acid battery	<i>Kidney failure CNS disorders Affect Gonads</i>
Cadmium	Battery, circuit boards, housing	<i>Bone problems, Accumulate in body</i>
Mercury	Batteries, switches, housing	<i>Brain, fetus, Liver, CNS</i>
Chromium VI	Decorative hardener, corrosion protection	<i>Genotoxic, Lung cancer</i>
Plastic	Computer mouldings, cabling	<i>Generates Furans, dioxins</i>

Bio-remediate/Degrade

FIGURE 17.2 Effects of e-waste components on human health.

Major drawbacks of e-waste management:

- Generation of e-waste in large quantities, which may be due to a lack of infrastructure to control e-waste properly.
- Insufficient behavior of e-waste and their mixture formed with metropolitan solid waste.
- Poor or incomplete inventory assessment of e-waste.
- Lack of knowledge for the toxic effects produced on human health, from the wrong practices of e-waste management.
- Lack of knowledge for the hazardous nature and toxicity of e-waste.
- Absence of legislation to regulate and control e-waste management such as exporting them from developed countries to developing countries for recycling and improper disposal of them.

### 17.6.1 Processing and recycling of e-waste

Different electrical and electronic products like printed circuit boards (PCB) are fabricated from many toxic chemical substances, which include heavy metals like cadmium, lead, and germanium, oxides, and polymers. In many countries, these e-wastes are disposed of by incineration that produce gases like furans or dioxins, which cause cancer and pose a serious threat to the environment. However, the physical or mechanical crushing process does not separate out reusable materials or any type of metals from e-waste. Therefore, it is essential to look for an alternate approach, which is sustainable and environment-friendly.

One such approach has been seen in the enhanced separation of chemical substances such as metals, oxides, and polymers from the PCB, which employs a cold “cryo-mill” procedure followed by dispersing the product into water. Briefly, PCBs obtained from the computers, smartphones, recording devices, medical devices etc. are ground into fine nano-sized dust at low temperatures ( $<0^{\circ}\text{C}$ ) using liquid nitrogen and are pulverized in the cold “cryo-mill” to separate it from the e-waste. At room temperature, the obtained nano dust powder is then dissolved in water, to separate chemical substances such as metals, polymers, and oxides, which can be further reused as raw materials for manufacturing paints, plastic chairs, or whiteboards (Tiwary et al., 2017). Polymer nanocomposites are used to synthesize e-waste-based nanoparticles (NPs), thereby recycling the waste material. The traditional methods of extraction of individual components from e-waste like PCBs have several limitations in comparison to newly developed methods. Chemical methods like hydrometallurgy and pyrometallurgy consume low energy but yield a high amount of chemical waste and extract oxides, whereas the physical methods based on mechanical crushing and heating at high temperatures involve a large amount of energy, which leads to the formation of a large quantity of waste like gases and slag. This physical method extracts only metals, thereby losing oxides and polymers in the process (Friege, 2012; Davar et al., 2015; De Gusseme et al., 2011; Kasper et al., 2011; Ongondo et al., 2015). Biometallurgy is an ecofriendly method that has been developed to extract moderately all types of components like metals, oxides, and polymers. In comparison to physical and chemical methods, this procedure uses low energy with a longer duration of a procedure resulting in a decreased rate of recovery. Nowadays, the preferred method of choice is low-temperature milling to prepare NPs, which can separate and recycle the pure components and is considered as an environment-friendly and scalable method. Many such ecofriendly and affordable methods need to be explored in order to sustainably recycle e-waste. The scanning electron microscope images as seen in Fig. 17.3 exhibited structures of raw PCB and bioleached PCB, the study illustrated importance of metals recovery from the e-waste (PCBs) using strains of *Actinobacteria* in bioleaching.

### 17.6.2 Hybrid technique for metal extraction

The process of biological leaching is an improved technique but it is time-consuming and tedious when it comes to the removal of a complete metal by biological leaching alone. In comparison, chemical leaching is a rapid, robust, and proficient technique, but it possesses its own disadvantages (Ren et al., 2009). Therefore, to overcome the shortcomings of both the processes, the chemical and biological leaching techniques are coupled together.

### 17.6.3 Biological leaching of e-waste

Bacterial species like *Acidithiobacillus ferrooxidans*, *Acidithiobacillus thiooxidans*, *Leptospirillum ferrooxidans*, and *Sulfolobus* sp. are the main contributors of heavy metals bioleaching from e-waste (Mishra and Rhee, 2010). As shown in Fig. 17.4, by using precipitation techniques at desired pH conditions, the minerals were successfully recovered

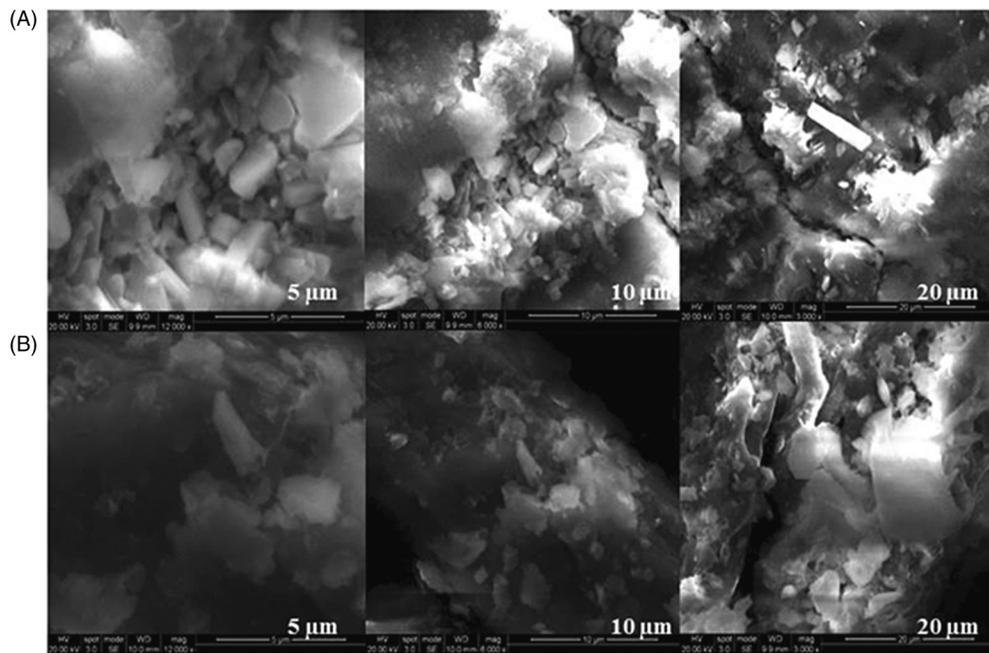


FIGURE 17.3 Scanning electron microscope images. (A) Raw PCB, (B) bioleaching residue. Reprinted with permission from *Dhanalashmi et al. (2019)*. Copyright © 2019 Springer Open.

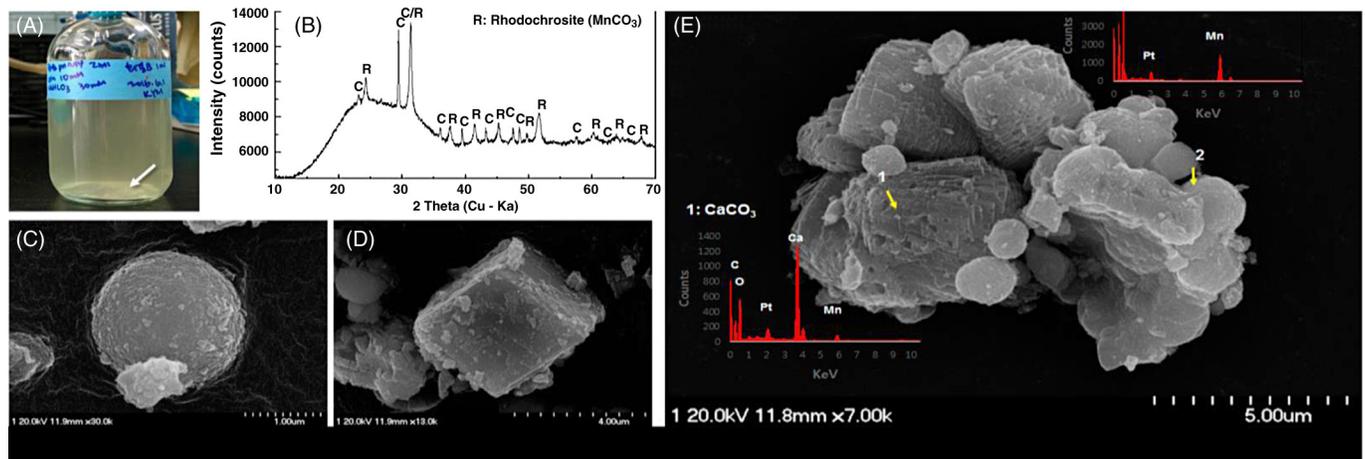


FIGURE 17.4 (A) A picture displaying the white settled precipitate; (B) XRD patterns; (C)–(E) SEM-EDS images of the biogenic carbonate minerals. Reprinted with permission from *Kim et al. (2018)*. Copyright © 2018 MDPI.

from PCBs (*Kim et al., 2018*). Furthermore, in acidic condition, microorganisms are constantly being used in the selective metal recovery and decomposition of inorganic and organic matter on the earth. Bioleaching is a natural process where microbes transform solid metallic products into its soluble and extractable form. Bacteria belonging to an autotrophic nature (*Thiobacilli* species), heterotrophic fungi (e.g., *Aspergillus* sp., *Penicillium* sp.) and heterotrophic bacteria (*Pseudomonas* sp., *Bacillus* sp.) are the three major groups of microorganisms involved in bioleaching of metals. As per *Fig. 17.5*, it is clearly observed that the biogenic carbonate minerals formation. The mineral decomposing microbes, called chemolithotrophs of an Iron and sulfur-oxidizing nature, also fix atmospheric  $\text{CO}_2$  (*Clark and Norris, 1996; Mishra and Rhee, 2010; Nagpal et al., 1993*).

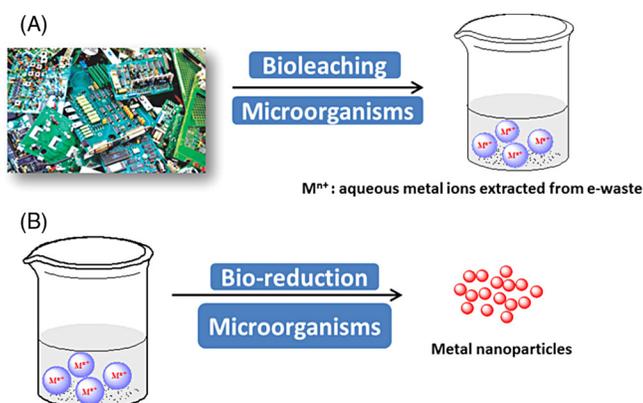


FIGURE 17.5 Represents extraction of metals from e-waste. (A) Bioleaching of metals from e-waste to aqueous metal ions through bacteria and fungi; (B) Bio-reduction of aqueous metal ions to metal nanoparticles through microorganisms and plant extracts.

## 17.7 Significance of nanoparticles in e-waste management

Countries are developing e-waste at higher pace and so it is the global concern for electronic waste or e-waste management systems. E-waste comprises of materials that are toxic to health and the environment. It is the need of the hour to analyze methods to manage and recycle of the e-waste components for the betterment of society. The decomposition of the waste material is a slow process involving many obstacles that need monitoring globally. The hazardous chemicals like mercury and lead are present in the most common equipment like televisions and computers (Bystrzejewska et al., 2009). The United Nations Environmental Program (UNEP) universally reports 20–50 million tons of waste that instigate many health- and environment-related problems. Nanotechnology has various applications (Fig. 17.6) such as remediation of ground water, solid waste, heavy metal, hydrocarbon, and filtration at the nanoscale, catalysts in the absorption and breakdown of pollutants, and wastewater management. A new area to focus on, however, is the use of microorganisms in the degradation of hazardous components. Biosynthesis of industrial products with the help of microorganisms would be rapid and safe to the environment directing toward green nanotechnology. Microorganisms would provide alternative methods when compared to conventional therapies (Garlapati, 2016).

### 17.7.1 Nanoparticles produced by bacteria

Bacteria have the capacity to reduce metal ions in various components at the nanoscale, thereby immobilizing them. This includes reduction of heavy metals like platinum, lead, cadmium, titanium, and palladium. Bacterial en-

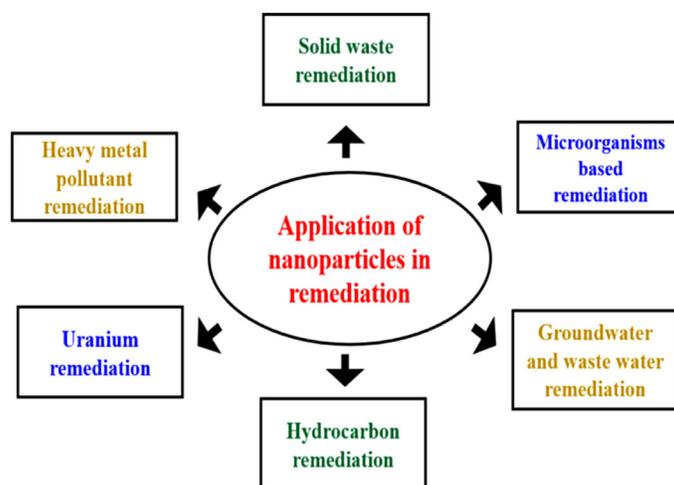


FIGURE 17.6 The application of nanoparticles in remediation.

zymes catalyze such reactions and are, thus, used in the synthesis of inorganic NPs. Such green-synthesized NPs are used for various applications (Yadav et al., 2017).

### 17.7.2 Nanoparticles produced by yeast and fungi

Yeast and fungi produce enzymes that essentially help in the reduction of heavy metals. The high biomass production from these sources has been exploited to produce NPs from the e-waste containing heavy metals on a large scale. Due to the wild abundance of fungi and yeast, the green synthesis of such NPs seems cost-effective too (Saxena et al., 2014).

### 17.7.3 Carbon nanotubes (CNs) and nanocrystals (NCs) remediation

CNs and NCs are carbon-based nanomaterials, which consist of exceptional tunable properties. These facilitate new technologies that have wide applications in the management of e-waste and globally prevent pollution. The CNs is of two types, single and multiwalled, generally used to eliminate Nickel ions from water and cationic dyes from aqueous solutions (Rizwan et al., 2014).

### 17.7.4 Heavy metal remediation (phytoremediation)

Many countries face severe problems of environmental pollution, due the presence of heavy metals in soil and water. According to a study, *Noaeamucronata* also called as thorny saltwort, has the capacity to gather Pb-NPs and reducing heavy metals (Mohsenzadeh and Rad, 2012).

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## 17.8 Synthesis and characterization of the nanoparticles

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### 17.8.1 Biorecovery of palladium (Pd)

Nowadays, the synthesis of metallic NPs from precious metals using a direct bio-reduction process has increased. Microorganism-assisted nanoparticle synthesis is beneficial as they are inexpensive and require ambient temperature and pressure. There are many reports of the microbial bio-reduction of Pd, which has been used to recover the element from leaching models of a catalytic conversion of chemicals and pollutants, and from the industrial automotive catalyst (Arda et al., 2019).

### 17.8.2 Biorecovery of gold (Au)

Biorecovery of Au from jewelry waste using microorganisms such as *Escherichia coli* and the bio-manufacturing of catalytically active Au nanomaterials for the oxidation of glycerol has been reported (Deplanche et al., 2007). This combination strategy of microorganism and surfactants facilitates the formulation of stable Au NPs and bio-Au nanocomposites. Further adding to these techniques, the bimetallic-synthesized Pd–Au nanocomposites from e-waste have been used for the dechlorination of potential environmental pollutants (De Corte et al., 2011).

### 17.8.3 Biorecovery of silver (Ag)

Synthesized membranes involve biogenic Ag (o) precipitates from wastes and have potential antiviral, disinfectant, and antifouling properties. In addition to these, the nanocomposite materials possessed antibacterial action and reduced biofilm formation by inhibiting bacterial adhesion (De Gusseme et al., 2011; Gusseme et al., 2010).

### 17.8.4 Recovery of copper (Cu)

The hydrometallurgical procedure has been commonly employed to recover Cu from e-waste in the form of NPs. Another ecofriendly and low-cost method is normally employed for extraction of the fine dust of PCBs, followed by the selective leaching of Cu in ammonium and ammoniacal salt solutions at room temperature, and finally the NPs are produced by using L-ascorbic acid and CTAB as a reducing agent and modifier, respectively. The characterization tests used in a study explaining this process are as mentioned below. This is suggested to be used in electrochemical

sensor technology and development processes. The recovered copper NPs have been characterized by employing various advanced analytical tools, powder X-ray diffraction (to explore lattice properties), and transverse electron microscopy (to know shape and size of the recovered NPs) (El-Nasr et al., 2020).

### 17.8.5 Carbon-based nanomaterials

Carbon nanomaterials like carbon dots and reduced graphene oxide have been produced by using TiO<sub>2</sub> NPs as a catalyst, and have shown enhanced photocatalytic activity for methylene blue dye degradation. This method can be efficiently utilized to fabricate different carbon nanocomposites employing metal oxides as a catalyst and much plastic waste as a carbon resource (Mohamed and Alsanea, 2020).

### 17.8.6 Recovery of zinc oxide (ZnO) nanoparticles

ZnO NPs possess excellent physical and optical properties, and are mostly used in gas sensors, energy storage, optoelectronics, etc. Different chemical processes like conventional solid-state process, precipitation, hydrolysis, pyrolysis, hydrothermal methods, and sol-gel have been mentioned for ZnO nanoparticle synthesis into different sizes and morphologies, which look for parameters like pH, temperature, reaction media, counter ions, and additives (Davar et al., 2015). A superficial thermal production methodology has been reported to produce ZnO NPs from used-up Zn-C batteries. This recovery of ZnO NPs from used-up Zn-C batteries requires exposure to 900°C under the influence of an inert argon gas using a horizontal quartz tube furnace (Rifat et al., 2018).

Recycling of electrode waste from spent domestic Zn-MnO<sub>2</sub> batteries has been reported by using a simple recovery, one-pot solvothermal process for ZnO NPs, which has enormous environmental significance. With manual dismantling, an electrode material from the batteries is collected and mixed with HCl and Cyanex 923 (phosphine oxide reagent) at 250°C for 30 min. This selected extract facilitates the efficient separation of pure Zn from Zn-MnO<sub>2</sub>. Furthermore, the recovery of high purity ZnO NPs upon ethanolic treatment that yielded almost 5 nm particle sizes (Akash et al., 2016).

### 17.8.7 Silicon carbide nanowires

The carbothermal reduction process has been employed for the synthesis of silicon carbide nanowires using a glass fraction of an obsolete computer monitor and a computer's plastic shell as a source of silica and carbon, respectively. A stoichiometric mixture of both electronic waste (e-waste) components was prepared and subsequently heat-treated (1550°C) in an inert atmosphere of argon gas for 20 min, which was further processed for characterization. It was found that the synthesized silicon carbide nanowires exhibited bamboo-like and hexagonal prism structures with diameters of 30–200 nm and lengths up to 10 μm (Samane et al., 2017).

### 17.8.8 Regulations and laws in e-waste management from a global scenario

The regulations for the management of e-waste are addressed partially because recycling processes have achieved support only in a few legislation policies. Green materials and eco-designs have been executed at operational levels, in addition to e-waste and material management (Irimia-Vladu, 2014). However, this sort of regulation and technical systems has yet to be achieved at the e-waste substance level. The e-waste management occurs in four levels, namely at the product, component, material, and substance levels. To succeed in e-waste management, it is now a prerequisite to address this problem from the product and component level to the levels of materials and substances. The general awareness in e-waste management and environmental risk, as well as ecotoxicology of harmful materials in recycled products should be well illustrated. The e-waste controlling board should take steps to curb toxic substances from entering downstream processes. The e-waste bio-separation technology, policy, and regulations should be properly addressed and revised. This may result in enhanced WEEE regulation for both nonregulated and regulated nation-states. The e-waste management at a global level has been addressed in developing and developed countries with much counter legislation and regulations, at different levels. The open-space incineration of e-waste (like wire piles, melting of electronic boards and discarding of metal bearing acidic solutions) are commonly practiced (Borthakur and Singh, 2017). The level of toxic organic compounds like polychlorinated biphenyls, polybrominated diphenyl ethers, polychlorinated dibenzo-*p*-dioxins, and dibenzofurans in air and water, is increasing at alarming levels, and further continues having harsh effects on the environment and human health. Apart from the contamina-

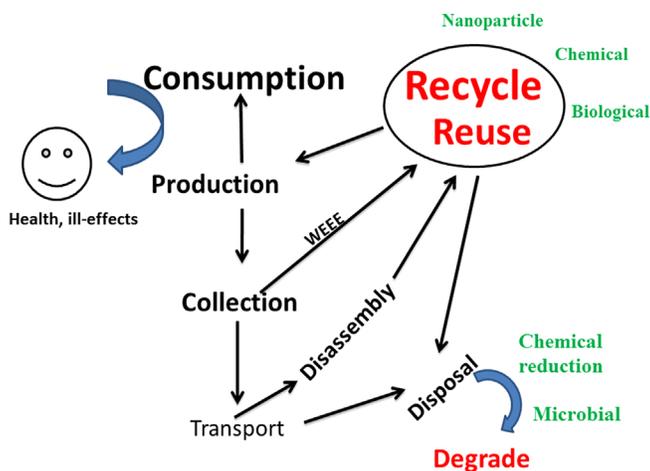


FIGURE 17.7 Pictorial representation of e-waste processing.

tion of these resources and its indirect impact on human health, it is also directly affecting us by accumulating in our food chain (Tue et al., 2014, 2016; Luo et al., 2011).

### 17.8.9 Producer responsibility organizations

E-waste management rules, 2016, jolted producers to set up a Producer Responsibility Organization (PRO) for the enactment of EPR responsibilities. The PROs take on the liability for setting up a collection and reprocessing mechanism as well as running responsive movements, which are essential for amenability under the e-waste rules. The intermediates, like PROs, may help in the collection and transfer of materials on behalf of the producers. The movement of e-waste for recycling will be under the effect of collectors, dismantlers, contractors, and mediators on behalf of producers with registered recyclers for end-of-life processing (Fig. 17.7). The middlemen act as PROs in addition to recyclers as well as capitalists. Therefore, PROs selection plays a crucial role in e-waste management and hence, the (Central Pollution Control Board (CPCB) sets a regulatory guideline for PROs permission. The importance of PROs is not certain because many government organizations do not consider a PRO as a certified entity to bid for their e-waste.

## 17.9 Challenges of e-waste management

The main tasks for the effective management of e-waste in India are similar to many other countries, in particular emerging economies. The prevailing conditions in emerging economies, like India and China, face many conducive environments that drag the tail of e-waste management systems. As shown in Fig. 17.8, the producers especially do not follow the regulatory guidelines of WEEE and hence lead to unwanted e-waste problems in India. The main challenges like infrastructure and ecosystem, skills and capacity, financing, awareness, standards, and monitoring are all interconnected. There is a lack of coordination between the producers, consumers, and recyclers. The recyclers mainly involved in recycling of e-waste, often fail to recollect e-waste from hidden areas, hence it may lead to pollution.

## 17.10 Conclusions and future perspectives

This chapter summarizes the importance of e-waste management in mitigating environmental pollution. The e-waste-driven pollution is rapidly growing environmental problems that need immediate attention and an answer. The lack of knowledge about e-waste problems like its disposable, chemical nature and its handling were leading to improper management and ultimately culminating in health ailments of the living world and the environment. The biological recovery of metal ions and toxins is being aimed through the use of NPs based on charge, ionic property, and molecular weight. The working group has to receive the information regarding the

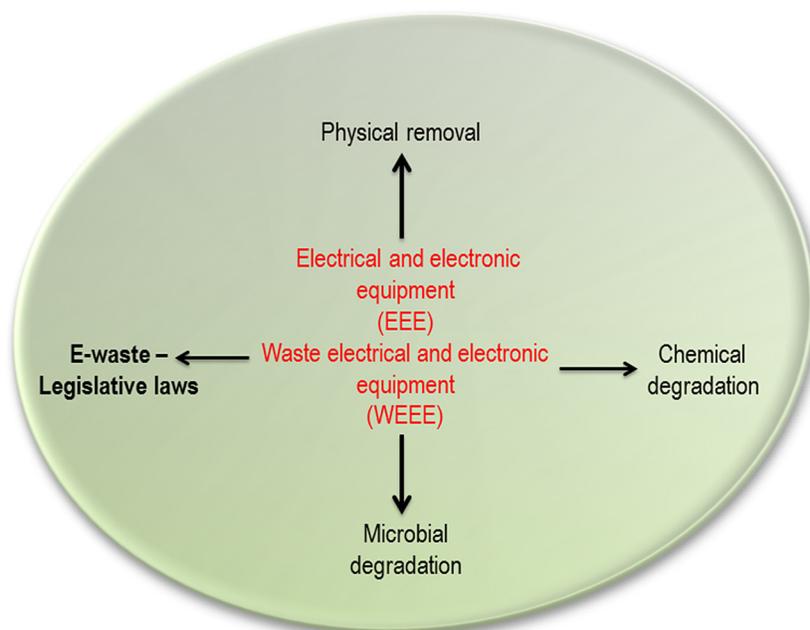


FIGURE 17.8 Schematic representation of e-waste management.

safety and handling of e-waste for personal protection and strict rules and regulations on e-waste should be followed in every country. The near futuristic practice newer technologies those involving the use of bacteria, fungi, and environmentally friendly entities will be given significance. The bio-recovery of heavy metals through bio-generated NPs will play a prime importance.

The biological food chain is also continuously affecting due to contamination caused by the use of e-waste. The toxicity of e-waste was lethal to the many life forms of living world; hence, its mitigation, bioremediation, and amelioration of environment are a major challenge of pollution boards to control it.

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# Lipid Peroxidation: A Signaling Mechanism in Diagnosis of Diseases

*Kalpana Sabanna Patil and Raju Ratan Wadekar*

## Abstract

Quantification of reactive oxygen species, is perplexing either *in vivo* or *in vitro* due to their short half-lives. Consequently, to define the magnitude of oxidative stress, the more stable oxidation products can be measured in biological samples. The oxidative stress leads to the lipid peroxidation that involves the initiation, termination and propagation of lipid radicals, wherein, the process involves the oxygen uptake, rearrangement of the double bonds in unsaturated lipids, that leads to polyunsaturated fatty acid deterioration. Subsequently, the toxic signaling end products are considered as biomarkers of free radicals that act both as signaling molecules and as cytotoxic products cause covalent alteration of lipid peroxidation products. The use of validated signaling mechanism (s) of Lipid peroxidation and products derived thereof exhibits its use clinical practice and basic clinical research as well as in clinical practice has become common place, and their presence as endpoints in clinical trials is now broadly accepted. This knowledge can be used to diagnose disease earlier, or to prevent it before it starts. The signaling markers can be used to excel the effectiveness of the prevailing medicines and to improve the new medicines.

**Keywords:** lipid peroxidation, isoprostanes, malondialdehyde, Alzheimer's disease, oxidative stress

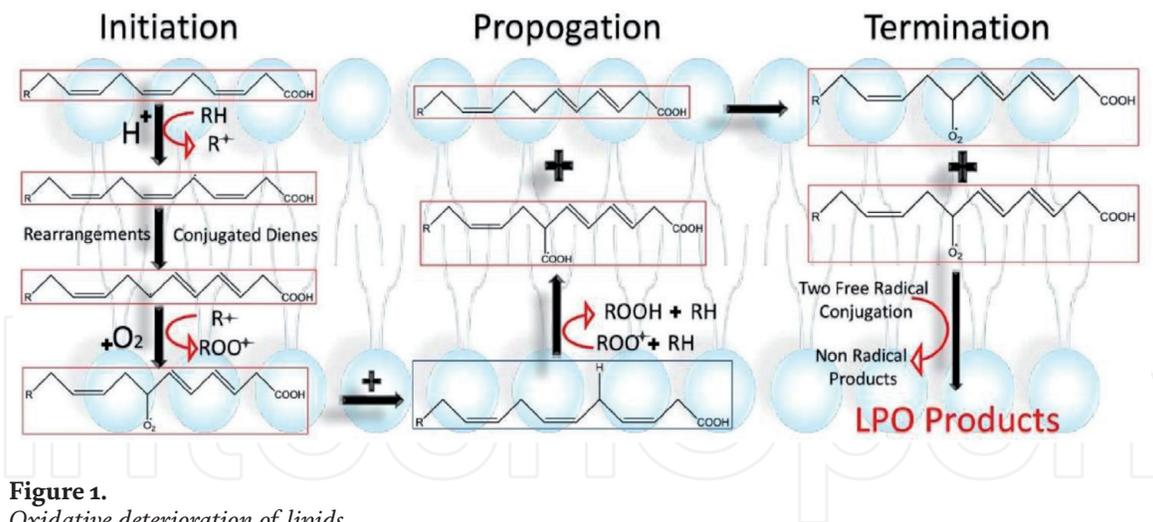
## 1. Introduction

Lipids are of two types: Polar and Non-polar. The polar lipids (Triglycerides), store in various cells but especially in adipose (fat) tissue, are usually the main source of energy for mammals. Polar lipids are underlying segments of cell layers, where in it contributes for the development of permeability barrier of cells and sub-cellular organelles in the form of a lipid bilayer [1]. The glycerol-based phospholipid is the significant type of membranous lipid bilayer and it is evidenced by the element that membrane lipids may regulate the biological functions of a membrane organelle by amending its biophysical characteristics, such as the divergence and absorptivity [2]. Lipids and its metabolite products facilitate a key ingredient in understanding the biology and serve as a signaling biomolecules in the diagnosis of diseases [3]. However, the leading enzymes that generate as lipid-signaling biomarkers are lipoxygenase, that intervene hydroperoxyeicosatetraenoic acids (HPETEs), lipoxins, leukotrienes, or hepoxilins biosynthesis after oxidation of fatty acids/arachidonic

acid (AA), cyclooxygenase that yields prostaglandins, and cytochrome P-450 (CYP) that produces epoxyeicosatrienoic acids, leukotoxins, thromboxane, or prostacyclin respectively [4, 5]. The signaling lipid biomarkers recruits via stimulation of a variety of receptors, including nuclear and G protein-coupled receptors. Moreover, several other types of lipid metabolites have been recognized as potent intracellular signal transduction molecules viz; i) diacylglycerol (DAG) and inositol phosphates (IPs) were derived from the phosphatidylinositol phosphates. DAG is a transcription nuclear factor- $\kappa$ B (NF- $\kappa$ B) which promotes cell survival and proliferation and also a physiological activator of protein kinase C [6, 7] and a small G protein [8]. On the other hand, IPs (lipid derived metabolites) are an extremely stimulating that intricate in signal transduction, results in activation of mTOR and Akt [9], and calcium homeostasis [10, 11]; ii) Sphingolipid derived from ceramide (sphingosine-1-phosphate), is an effective messenger molecule engaged in proliferation, adhesion, migration and also regulates calcium mobilization at molecular and cellular level of the organism [12–14]; iii) oxidative stress induced fatty acid derived eicosanoid and prostaglandins involved in inflammation [15, 16] and immunity [17]; iv) phosphatidylserine, (a phospholipid) that plays crucial role in a number of signaling pathways, includes fusogenic proteins, kinases and small GTPases [18]; v) the sex and growth hormones such as testosterone, progesterone, estrogen and cortisol that monitored a host body activities such as reproduction, blood pressure metabolism, inflammation, oxidative stress response etc. [19].

Molecular mechanism of lipid damage: The process of lipid peroxidation (LPO), is the resultant of oxidative stress and free radical production. Specifically, reactive oxygen species (ROS) attack polyunsaturated fatty acids (PUFAs) of cellular membranes and leads to the insult of functional and/or structural integrity of cell membranes, subsequently producing 4-hydroxy-2-nonenal (HNE), malondialdehyde (MDA) and acrolein (a group of  $\alpha$ ,  $\beta$ -unsaturated highly reactive aldehyde) [20, 21]. Therefore, these strong reactive aldehydes are significantly diffusive, able to attack and form covalent linkages with auxiliary cellular constituents. Moreover, the lipid peroxidation process continues as self-propagation followed by initiation of chain reactions and termination either with complete substrate utilization or through interaction with antioxidants such as tocopherol (Vitamin E). Neuroprostanes (neuroPs), isoprostanes (IsoPs) are the additional LPO products of arachidonic acid and docosahexaenoic acid (DHA), that are quantified in the biological fluids to diagnose the severity of the disease. Furthermore, the cyclized fatty acids proliferate further and metabolize the cellular membrane components, mainly lipids and proteins, and propagates the other LPO products in the body fluids [22].

Quantification of reactive oxygen species, is perplexing either *in vivo* or *in vitro* due to their short half-lives. Consequently, to define the magnitude of oxidative stress, the more stable oxidation products can be measured in biological samples. The oxidative stress leads to the lipid peroxidation that involves the initiation, termination and propagation of lipid radicals, wherein, the process involves the oxygen uptake, rearrangement of the double bonds in unsaturated lipids, that leads to polyunsaturated fatty acid deterioration. Subsequently, the toxic signaling end products are considered as biomarkers of free radicals that act both as signaling molecules and as cytotoxic products cause covalent alteration of lipid peroxidation products [23]. In respect of their oxidative-induced damage properties, these compounds are considered as disease mediators in the pathophysiology of many neurodegenerative diseases (NDs), including Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS), Diabetes, Atherosclerosis, Chronic inflammation, Asthma and liver injury that serve as potential biomarkers in the signaling mechanism in diagnosis of diseases [24]. Thus, it is necessary to understand the oxidative deterioration of lipids in a sequential five-step procedure



**Figure 1.**  
 Oxidative deterioration of lipids.

in which oxidants, either radical or non-radical species, attack lipids containing C-C double bonds [25, 26]. On the contrary of enzyme-based lipid metabolism, lipid peroxidation does follow a non-enzymatic process that continues in ahystericalmode: Initiation, propagation and termination (**Figure 1**) [27].

## 2. Mechanism of action of lipid peroxidation (LPO)

The process of LPO on membrane influences discrete functions from the increased rigidity of membrane, reduced action of membrane-confined enzymes, impairment of membrane receptors and modified permeability of the cell membrane. Similar to phospholipid impairment, radicals can also directly attack lipid-protein and membrane proteins mediate as well as protein-protein interconnection, subsequently affect the membrane integrity [28]. LPO products persuade such a loss of membrane integrity that ultimately leads to unadorned cytotoxicity, and could result in unrestrained cellular growth or even apoptosis. Rationally, the perturbation of the above-mentioned functions ensued by polyunsaturated fatty acids, along with the resultant metabolites and protein insults modifies the neuronal homeostasis, and leads to the multi-organ organ dysfunction [29–31].

## 3. Lipid peroxidation (LPO) products as biomarkers in neurodegenerative disorders

LPO products are significantly associated to the development of Alzheimer's diseases (AD); and hence, they are studied as potential disease signaling biomarkers in neurodegenerative disorders. LPO products such as MDA, IsoPs, TBARS, and fluorescent lipofuscin-like pigments (LPF) extensively studied and found in different human samples (plasma, serum and urine) of the patients suffering from neurodegenerative disorders. (Summarized in **Table 1**).

Histopathological studies revealed a co-localization of lipid peroxidation products and  $\beta$ -amyloidplaques in the brain of the AD. Also, the study evident for the presence of fatty acids in AD brain lesions produced a neurotoxic effect in cell culture increasing oxidative stress [41]. Since the brain contains high lipid content and high oxygen consumption, lipid peroxidation seems to play fundamental role in AD early detection. Similarly, IsoPsand its isomers produced via diverse actions that, are encountered as marginal oxidation products of the arachidonic acid [42]. Whereas, neuroPsenriched in the neuronal tissue and vital component

Sr. no	Biomarkers	Biological sample	Analytical technique	Results	Reference
01	8-Isoprostane	Urine	EIA	AD <DrD* AD+DM < DrD	[32]
02	Isoprostanes oxidized LDL	Urine	ELISA	Not differences between groups	[33]
03	8-Isoprotanes	Serum	ELISA	Non-frail AD < Pre-frail AD*	[34]
04	Isoprostanes	Urine	EIA	Non-frail AD < frail AD*	[35]
05	Isoprostanes, Neuroprostanes, dihom-isoprostanes	Urine	RIA	AD + placebo > AD treatment	[36]
06	MDA	Urine	GC-MS	Not differences between groups after the treatment	[37]
07	MDA	Urine	UPLC-MS/MS	Significant differences in groups	[38]
08	MDA	Plasma	HPLC-fluoresce	aMCI converted >aMCI stable	[39]
09	MDA	Blood	HPLC-MS	MDA blood levels do not correlated with different cognitive tests	[40]

**Table 1.**  
*Signaling mechanism of lipid peroxidation in biological samples of patients.*

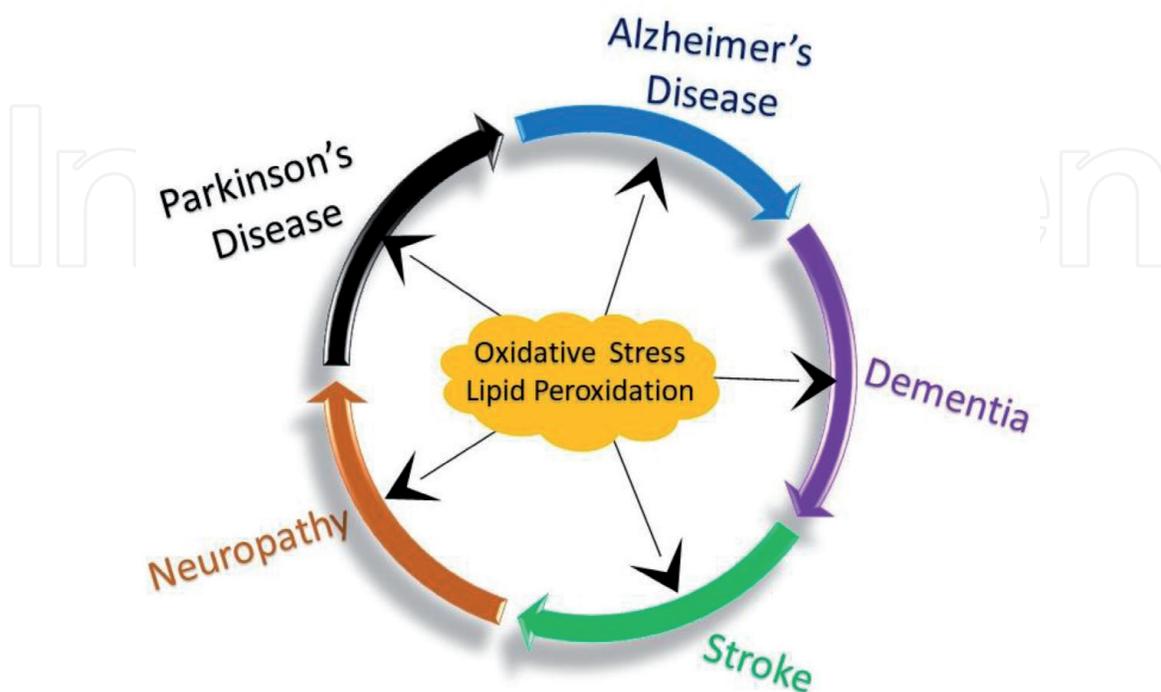
of the nervous tissues, awfully susceptible to oxidation [43]. Thus, the quantitative estimation of neuroPsaffords a significantsource of oxidative neuronal impairment-corresponding to IsoPs [44].

Malondialdehyde (MDA) a signaling molecule of LPO has ability to interact with micro-macromolecules such as nucleic acid bases, developingdivergent adducts, and can also react with proteins in a synergistic and covalent manner, subsequently, leads to the stimulation of strong immune responses and exhibits pro-fibrogenic and pro-inflammatory properties/mediators such as interleukins, cytokines etc. Furthermore, accumulation of MDA modifies membrane integrity by inducing increased intra and extracellular permeability and damage the fluidity of membrane lipid bilayer. Being a most mutagenic, MDA is capable of reacting with deoxyadenosine in DNA and deoxyguanosine, thus generating mutagenic DNA adducts [21, 31].

As the consequence of peroxidation of PUFAs (linoleic and arachidonic acid), Hydroxy-2-nonrenal (HNE) are formed, since they are the most abundant in fatty acids. The HNE, specifically, bind to amino acids mainly: cysteine, histidine and lysine proteinaceous residue addition by either the amino and thiol groups. The conjugates of protein residue and HNE, leads to the impairment of the normal protein function as well as structure, and also HNE exhibits reactivity with vital nucleic acids, lipids, signaling biomolecules and vitamins. Documented reports, suggests that, the HNE accumulates in extremely low concentration (10 µM), in response to oxidative stress and induces cytotoxicity and selective suppression of inducible and basal NF-kB factors. Therefore, increased levels of HNE results in Ca<sup>2+</sup> homeostasisimbalance, disruption of glutamate transport, membrane impairment, microtubule function, and cellular death via the activation of caspase pathways [28, 45].

Threonine metabolite product, acrolein generated by the bio activation of phagocytes and cyclophosphamide. Wherein, acrolein targets histidyl, lysyl and cysteinyl residue of protein side chain as well as reacts with nucleophilic sites in DNA, that results in DNA and protein adducts and, thus, initiates cytotoxicity specifically related to its ability to reduce glutathione [46]. Docosahexaenoic acid (DHA) enriched in neurons, and is a vital compound of the nervous tissue. It is a vital compound of the nervous tissue and enriched in neurons and extremely-susceptible to oxidation. DHA on oxidative stress, leads to the production of Neuroprostanes (F4-isoprostanes). In a biological aspect, neuroPs illustrates anti-inflammatory properties by inhibiting proteasome concentrated in the neurons membrane [45]. Nevertheless, the central nervous system (CNS) is one of the major targets of the LPO and peroxyl chain reactions induced by ROS, which eventually result in LPO products [47]. The role of LPO quantification in the pathogenesis of NDs is significant and extremely importance for the early detection of neurodegenerative disorders [45].

The most frequently exploited LPO products such as lysine residues and unsaturated aldehydes, including HNE and acrolein [48]. Several research studies have been probing the LPO products and disease state interrelation, and its application as possible biomarkers in order to assess prognosis and establish early detection of the disease [49]. Among the above-mentioned potential biomarkers, IsoPs signifies the most reliable and robust outcomes. Moreover, the IsoPs accurately process and assessed the oxidant stress *in vivo* via quantification of plasma and urinary sample. Also, *in situ* phospholipids composed of IsoPs that locates the free radical production and release from the cellular membrane via phospholipases in the plasma. IsoPs detected and quantified in a plethora of biological fluids including plasma cerebrospinal fluid, exhaled breath condensate, urine and bile [50]. On the other hand, neuroPs are a fundamental component of the nervous tissue, enriched in the neuronal tissue and extremely susceptible to oxidation [51]. Thus, the quantification of neuroPs provides a signaling biomarker of oxidative neuronal damage compare to IsoPs quantification. In addition, the quantity of neuroPs produced



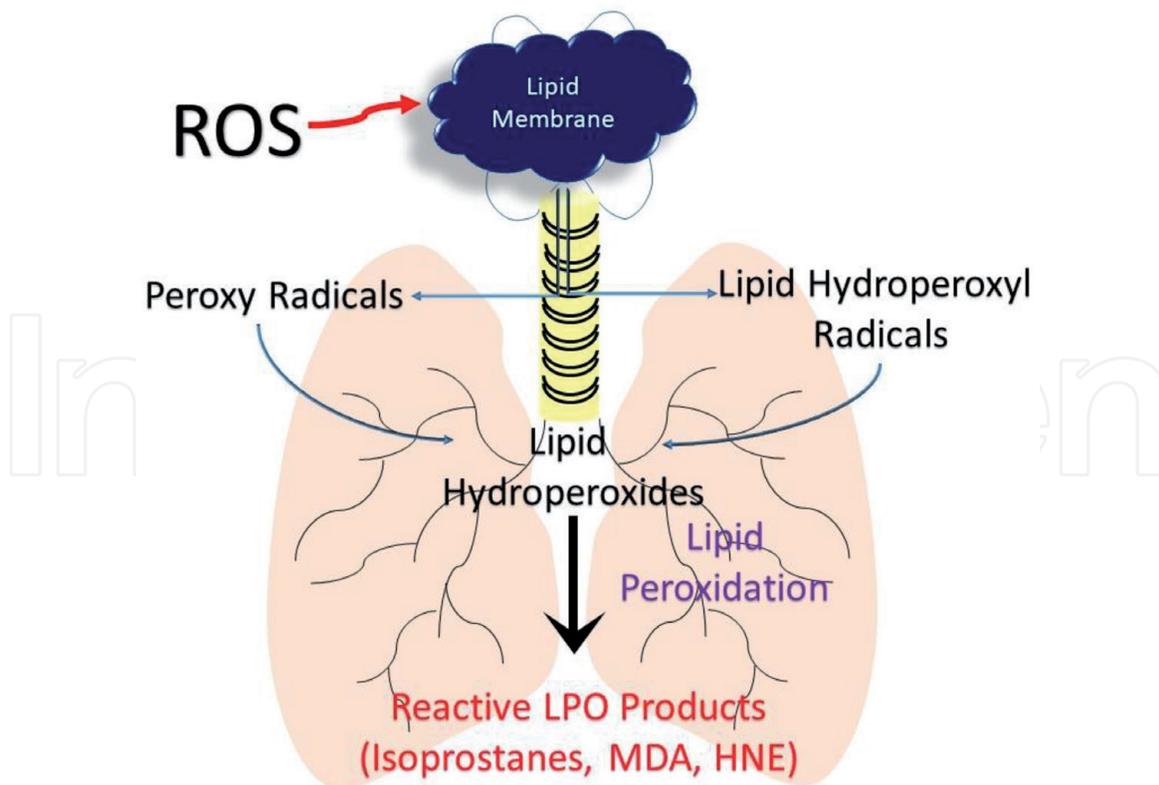
**Figure 2.**  
*Lipid peroxidation (LPO) products as biomarkers in neurodegenerative disorders.*

from DHA surpass that of IsoPs from arachidonic acid by 3.4 folds. NeuroPs are elevated in the cerebrospinal fluid and brain tissue in ND, such as Parkinson and Alzheimer's disease. Hence, quantification of neuroPs levels is a vital tool in evaluating brain oxidative impairment [52]. Whereas, crosslinking is a major factor in the development of pathology due to the promotion of intramolecular or intermolecular DNA and protein cross-linking, which results in intense change in the biochemical properties of various biomolecules (**Figure 1**). This articulated process is assumed to be a channel of interrelation chain reactions with covalent nucleophilic compounds. Also, the translated and interconnected experimental indicators with precise altered proteins in the CNS exhibited those definite cellular amendments are in concomitant with pathophysiology of Neurodegenerative diseases. Thus, the revival of scientific data affords a comprehensive knowledge in the advancement and employment of LPO products as potential biomarkers in the early diagnosis of the disease, altered biological processes, revealing potential active sites to target disease progression (**Figure 2**).

#### **4. Lipid peroxidation metabolites as influential signaling biomarkers in asthma and airway inflammation**

Oxidative stress at molecular and cellular level can have many detrimental effects on airway function, including airway smooth muscle contraction, induction of airway hyperresponsiveness, mucus hypersecretion, vascular exudation and shedding of epithelial cells. Furthermore, ROS can induce cytokine and chemokine production through induction of the oxidative stress-sensitive transcription of nuclear factor- $\kappa$ B in bronchial epithelial cells [53]. Recently discovered series of bioactive prostaglandin (PF)F<sub>2</sub>-like compounds were produced independently of the cyclooxygenase enzymes via the peroxidation of arachidonic acid, catalyzed by free radicals. The pathway leads to formation of 64 isomeric structures, of which 8-iso-PGF<sub>2</sub> $\alpha$  is most well characterized. Evidence suggests that 8-iso-PGF<sub>2</sub> $\alpha$  may act in part through the vascular thromboxane A<sub>2</sub>/PGH<sub>2</sub> (TP) receptor [54]. 8-iso-PGF<sub>2</sub> $\alpha$  has been found to elicit airway hyperresponsiveness in isolated perfused mouse lungs, and cause airway obstruction and air plasma exudation in guinea pigs *in vivo* [55]. These experimental findings offer assumption about the contribution of Isoprostanes to the airway narrowing that is characteristic of asthma and in addition to being reliable signaling marker of lipid peroxidation, Isoprostane may prove to have an important biological role in the pathological of asthma. A significant elevation of reactive oxygen species, MDA formation (A product of Lipid peroxidation) and Isoprostane was estimated in the broncho-alveolar lavage (BAL) fluid within 24 hrs of allergen-induced asthma. This clearly indicates, Isoprostane is produced as a biomarker in respiratory tract tissues that leads to the late observed physical symptoms in allergen-induced asthma [56].

A recent study demonstrated that concentrations of exhaled ethane were increased in patients with more severe bronchoconstriction (forced expiratory volume in one second (FEV<sub>1</sub>) <60%), compared with less-constricted patients (FEV<sub>1</sub> > 60%) and provides evidence that lipid peroxidation is related to asthma severity. These relationships between markers of oxidative stress and disease severity suggest that such tests may indicate the clinical status of asthma patients [57]. The increased level of 8-iso-PGF<sub>2</sub> $\alpha$  concentrations has been observed in chronic obstructive pulmonary diseases and asthma [58]. The discovery of Isoprostane has generated attention, as they provide a reliable index of oxidative stress *in vivo*. Isoprostane are structurally stable, are produced *in vivo* and are present in relatively high concentrations [59]. Traceable levels of F<sub>2</sub>-isoprostanes can be found in all normal animal and



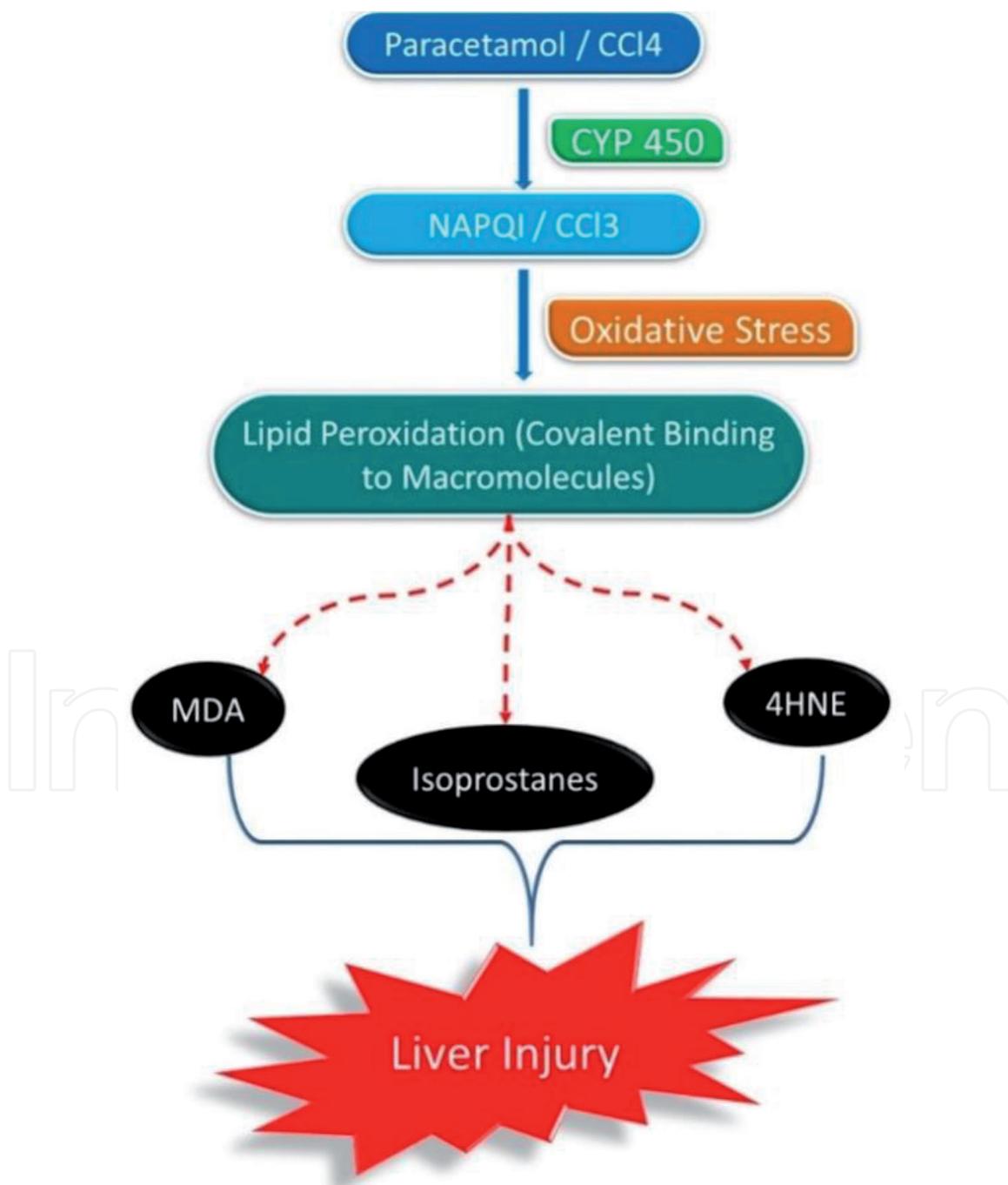
**Figure 3.**  
*Lipid peroxidation metabolites as influential signaling biomarkers in lung diseases.*

human biological fluids (including plasma, urine, bile, gastric juice, synovial fluid and cerebrospinal fluid)), and esterified in normal animal tissues. Thus, they overcome many of the methodological problems associated with other signaling markers. Determination of 8-iso-PGF<sub>2</sub> $\alpha$  as a marker of oxidative stress, of carbon tetrachloride (CCl<sub>4</sub>)-induced lipid peroxidation has been shown to be 20 times more sensitive than measurement of Thiobarbituric acid reactive substances (TBARS). Thus, the reliability of isoprostanes as *in vivo* markers of lipid peroxidation makes them an extremely valuable signaling biomarker for defining the potential of antioxidant agents (Vitamin C, E and  $\beta$ -carotene) in humans [60]. A significant amount of elevated ethane produced following lipid peroxidation has been observed in plasma and breath condensate of asthmatics as a biomarker indicator of acute airway inflammatory diseases. Moreover, measurement of auto-antibodies directed against oxidative modifications of low density lipids (LDL) is a recently developed technique that provides an *in vivo* marker of lipid peroxidation. Enzymes-linked immunosorbent assays are available in kit form, providing a quick and simple methodology. Thus measurement of isoprostanes in breath condensate should provide useful information concerning the degree of oxidant stress and success of antioxidant therapy in asthma (**Figure 3**).

## 5. Lipid peroxidation: a signaling mechanism in diagnosis of liver injury

Oxidative stress is one of the mechanisms involved in the pathogenesis of drug-induced reactive oxygen species which lead to the depletion of intracellular antioxidants, causing an imbalance in the redox status of the hepatic cells [61]. Rapid, extensive lipid peroxidation of the membrane structural lipids due to oxidative stress mechanism involved in the pathogenesis of drug-induced had seen proposed as the basis of drug-induced hepatocellular toxicity. The most of the xenobiotics such as Acetaminophen, Isoniazid and Rifampicin are well-known to

induced hepatic damage directly or indirectly via lipid peroxidation [62]. However, peroxy radical attribute to lipid peroxidation, thus known for the destabilization and disintegration of the cell membrane, that further causes arteriosclerosis, hepatic and kidney damage. The increased serum markers such as MDA formation are of diagnostic importance of hepatic injury because they are released due to the damage of hepatocytes and consequently participate in endogenous enzymatic antioxidant system imbalance [63]. CCl<sub>4</sub>-enhanced lipid peroxidation has been observed in liver tissue homogenates, isolated hepatocytes and in vivo, and this has been associated with changes in endoplasmic reticular enzyme activity, in vivo fatty acid export and protein synthesis [64]. CCl<sub>4</sub> metabolism enhances production of malondialdehyde in vitro and increase ethane production and lethality in vivo (**Figure 4**). Consequently, lipid peroxidation initiated by free radical reactions and unchecked by compromised cellular defenses, provides a possible link between



**Figure 4.** Lipid peroxidation: a signaling mechanism in diagnosis of liver injury.

ethanol metabolism and associated liver disease [65]. The lipid peroxide content of liver is elevated by both short and long-term ethanol exposure and an enhanced rate of lipid peroxide formation following ingestion has been ascertained by MDA production, diene conjugate formation and *in vivo* ethane and pentane exhalation. Lipid peroxidation might merely be a sign of oxidative processes which occur after reduced glutathione is depleted concomitant with free radical attack on cellular protein and nucleic acid. The elevated MDA formation as a product of lipid peroxidation in drug-induced liver damage provide a significant biological signaling marker for the early detection or diagnosis of liver injury.

## 6. Conclusion

The oxidative stress inducing compounds mediates metabolic process of lipids mainly via peroxidation that leads to the production of macromolecules such as Isoprostane, MDA, 4-HNE in the biological fluids. Moreover, the aldehyde like molecules produced via lipid peroxidation targets and modifies proteins and DNA substantially at macromolecule level. Furthermore, MDA and 4-HNE known to promote cross linking of protein/DNA reactions that significantly alleviates and alters the biomarkers biochemical property, thereby develops a clinical symptomatic states. The use of validated signaling mechanism (s) of Lipid peroxidation and products derived thereof in basic and clinical research as well as in clinical practice has become common place, and their presence as endpoints in clinical trials is now broadly accepted. This knowledge can be used to diagnose disease earlier, or to prevent it before it starts. The signaling markers can be used to improve the efficacy and safety of existing medicines and to develop new medicines.

## Conflict of interest

The authors declare no conflict of interest.

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# Study of Losartan's Effects on Different Biochemical Parameters in Essential Hypertensive Patients

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## ABSTRACT

The renin angiotensin system (RAS) provides the most powerful regulation of blood pressure and angiotensin II is the primary mediator in this system. The binding of angiotensin II to AT<sub>1</sub> receptors produces a number of potentially harmful effects that include increase in blood pressure, progression of atherosclerosis, myocardial and vascular hypertrophy. Losartan was the first angiotensin receptor blocker (ARB) which was found to reduce the risk of stroke and new-onset diabetes along with a proven benefit in stroke. The present study was designed to evaluate the effects of losartan on different biochemical parameters.

**Objective:** To study effects of monodrug (Losartan) therapy on blood sugar, lipid profile, uric acid and serum electrolytes over a period of six months.

**Methods:** Twenty-nine newly diagnosed patients of either gender with essential hypertension were included in the study. Baseline readings of lipid profile, serum electrolytes, fasting blood sugar and uric acid were recorded before starting losartan monotherapy and were repeated after six months.

**Results:** After comparing the means, there was a significant increase in HDL cholesterol and a significant decrease in serum uric acid levels after six months of losartan therapy. No significant difference was found in blood sugar and electrolyte levels.

**Conclusion:** These findings suggest that losartan can be an attractive option for the treatment of hypertension and for metabolic syndrome.

*Keywords: Lipid profile; BSL; serum electrolytes; SUA (serum uric acid); losartan; essential hypertension.*

## 1. INTRODUCTION

Hypertension is a major, common health problem, usually a progressive disorder and one of the leading causes of death and disability worldwide. It is a major risk factor for cardiovascular diseases [1,2]. Lowering of elevated blood pressure decreases morbidity from cardiovascular, cerebral and renal failure [3]. Essential hypertension is a condition where the cause for rise in blood pressure is not known [4]. The beneficial effects of antihypertensive agents on cardiovascular system can be counter balanced by the induction of metabolic disorders. The modifications in various metabolic parameters (like lipids, serum electrolytes, serum uric acid, blood sugar level etc.) are responsible for different adverse drug reactions of antihypertensive drugs. It might also have potential to produce secondary morbidities after long term use.

Several studies comparing antihypertensive agents have shown differences in risk reduction in cardiovascular diseases (CVD) with a similar blood pressure lowering effect, suggesting that specific pharmacological mechanisms may be involved [2,3]. The renin angiotensin aldosterone system (RAAS) is targeted by some of the most widely used antihypertensive medication classes like angiotensin receptor blockers (ARBs), aldosterone antagonists ACEI (Angiotensin converting Enzyme Inhibitors) and direct rennin inhibitors [5,6]. ARBs are increasingly used in the treatment of

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hypertension because of fewer side effects with blood pressure lowering abilities. Losartan was the first ARB to be discovered. It is a competitive antagonist and inverse agonist with  $10^4$  times more selectivity for AT<sub>1</sub> than AT<sub>2</sub> receptors. It generates active metabolite which is more potent and non-competitively blocks the AT<sub>1</sub> receptor with higher affinity. Thus, blockade of AT<sub>1</sub> receptors causes inhibition of vasoconstriction, sodium retention and reduces blood pressure [7,8].

The present study was designed to evaluate the effect of losartan monodrug therapy on different biochemical parameters. Various studies carried out with losartan showed no significant changes in the biochemical parameters. However, there have also been some studies which have shown significant favorable changes in the various parameters [9]. Therefore, the present study was designed to observe the effect of Losartan on different biochemical parameters in essential hypertension.

## 2. METHODS

It is an open prospective study conducted in OPD of medicine department of 50 bed multi-specialty private hospital in Western Maharashtra. Newly diagnosed patients of either sex were selected as per JNC 8. The patients with either gender in the age group 18-70 years, newly diagnosed as per JNC 8, stage I and II of essential hypertensives without comorbidities were included in the study. The patients excluded from the study were those taking hypolipidemic, hypoglycemic, uricosuric drug therapy, combination/ multidrug antihypertensive treatment, chronic drug therapy, steroids or estrogen, subjects with any hepatic or renal diseases, pregnant, lactating females, females on contraceptives and subjects with chronic history of smoking and alcoholism.

Twenty-nine patients, newly diagnosed, with mild to moderate hypertension were enrolled after taking informed and written consent. Before administering losartan, baseline blood pressure and biochemical parameters like lipid profile, serum electrolytes (sodium, potassium and calcium) uric acid, fasting blood sugar level (BSL) were recorded. After overnight fasting of 12-14 hours, blood sample was taken for laboratory investigation. Mono therapy with losartan (Dose range: 20- 50 mg OD) was started and follow up of blood pressure was carried out every month. The same biochemical parameters were measured after six months of losartan mono drug therapy. Institutional Ethics Committee (IEC) approval was taken prior to the initiation of the study. Study protocol and informed consent forms were also approved by Ethics Committee. Statistical analysis was done using version 20.0 SPSS software. Student's 'paired t' test was applied for statistical analysis of data. The data was expressed as mean  $\pm$  SD with t- value, p- value and  $p < 0.05$  was considered as statistically significant.

## 3. RESULTS

In the present study, it was observed that there was non-significant decrease in TC, TG, VLDL, LDL and very highly significant increase in HDL. Also, very highly significant decrease in serum uric acid (SUA) level was observed with losartan monotherapy. There was non-significant decrease in fasting BSL after receiving losartan. There were no changes in sodium, potassium and calcium levels.

**Table 1. Effect of losartan on lipid profile**

Losartan (n=29) 20mg – 50mg		Mean $\pm$ SD		t-value	p-value
		Before	After		
Lipid Profile (mg/dl)	TC	191.59 $\pm$ 26.40	188.69 $\pm$ 23.39	0.8400	0.4070
	TG	118.97 $\pm$ 14.05	118.24 $\pm$ 11.82	0.4200	0.6780
	HDL	43.97 $\pm$ 7.58	47.79 $\pm$ 8.12*	-4.5400	<0.0001
	LDL	123.79 $\pm$ 22.40	117.24 $\pm$ 17.01	1.9900	0.0560
	VLDL	23.82 $\pm$ 2.79	23.6 $\pm$ 2.38	0.5000	0.6240

*Student's paired t-test: \*p<0.05*

*Value expressed as mean  $\pm$ SD; paired t test \*\*\* p< 0.0001 very highly significant (baseline vs 6 months).  
 Abbreviations:- TC- Total Cholesterol, TG- Triglycerides, VLDL- Very low density lipoproteins, LDL- Low density lipoproteins, HDL- High density lipoproteins*

**Table 2. Effect of losartan on serum electrolytes, serum uric acid and fasting blood sugar level**

Losartan (n=29) 20mg – 50mg		Mean ± SD		t-value	p-value
		Before	After		
Electrolytes (mEq/ L)	Na <sup>+</sup>	139.51±3.66	138.41±3.05	1.5400	0.1350
	K <sup>+</sup>	4.13±0.36	4.04±0.25	1.3100	0.2000
	Ca <sup>++</sup>	9.47±0.60	9.53±0.51	-0.6900	0.4940
SUA (mg/ dl)		4.02±0.72	3.61±0.45***	4.7600	<0.0001
Fasting BSL (mg/ dl)		83.97±12.66	81.21±11.44	1.7200	0.0970

*Student's paired t-test: \*p<0.05*

*Value expressed as mean ±SD; paired t test \*\*\* p< 0.0001 very highly significant (baseline vs 6 months).*

*Abbreviations:- F BSL- Fasting blood sugar level, Na<sup>+</sup>- Sodium, K<sup>+</sup>- Potassium, Ca<sup>++</sup>- Calcium, SUA- Serum Uric acid.*

## 4. DISCUSSION

### 4.1 Effects on Lipids

Dyslipidemia is more common in untreated hypertensives than normotensives where increase in lipid levels is seen as the blood pressure (BP) is increased. Many studies have shown that total cholesterol, TG and virtually all fractions of lipoproteins are frequently abnormal among hypertensive patients when compared to the normal population [10]. High levels of serum cholesterol are known to increase the risk of developing macrovascular complications such as coronary heart disease and stroke. Plasma HDL levels are inversely related to the risk of atherosclerosis and CVD [11]. The main objective of this study was to compare baseline levels of lipid profile with lipid levels obtained after six months of losartan mono drug therapy [12].

The present study showed that on administration of losartan, there was a slight decrease in the levels of TC, TG, LDL and VLDL. However, these changes were statistically insignificant while there was a significant increase in HDL levels. There are numerous studies which are in line with the present study result [13,14,15]. An increase in adiponectin levels have also been observed with ARBs [16]. They are reported to be linked to an elevation in HDL cholesterol [17] which is an observation that supports our present findings. Hanefeld M et al in their study, observed the effect of ARB (Valsartan) on lipid profile [6]. There were no significant changes in levels of TG, VLDL and marked decrease in LDL levels were seen with valsartan monotherapy. According to them, the possible mechanism that contributed to the beneficial effects on lipids was a reduction in catecholamine levels by AT<sub>1</sub> receptors antagonists [18]. Various studies are in contrast to the present study findings [19,20]. This contrast may arise due to variation between doses and the duration of drug treatment in various studies.

The wide uses of ARBs for the treatment of hypertension and hypertension related organ damage have succeeded in reducing the onset of cardiovascular diseases, preventing organ damage and cardiac death. These beneficial effects of ARBs are largely dependent upon their primary effects on lowering of blood pressure. This group of agents exerts a wide variety of biological effects on vascular metabolism including antioxidative and anti-inflammatory actions [21]. These pleiotropic actions therefore play a role in cardiovascular protection.

### 4.2 Effects on Blood Sugar Levels

In the present study, a slight decrease in blood sugar levels were observed, which was insignificant. There are number of studies which demonstrate that ARBs do not show any significant changes in blood sugar levels [13,14,22]. Certain studies stated that treatment for longer periods or with higher doses, was associated with a significant fall in the BSL [23]. The fall in BSL, be it significant or non significant, can be explained on the basis of following mechanism.

#### 4.2.1 Activation of PPAR<sub>γ</sub>

Peroxisome Proliferator – activated receptor gamma (PPAR<sub>γ</sub>) represent a family of ligand activated nuclear receptors involved in glucose and lipid metabolism [22,24,25]. Pharmacological activation of

PPAR $\gamma$  improves glucose tolerance and insulin sensitivity in type 2 diabetes patients, thus proving that PPAR $\gamma$  agonists are clinically useful in ameliorating type 2 diabetes [26]. Another underlying mechanism possibly involved in the reduction of new-onset diabetes is RAS inhibition [27]. From a theoretical point of view, preventing type 2 diabetes mellitus by RAS inhibition may result from a preservation of  $\beta$  cell function and/ or an enhancement of insulin sensitivity, thereby decreasing the need for pancreatic insulin secretion [28]. Targeting RAS may lead to alterations in microcirculation and changes in ionic status that indeed could potentially affect the islet insulin secretion as well as the cellular insulin action. However unexpected insulin mechanism may also play a role, as newly recognized components of the RAS have been observed to modulate cardiovascular and renal regulation or even adipocyte turnover [29]. Besides, a pure haemodynamic effect on cellular insulin action, by blocking angiotensin II has also been described [30].

Therapy with ARBs shows improvement in glucose metabolism. Large clinical trials has evaluated the effects of ARBs on cardiovascular end points. An analysis of comorbidity showed that such therapy with ARBs substantially lowers the risk for type 2 diabetes when compared with other antihypertensive drugs and placebo [31].

### **4.3 Effect of Angiotensin Receptor Blocker (ARBs) on SUA**

Hyperuricemia has been associated with endothelial dysfunction, impaired oxidative metabolism, stimulation of granulocyte adherence, increased platelet aggregation and all these are implicated in the pathogenesis of hypertension. Hyperuricemia may be a precursor of hypertension or be a reflection of subclinical renal dysfunction may cause both increase in serum uric acid level and increase in blood pressure [32]. Elevated serum uric acid in hypertensive patients has been associated with 3-5 folds increased risk of coronary artery disease or cerebrovascular disease compared with normal uric acid level. Lowering serum uric acid level might be beneficial in slowing progression of CVD (Cardiovascular Disease) in hypertensive patients [33,34].

The presence of elevated uric acid defined as  $\geq 7\text{mg/dl}$  levels has been linked to multiple comorbidities including gout hypertension chronic kidney disease (CKD), diabetes, obesity & heart failure. In our study, a highly significant fall in serum uric acid (SUA) level was observed with losartan monotherapy. There are numerous studies which shows that ARBs and in particular losartan demonstrates a significant reduction in SUA levels [35].

The mechanism involved in this process may be explained as follows:

#### **4.3.1 Reabsorption of uric acid transporter URAT<sub>1</sub> and secretion via other transporters**

URAT<sub>1</sub> mainly contributes to renal absorption of uric acid across the apical membrane of proximal tubular epithelial cells. Since URAT<sub>1</sub> is an anion/ uric acid exchanger and compounds like PZA (Pyrazine carboxylic acid) and lactic acid stimulate the reabsorption of acid, modulation of URAT<sub>1</sub> may occur due to reduction and increment of SUA levels by cis inhibition and trans stimulation of URAT<sub>1</sub> respectively by ARBs. Losartan exhibited inhibitory effects on the uptake of uric acid by URAT<sub>1</sub>. The hypouricemic effect of Losartan may be due to the fact that Losartan targets the urate anion exchange and decrease urate absorption in the proximal convoluted tubule. As a result, urate excretion is increased which leads to increased renal uric acid excretion [36]. However, there are certain studies that show ARBs do not any effect on SUA levels [37]. Such studies are in contrast with our study findings.

### **4.4 Effect of ARBs on Serum Electrolytes (Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>++</sup>)**

Losartan showed no change in sodium, potassium and calcium levels in the current study. There are studies which display non significant changes in serum electrolytes on treatment with ARBs. The present study shows a decrease in sodium levels, but not significant. This decrease can be explained by the action of ARBs in promoting renal excretion of sodium and water (natriuretic and diuretic effect) by blocking the effect of angiotensin II in the kidney and by blocking ang II stimulation of aldosterone secretion [38].

In some studies, hyperkalaemia has been observed on the treatment of ARBs, which can be explained on the basis of following mechanism- Bakris GL et al investigated the impact of ACEI and ARBs on potassium in renal failure. They exhibited that in presence of renal insufficiency, the ARBs do not raise serum K<sup>+</sup> (to the same degree as ACEIs). Effect on serum K<sup>+</sup> is related to a relatively smaller reduction in plasma aldosterone by ARBs and not related to changes in GFR. Thus, treatment with ARBs, especially in patients with renal insufficiency is less likely to affect the serum K<sup>+</sup> levels [39]. In present study, ARBs have shown, a non significant decrease in levels of potassium wherein the values lie within normal limits.

## 5. CONCLUSION

The results of present study are an important step to better understand the clinical efficacy of losartan especially in hypertensive Indian population. In conclusion, losartan is an efficacious antihypertensive but offers highly significant increase in HDL and highly significant decrease in SUA level. Thus, the metabolic effect of antihypertensive drugs could be of special importance in long term treatment of essential hypertension. It suggests that losartan is an attractive option for treatment of hypertension as well as in hypertension associated with hyperuricemia, gout, hyperlipidemia, type 2 diabetes patients and in patients with metabolic syndromes.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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# Surgical Techniques in Pediatric and Adolescent Urology



**Mohan S Gundeti**



# CONTENTS

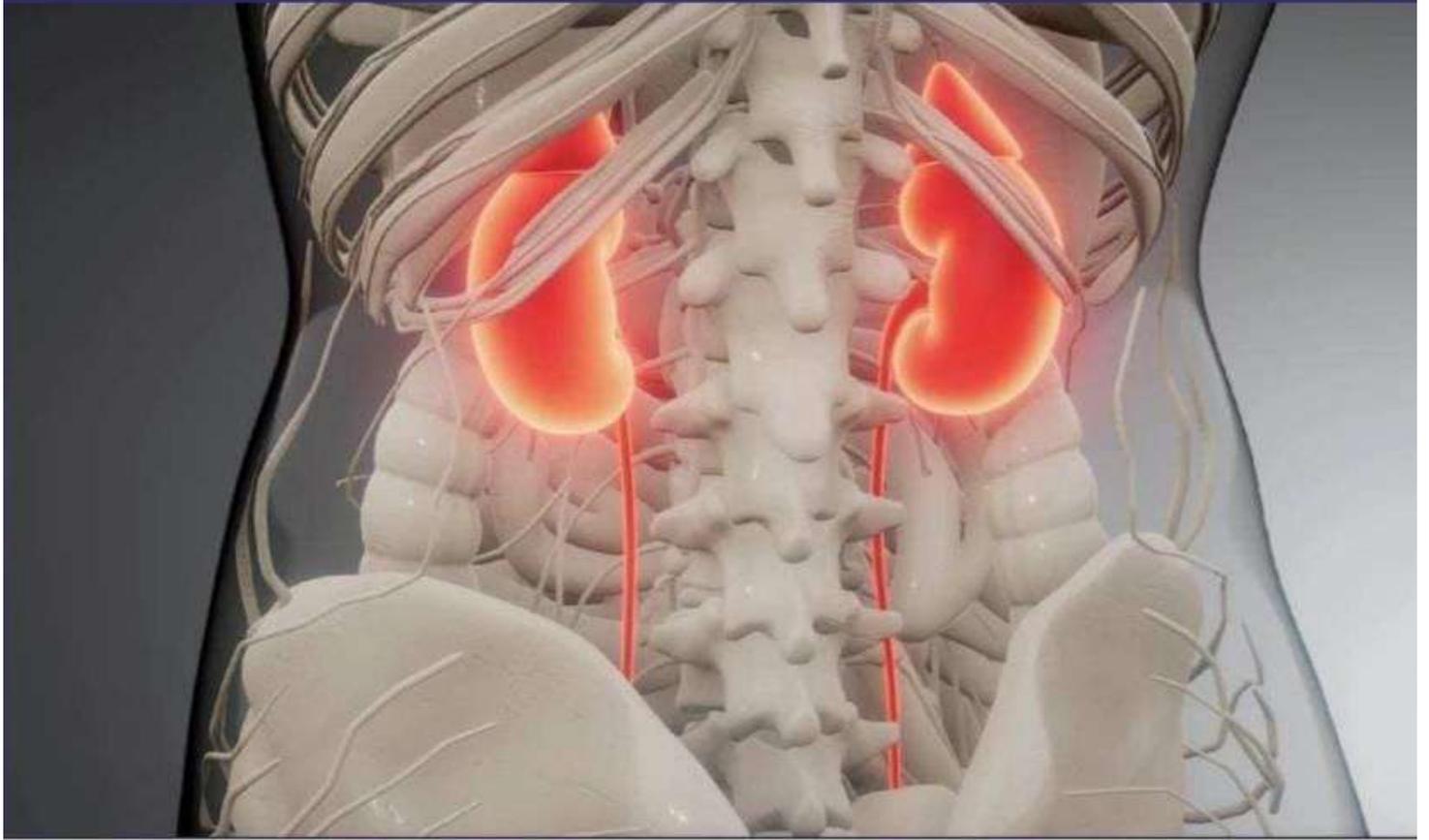
## SECTION 1 History, Anesthesia and Basic Surgical Principles and Training

<b>Chapter 1. History of Pediatric Urological Reconstructions .....</b>	<b>3</b>
<i>Duncan R Morhardt, David A Bloom</i>	
<b>Chapter 2. Ethical Consideration in Pediatric Surgical Reconstructions .....</b>	<b>9</b>
<i>Mindy B Statter, Peter Angelos</i>	
<b>Chapter 3. Special Anesthetic Consideration in Infants Toddlers .....</b>	<b>17</b>
<i>Annie Amin, Igor Tkachenko</i>	
<b>Chapter 4. Postoperative Pain Control and Regional Anesthesia .....</b>	<b>23</b>
<i>Ashish Gupta, Andrew Wuenstel</i>	
<b>Chapter 5. Recent Advances on Long-term Effects of Anesthesia on Children .....</b>	<b>30</b>
<i>Roshan Patel, Zheng Xie</i>	
<b>Chapter 6. Fluid, Electrolyte Balance and Parenteral Nutrition .....</b>	<b>39</b>
<i>Sudhir Sriram, Jaideep K Singh</i>	
<b>Chapter 7. Basic Surgical Principles of Pediatric Surgery .....</b>	<b>50</b>
<i>Nikunj K Chokshi, Mark B Slidell</i>	
<b>Chapter 8. Plastic Surgical Principles: Skin Flaps/Tissue Transfer/Myocutaneous Flaps in Consideration of Urological Reconstructions .....</b>	<b>60</b>
<i>David H Song</i>	
<b>Chapter 9. Surgical Scars, Prevention, Excisions and Revisions .....</b>	<b>67</b>
<i>Lydia Willimas, Russell R Reid</i>	
<b>Chapter 10. Basics of Instrumentation, Suture Material and Equipment for Open Surgery .....</b>	<b>73</b>
<i>Gursev Sandlas</i>	
<b>Chapter 11. Surgical Training in 21st Century (Role of Simulation/Inanimate Models) .....</b>	<b>77</b>
<i>Thomas G Leffler, Alison C Keenan, Patrick H McKenna</i>	
<b>Chapter 12. Role of Simulation in Current Era of Surgical Training .....</b>	<b>86</b>
<i>Prasad Patki, Srivathsan Ramani</i>	

**SECTION 3 Male Genital Reconstruction**

<b>Chapter 14. Anatomy of Penis and Neural Innervation in Respect to Hypospadias and Epispadias Reconstructions</b> .....	123
<i>Natalija Kovacevic, Yegappan Lakshmanan</i>	
<b>Chapter 15. Surgical Reconstructions of Distal Hypospadias: The University of Chicago Experience</b> .....	129
<i>Nimrod S Barashi, Mohan S Gundeti</i>	
<b>Chapter 16. Two-stage Repair of Proximal Hypospadias</b> .....	142
<i>Christopher Long, Mark R Zaentz</i>	
<b>Chapter 17. Different Methods of Repair for Chordae Corrections without Hypospadias</b> .....	152
<i>Marcos Perez-Brayfield, Ramphis A Morales-López</i>	
<b>Chapter 18. Inconspicuous Penis: Different Surgical Approaches</b> .....	162
<i>Nothale Webb, Ashish Jwani, Juan I Bortogony</i>	
<b>Chapter 19. Repair of Urethral Diverticulum Congenital and Acquired</b> .....	174
<i>Matthew D Timberlake, Micah A Jacobs</i>	
<b>Chapter 20. Redo Hypospadias Repair</b> .....	179
<i>Lisieux Eyer de Jesus, João Luiz Pippi-Salle</i>	
<b>Chapter 21. Redo and Secondary Procedures in Adolescent Adult Life Hypospadias</b> .....	188
<i>Maneer K Hanna, Adam S Howie</i>	
<b>Chapter 22. Preputioplasty in Hypospadias Repair</b> .....	201
<i>Amilal Bhat, Vikash Singh Tomar, Mahakshit Bhat</i>	
<b>Chapter 23. Penile Torsion</b> .....	207
<i>Amilal Bhat, Mahakshit Bhat, Vikash Singh Tomar</i>	
<b>Chapter 24. Scrotoplasty in Penoscrotal Transposition in Hypospadias</b> .....	223
<i>Amilal Bhat, Gordhan R Choudhary, Akshita Bhat</i>	
<b>Chapter 25. Urethroplasty and Urethral Reconstructions for Trauma in Pediatric Patients</b> .....	229
<i>Joseph J Pariser, Richard A Santucci</i>	

<b>Chapter 26. Duplex Urethra Repairs</b> .....	241
<i>MS Ansari, Ankur Bansal, Ashwin P Sekhar, Priyank Yadav</i>	
<b>Chapter 27. Male and Female Epispadias Repair</b> .....	247
<i>Alexander Cho, Pankaj Mishra, Imran Mushtaq</i>	
<b>Chapter 28. Radical Soft Tissue Mobilization</b> .....	263
<i>Marc-David Leclair, Sébastien Faraj</i>	
<b>Chapter 29. Male Bladder Exstrophy Repair: Different Approaches</b> .....	266
<i>Matthew C Rasprenski, John P Gearhart</i>	
<b>Chapter 30. Circumcision and Meatotomy: Techniques and Other Considerations</b> .....	281
<i>Stephen R Nold, Mark A Faasse</i>	
<b>Chapter 31. Inguinal Hernia and Hydrocele</b> .....	290
<i>Yolanda Pullin, Juan Manuel Morales, Pedro-José López E</i>	
<b>Chapter 32. Open Inguinal Orchiopexy</b> .....	297
<i>Stuart O'Toole</i>	
<b>Chapter 33. Surgery for Testicular Torsion</b> .....	
<i>Gregory Shepherd, Nila Fraser, Manoj Shenoy</i>	
<b>Chapter 34. Childhood Reconstruction of Aphallia</b> .....	
<i>YJL (Yves) Bodar, Aseem R Shukla</i>	
<b>Chapter 35. Phalloplasty: Surgical Techniques</b> .....	317
<i>Jonathan Kaye, Blake W Palmer, Bradley P Krapp</i>	
<b>Chapter 36. Varicocele Ligations: Open Surgical and Different Approaches</b> .....	330
<i>Rajendra B Nerli, Mallikarjuna Reddy N, Shridhar C Ghagane</i>	



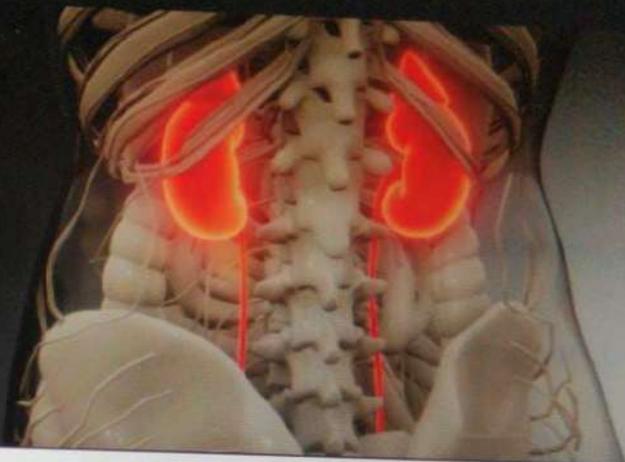
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# Recent advances in hypospadias

Epidemiology, Diagnosis and Treatment

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Hypospadias is an abnormality of anterior urethral and penile development in which the urethral opening is ectopically located on the ventral part of the penis proximal to the tip of the glans penis, which, in this, is splayed open. The earliest medical text describing hypospadias dates back to the second century CE and was the work of Galen, the first to use the term. During the first millennium, the primary treatment for hypospadias was amputation of the penis distal to the meatus. Since that time, many have contributed to development of modern hypospadias repair. More than 300 different types of repairs have been described in the medical literature. Although most reports have been in the past 60 years, most basic techniques were described over a century ago. Modern anesthetic techniques, fine instrumentation, sutures, dressing materials, and antibiotics have improved clinical outcomes and have, in most cases, allowed surgical treatment with a single-stage repair within the first year of life on an outpatient basis.



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Practical and Clinical Guide  
for  
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# Progress in Medicine

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# Obstetric Hemorrhage

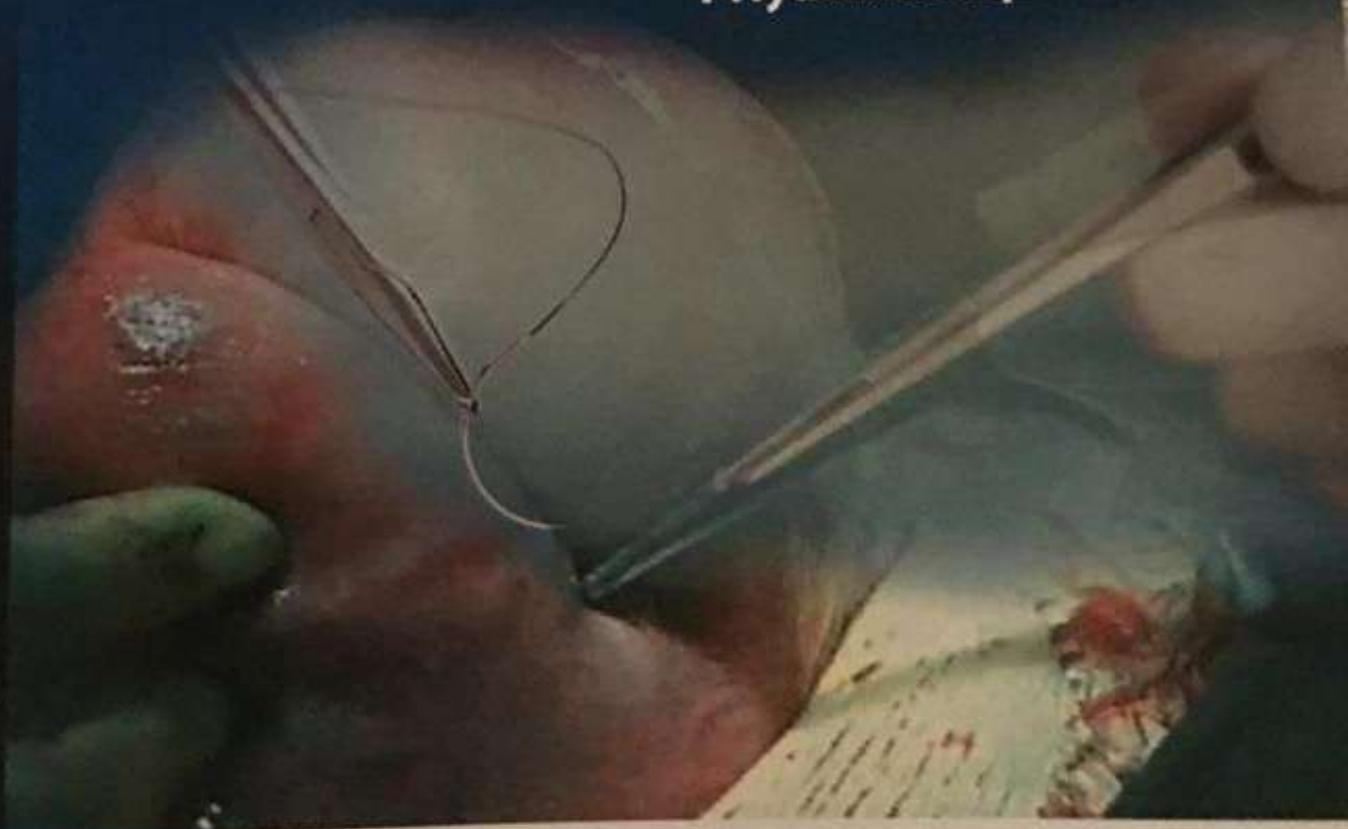
Evidence-based Management  
and Recent Advances

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*Forewords*

**CN Purandare • Nandita Palshetkar • Sabaratnam Arulkumaran**



# Obstetric Hemorrhage: Prevention and Management (Golden Hour)

MB Bellad

*A profuse hemorrhage occurring prior to or shortly after the birth of the child is always dangerous and not infrequently a fatal complication.*

—J Whitridge Williams (1903).

## INTRODUCTION

Obstetrics is a bloody business as rightly said. Following are the important causes of obstetric hemorrhage excluding accidental and incidental causes.

Obstetric hemorrhage with hypertension and infection to be one of the dangerous "red" of maternal death causes. It also is a leading cause for admission of pregnant and postpartum women to intensive care units.

**Bleeding in early pregnancy:** Miscarriage related, ectopic pregnancy, molar pregnancy, and others.

**Antepartum hemorrhage (APH):** Placenta previa, abruptio placenta, and others.

**Postpartum hemorrhage (PPH):** 4 Ts—(1) tone, (2) trauma, (3) tissue, and (4) thrombin.

**Shock index (SI):** Heart rate or systolic blood pressure (SBP).

This is an important that helps in the management even when the hypertensive woman who after bleeding still has normal range of blood pressure.

**Shock index:**

< 0.9 = Normal

0.9-1.69 = Mild shock

> 1.7 = Severe shock, this is a very simple

## ■ BLEEDING IN EARLY PREGNANCY

Three important causes—(1) miscarriage (abortion), (2) ectopic pregnancy, and (3) molar pregnancy.

### Prevention in General

Optimal age of conception plays an important role as extremes of reproductive ages are associated with increased chromosomal defects.

**Preconceptional health and care:** Optimal state of health at the entry of pregnancy is single important factor for good pregnancy outcome. Treatment and correction of common health conditions like anemia, hypothyroidism, hyperglycemia, and other conditions (that impair both maternal health, conception, embryo, and fetus) play an important role to ensure healthy pregnancy. Immunization against rubella is important.

To ensure good health, of women before and during pregnancy, it is important to give good health facilities and adequate nutrition to the girl child and adolescent. In government surveys, eligible couple survey should be used to ensure this.

### Case Scenario 1

*Miscarriage or Abortion Related*

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To

The Spl Officer to Vice Chancellor  
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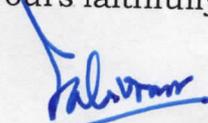
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Yours faithfully,

  
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# Hyperglycemia and Hypoglycemia in the Long-term Care of Elderly Diabetics

MV Jali

## ABSTRACT

With the aging of the population and longer life expectancies, the prevalence of population with multiple chronic medical conditions has increased. It is difficult to manage these conditions as people age has led to more individuals with multiple medical conditions admitted to the long-term care facilities. Older adults with diabetes residing in the long-term facilities represent the most vulnerable of this cohort. They are at a higher risk of hypoglycemia for many reasons, including insulin deficiency and progressive renal insufficiency. Also, older adults tend to have higher rates of unidentified cognitive deficits, causing difficulty in complex self-care. Older patients with type 2 diabetes mellitus (T2DM) are at a higher risk of developing cognitive impairment and, therefore, are in danger of being unable to self-manage their disease. To prevent further complications from T2DM, patients can self-manage their glucose levels and medication intake. Hypoglycemic events should be meticulously monitored, and glycemic targets may need to be adjusted to accommodate the changing requirements of the older adult.

## INTRODUCTION

The elderly population is one of the most discussed global phenomena in the present day.<sup>1</sup> Countries with an increasing population like India have a large number of people now aged over 60 years or more. In the last five decades, the people over 60 years has tripled and increased shortly. According to census 2011, older people are 8.14% of the total population. The projections for the people over 60 years in the next four censuses are 133.32 million (2021), 178.59 (2031), 236.01 million (2041), and 300.96 million (2051).<sup>1</sup> The increase in the elderly population is the result of changing fertility and mortality regimes over the last five decades. Older individuals are highly prone to mental morbidities due to the aging of the

brain, problems associated with physical health, cerebral pathology, socioeconomic factors such as the breakdown of the family support systems, and a decrease in economic independence. The mental disorders frequently encountered include dementia and mood disorders.<sup>2</sup> Other complications include neurotic and personality disorders, drug and alcohol abuse, delirium, Alzheimer's, and mental psychosis. Nevertheless, understanding the aging process remains a challenge. Many different clinicians practice geriatric medicine in a wide variety of settings: Hospital wards, outpatient clinics, day hospitals, general practitioner surgeries, care homes, and the patient's own home.<sup>3</sup>

Diabetes is a significant health condition for the aging people; at least 20% of patients over the

TABLE 1: Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes.

Patient characteristics/health status	Rationale	Reasonable A1c goal <sup>‡</sup>	Fasting or preprandial glucose (mg/dL)	Bedtime glucose (mg/dL)	Blood pressure (mm Hg)	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5%	90–130	90–150	<140/90	Statin unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0%	90–150	100–180	<140/90	Statin unless contraindicated or not tolerated
Very complex/poor health (long-term care or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5% <sup>†</sup>	100–180	110–200	<150/90	Consider the likelihood of benefit with a statin (secondary prevention more so than primary)

(ADL: activities of daily living)

\* Coexisting chronic illnesses are conditions severe enough to require medications or lifestyle management and may include arthritis, cancer, congestive heart failure, depression, emphysema, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. By "multiple," we mean at least three, but many patients may have five or more.<sup>6</sup>

\*\* The presence of a single end-stage chronic illness, such as stage 3–4 congestive heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy.

<sup>†</sup> A1c of 8.5% equates to an estimated average glucose of ~200 mg/dL. Looser glycemic targets than this may expose patients to acute risks from glycosuria, dehydration, hyperglycemic hyperosmolar syndrome, and poor wound healing.

<sup>‡</sup> A lower A1c goal may be set for an individual, if achievable without recurrent or severe hypoglycemia or undue treatment burden.

Note: This represents a consensus framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes. The particular patient categories are general concepts. Not every patient will undoubtedly fall into a specific group. Consideration of patient and caregiver preferences is an essential aspect of treatment individualization. Additionally, a patient's health status and preferences may change over time.

Source: American Diabetes Association. Older Adults: Section 10. Standards of Medical Care in Diabetes—2015. Diabetes Care. 2015;38(Suppl. 1):S67-9. Ref. Footnotes

and unpredictable hypoglycemia, as the geriatric population is less likely to take advantage of reducing the risk of microvascular complications and more likely to suffer serious adverse effects from hypoglycemia.<sup>9</sup>

Dorner guidelines allow for liberalization of the dietary treatment of diabetes in people

with type 2 diabetes mellitus (T2DM) in long-term care facilities.<sup>10</sup> The care team should work together to promote specific policies and protocols in the facility to address how individual T2DM patients assessed, and which diets offered as an adjunct to treatment. Careful monitoring of blood glucose levels, medications,

and response to treatment may allow for more liberalization of the food. Diet liberalization can help to promote better health and improved quality of life for our elderly residents. Although hyperglycemia control may be necessary for older individuals with diabetes, more significant reductions in morbidity and mortality are likely to result from control of other cardiovascular risk factors rather than from tight glycemic control alone. There is substantial evidence from clinical trials of the value of treating hypertension in the elderly.<sup>7,8</sup> There is less evidence for lipid-lowering and aspirin therapy, although the benefits of these interventions for primary and secondary prevention are likely to apply to older adults whose life expectancies are equal or exceed the time frames seen in clinical trials.<sup>11</sup>

### ■ HYPOGLYCEMIA AND HYPERGLYCEMIA

With the aging of the population and longer life expectancies, the prevalence of population with multiple chronic medical conditions has increased. It is difficult to manage these conditions as people age (because of changes in physical, functional, or cognitive abilities and the complexity of many treatment regimens) has led to more individuals with multiple medical conditions admitted to the long-term care facilities. Older adults with diabetes residing in the long-term care facilities represent the most vulnerable of this cohort. Studies that specifically target diabetes management in older population are lacking, and those that focus diabetes management in the extended care facilities are even fewer. The lack of knowledge regarding the care of the elderly residing in long-term care with diabetes may lead to treatment failure and a higher risk of hyperglycemia as well as hypoglycemia. In aging populations, hypoglycemia has the potential for catastrophic consequences. To avoid this, the management of older population with diabetes and other medical comorbidities residing in long-term care facilities requires a more holistic approach compared with focusing on individual chronic disease goal achievement.<sup>12</sup>

Older adults are at a higher risk of hypoglycemia for many reasons, including insulin deficiency and progressive renal insufficiency. Also, older adults tend to have higher rates of

unidentified cognitive deficits, causing difficulties in complex self-care activities (e.g., glucose monitoring and adjusting insulin doses). These deficits have been associated with increased risk of hypoglycemia and with severe hypoglycemia linked to increased dementia. Therefore, it is essential to screen older adults for cognitive dysfunction routinely and discuss findings with the caregivers. Hypoglycemic events should be meticulously monitored and glycemic targets may need to be adjusted to accommodate the changing requirements of the older adult.<sup>7,8</sup>

### ■ PHARMACOLOGICAL THERAPY

Particular care is required in prescribing and monitoring pharmacological treatment in older adults. Cost may be a significant factor, mainly since older adults tend to be on many medications. Metformin is contraindicated because of renal insufficiency or significant heart failure. Thiazolidinediones, used at all, should be used very cautiously in those with, or at risk for, congestive heart failure and have associated with fractures. Sulfonylureas, other insulin secretagogues, and insulin can cause hypoglycemia. Patients or caregivers must have excellent visual and motor skills and cognitive ability, if insulin use is required. Glucagon-like peptide-1 (GLP-1) agonists and dipeptidyl peptidase-4 (DPP-4) inhibitors have few side effects, but their costs may be a barrier to some older patients. A clinical trial, SAVOR-TIMI 53 (Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus—Thrombolysis in Myocardial Infarction 53), evaluated saxagliptin (a DPP-4 inhibitor) and its impact on cardiovascular outcomes.<sup>12</sup>

### ■ CONCLUSION

In old T2DM, treatment of hyperglycemia has to be integrated into global and individualized care. Geriatric assessment in addition to avoiding lethal complications of diabetes, the prevention of decrease in the level of functional independence is the primary goal of this care and implemented by taking into account the type of patient, vigorous, or frail. For the dependent patient, maintaining comfort becomes the

dyslipidemia in older  
 Lipids  
 Statin unless contraindicated or not tolerated  
 Statin unless contraindicated or not tolerated  
 Consider the likelihood of benefit with a statin (secondary prevention more so than primary)  
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priority goal. From this assessment, ensure the therapeutic and glycemic goals. The choice of therapeutic tools is a function of fixed goals, of comorbidities, of the organization of care at home or in nursing homes, and of the iatrogenic risk, in particular, the undernutrition and the hypoglycemia.<sup>13</sup> Older patients with T2DM are at a higher risk of developing cognitive impairment and, therefore, are in danger of being unable to self-manage their disease, according to a new study. To prevent further complications from T2DM, patients can self-manage their glucose levels and medication intake. However, older patients who have had diabetes for a more extended period may experience memory loss and other cognitive dysfunctions, which can hinder their ability to manage their disease properly. "Older people with T2DM are at increased risk for cognitive dysfunction," researchers concluded. "Changes in cognition may negatively affect diabetes self-management behaviors, influencing self-care outcomes."<sup>14</sup> The development of referral criteria, modes of rapid assessment, joint working practices, and "outreach" to all care settings and diagnostic groups are essential components, which are not yet fully developed. Geriatrician must be able to work effectively in acute hospitals, long-term care facilities, and the community, including the older patient's home.<sup>3</sup> Thus, geriatric medicine maintains the art of medical practice, using the recent knowledge in biology and medical sciences, and deals with the population with the highest level of morbidity and lowest function.

### EDITOR'S NOTE

The management of T2DM in older adults requires a holistic understanding of the relationship between the disease and the functional, psychological/cognitive, and social geriatric issues, so as to individualize both glycemic targets and therapeutic approaches. In this article, Dr Jali highlights the clinical and functional heterogeneity that complicates the long-term care of elderly diabetics, the risk factors for hyperglycemia/hypoglycemia in this population, the balance of glycemic target goals, and the choice of pharmacological therapies in this patient group. Treatment and management

of elderly diabetics should adopt 'geriatric medicine approach' that takes account of a broad range of comorbidities, functional abilities, socioeconomic status, and life expectancy.

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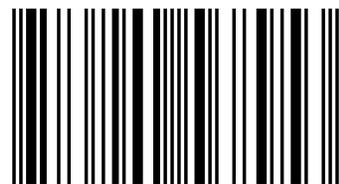
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Provisional fixed prosthodontic treatment involves a multifaceted array of clinical activities, special knowledge, material selection and management. Contemporary treatment incorporates both natural teeth and dental implants. Although provisional restorations are usually intended for short term use and then discarded, they can be made to provide pleasing esthetics, adequate support and good protection for teeth while maintaining periodontal health. They may be fabricated in the dental office from any of several commercially available materials and a number of practical methods. The success of fixed prosthodontics often depends on the care with which the provisional restoration is designed and fabricated.



Prosthodontist with special area of interest in material science research.



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Acharya, K., Rao

Aditya Acharya  
Lekha K.  
Adithi Rao

# Materials and techniques for provisional restorations

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with currently available materials and newer  
techniques

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**Imprint**

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## CONTENTS

1. Introduction.....	5
2. Review of literature.....	9
3. Discussion.....	19
A. Requirements of provisional restorations:	
i. Biologic requirements	
ii. Mechanical requirements	
iii. Esthetic requirements	
B. Summary of rationale and requirements	
C. Materials and Procedures:	
i. External surface form	
- Custom made	
- Preformed	
ii. Tissue surface form	
- Indirect procedure	
- Direct procedure	
- Indirect-direct procedure	
D. Provisional restorative materials	
i. Ideal properties	
ii. Currently available materials	

- Custom fabricated materials
- Preformed materials

E. Influence of material properties on treatment outcome:

- i. Marginal accuracy
- ii. Color stability
- iii. Gingival response
- iv. Pulpal response
- v. Hypersensitivity

F. Strengthening provisional materials

G. Provisional luting materials

4. Clinical considerations for provisional treatment involving natural teeth.....73

- A. Provisional restorations as a part of comprehensive treatment
- B. Diagnostic provisional treatment
- C. Occlusal diagnosis and treatment
- D. Esthetic and phonetic diagnosis and treatment
- E. Periodontal treatment and maintenance
- F. Orthodontic conjoint treatment
- G. Provisional fixed prosthesis fabrication
  - i. General concepts

- ii. Adaptation to a prepared tooth
  - iii. Cavosurface adaptation
  - iv. Clinical methods
- H. Provisional treatment for All Ceramic veneer restorations
- I. Esthetics
- 5. Clinical considerations for provisional treatment involving implants:..90
  - A. Single tooth implant provisional treatment
  - B. Partially edentulous and edentulous implant retained provisional treatment
  - C. Immediate fixed transitional restoration
  - D. Dental implant provisional treatment: Materials and methods
  - E. Material strength and provisional prosthesis durability
- 6. Procedures for fabrication of provisional restoration with different techniques.....110
  - A. Technique for prefabricated provisional restorations
  - B. Technique for custom provisional restorations
  - C. Template fabricated provisional fixed partial denture
  - D. Template fabricated VLC provisional restoration
  - E. Shell fabricated provisional restoration
  - F. Over impression fabricated Bis-acryl composite crown

G. Provisional crown for an endodontically treated tooth

H. Preformed anatomic metal crown

I. Techniques for provisional restorations for implants

7. Summary.....150

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## INTRODUCTION

Prosthodontic treatment, whether involving complete or partial coverage and natural tooth or dental implant abutments, commonly relies on indirect fabrication of definitive prostheses in the dental laboratory. Historically, the necessity for provisional treatment has been primarily derived from this methodologic process. The importance of interim treatment, however, is more far reaching than is portrayed by this procedural necessity and the requirement for satisfactory provisional restorations differ only slightly from the definitive treatment they precede'. Kaiser<sup>2</sup> and others<sup>3,4</sup> identified multiple areas of concern with provisional restorations including the esthetics, comfort, speech and function, periodontal health, maxillomandibular relationships, and continued evaluation of treatment plan. Biologically acceptable fixed prosthodontic treatment demands that prepared teeth be protected and stabilized with provisional restorations that resemble the form and function of the planned definitive treatment<sup>5</sup>. They can assist in the maintenance of periodontal health and promote guided tissue healing by providing a matrix for surrounding gingival tissues. This is especially useful with treatment involving highly esthetic areas.

Besides the immediate protective, functional and stabilizing value, interim restorations are useful for diagnostic purposes where the functional, occlusal and esthetic parameters are developed to identify an optimum treatment outcome before the completion of definitive procedures. A provisional restoration will provide a template for defining tooth contour, esthetics, proximal contacts and occlusion and for evaluating the potential consequences from an alteration in the vertical dimension of occlusion. Provisional treatment can also provide an important tool for the psychological management of patients where a mutual understanding of treatment outcome and the limitation of treatment can be identified.

The use of provisional restoration relies on a reasonable turnaround time from tooth preparation to completion of definitive treatment. Provisional treatment is usually well tolerated when this occurs. Longer periods of use can promote tooth sensitivity and potential pulp damage. Occasionally, however, interim treatment has to function for extended intervals and provide long time tooth protection and stability while conjunctive treatment is accomplished. These procedures are especially useful while the periodontal health status of an abutment tooth over an extended period of time is evaluated. Long time provisional treatment also allows for improved interproximal access during periodontal therapy.

Maintenance of long term provisional restoration in concert with procedures such as alveoloplasty, tissue augmentation, dental implant placement, endodontic therapy, and orthodontics are frequently useful.

It can be challenging for practitioners to justify the use of provisional treatment because of its "temporary" nature, especially when the time required to produce a suitable interim restoration equals that spent for tooth preparation and impression making. However, exclusion of this essential step and the quality of provisional restoration can be the difference between overall treatment success and failure. The terms provisional, interim, or transitional have been routinely used interchangeably in the literature. The use of term 'temporary' however, is controversial and is considered inappropriate by some because provisional restorations serve many functions, and "temporary" treatment may be interpreted as one of lesser importance or value. Provisional restorations should be same as definitive restorations in all the aspects, except for the material from which they are fabricated. Provisional treatment, as an adjunct to some procedures such as porcelain veneers or implant prosthodontics may be occasionally unnecessary.

The objective of this dissertation is to review provisional fixed prosthodontic treatment and to focus on the material science and clinical considerations involving natural teeth and dental implants and the interrelationship between provisional and definitive fixed prosthodontic treatment. Materials used with provisional treatment are discussed in terms of clinical selection and the influence of their physical properties on treatment outcome.

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## REVIEW OF LITERATURE

**Talkav L (1952)<sup>6</sup>** described and classified different materials and methods used for the fabrication of temporary acrylic fixed bridgeworks and splints. He classified the materials into those made with cold cure acrylic and those made with heat cure acrylic. He also described three techniques, namely the plastic crown form, aluminum shell and crowns prepared from alginate impression of prepared teeth.

**Leff A (1953)<sup>7</sup>** described a technique of forming temporary restoration using alginate impression and self-cure acrylic resin.

**Langeland K and Langeland LK (1965)<sup>8</sup>** studied the reaction of pulp to preparation, temporary restoration and final cementation. The authors cautioned against the use of self-curing resin in direct contact to the prepared abutments and recommended a well-fitting preformed crown with thick mix of ZOE cement for favorable pulp response.

**Ragman SS (1965)<sup>9</sup>** emphasized the need for proper contouring of the temporary restoration to promote deflective protection of gingival sulcus and to permit proper stimulation of gingival tissues.

**Fisher OW, Shillingburg HT and Dewhirst RB (1971)<sup>10</sup>** showed that fit of the temporary restoration is improved by using indirect technique

by allowing the acrylic to cure on plaster cast rather than on tooth.

**Sotera AJ (1973)<sup>11</sup>** listed out the functions of a provisional restoration should protect the prepared tooth structure, should be contoured to protect gingival margin and prevent gingival inflammation, should maintain occlusal contacts to prevent extrusion of opposing teeth, should keep abutment teeth in proper relationship to each other by placing some load on the abutment teeth and it will decrease the changes of sensitivity in the final restoration.

**Fritts KW and Thayer KE (1973)<sup>12</sup>** stated that accurately fitting crown margin is less damaging to gingiva, particularly in those preparations that extended sub-gingivally.

**Jones EE (1973)<sup>13</sup>** reported a case of a patient who became sensitive to self-polymerizing resin. The reaction was erythema multiforme, which was treated by removing the residual monomer. The diagnosis of allergy was corroborated by patch test.

**Crispin BJ, Watson JF and Caputo AA (1980)<sup>14</sup>** evaluated the accuracy of nine temporary restorative materials using direct and indirect technique. They concluded that the marginal accuracy produced by the indirect technique was significantly better than those made by direct technique.

**Oliva RA (1980)<sup>15</sup>** described a technique for custom shading of temporary acrylic resin crowns. He advocated the use of non toxic colored chalk shavings instead of using available commercial acrylic resin staining kits. He also found no apparent effect on either the strength or the setting time of the temporary cements.

**Jordan RD, Zakaraisen K and Turner KA (1982)<sup>16</sup>** described a technique of temporization for an extensively fractured anterior tooth. He used an endodontic file covered with acrylic resin to form a temporary post and core and a polycarbonate crown sealed with acrylic resin.

**Garvin PH, Malone WFP, Toto PD and Mazur B (1982)<sup>17</sup>** studied the effect of self cure resin on crevicular fluid volume and concluded that self cure acrylic resins lead to an increase in crevicular fluid volume. The periodontal inflammation process can be a reversible process provided that the amount of gingival irritation is minimal and restoration is of short term.

**Clements WG (1983)<sup>18</sup>** proposed a method to develop anterior determinants that are comfortable and pleasing to the patient, who participates in the development of their anterior esthetics and phonetics. He advocated the preoperative restoration to their final size and shape, which will help in making the conservative preparation and also provide guidelines

for final ceramo-metal restoration.

**Miller SD (1983)<sup>19</sup>** summarized the requirements of an acceptable temporary restoration

- acceptable marginal adaptation
- retention and resistance to masticatory load.
- highly polished plaque resistant surfaces with physiologic contours and embrasures which are conducive to oral hygiene maintenance
- esthetically satisfying
- easy to repair and remove.

**Kaiser DA and Cavazos E (1985)<sup>2</sup>** advocated temporization techniques using Self-curing acrylic resin, Heat cure acrylic resin, Vinyl polyethyl methacrylate, Ethyl amine Derivatives, and Light Cure composites and Preformed metal crown, both direct and indirect methods They also said that the temporary crown should resemble the natural tooth in colour and function and should not exert pressure on free gingiva or edentulous ridge.

**Monday JJL and Blais D (1985)<sup>20</sup>** studied marginal adaptation of acrylic temporary restoration and found that indirect technique, vacuum formed and acrylic reline was most accurate. More subgingival the margin, less acceptable was the adaptation of the provisional restoration.

**Rosenstiel SF and Gegauff AG (1988)**<sup>21</sup> studied the effects of provisional cements on temporary restorative resins. They found that ZOE cements soften the set resin and also inhibit polymerization of added resin. This is clinically important where reline or repair is a consideration. Non eugenol cements may be used with little effect on hardness.

**Hochwald DA (1991)**<sup>22</sup> proposed a method of Surgical template impression during stage I surgery for fabrication of a provisional restoration to be placed at stage II surgery.

**Roberts DB (1992)**<sup>23</sup> described a procedure for making indirect interim restorations from a cast die made from polyvinyl siloxane impression material. The use of these flexible casts and dies facilitates the removal of polymerized resin from the cast and rapid set of polyvinyl materials reduce time involved in making the indirect interim restorations. This method is particularly useful when replication of a specific irregular tooth arrangement is mandated.

**Cho GC and Chee WWL (1993)**<sup>24</sup> described a method of fabrication of esthetic custom provisional restoration that provide optimum esthetics and function accomplished with minimum chair side time. The effect of mamelons, translucency and incisal halos is produced to mimic natural

dentition. The technique is based on a provisional shell that is made in laboratory and relined intraorally for a more precise fit.

**Reikie DF (1993)**<sup>25</sup> reviewed many esthetic and functional considerations for partially edentulous implant patient. He said that with the availability of adjunctive grafting procedures, it is time for the implant team to change the traditional treatment planning approach that allows patient anatomy to dictate implant position and prosthesis design.

**Breeding LC (1995)**<sup>26</sup> described the procedure which provides an esthetic mean for inserting a provisional fixed restoration immediately after implant placement surgery. When this procedure is used, it is not necessary to prepare the abutment teeth adjacent to the surgical site for subsequent fixed restorations.

**Liebenberg WHO (1996)**<sup>27</sup> stressed on the need of maintenance of periodontal health and tooth position, while restoring the teeth with provisional restorations.

**Biggs WF (1996)**<sup>28</sup> advocated the placement of a custom implant provisional restoration at the second stage of surgery for improved gingival management.

**Tjan AH, Jacob Castelnovo J and Shiotsu G (1997)**<sup>29</sup> advocated the curing provisional resinous crowns with use of polyvinyl siloxane impression as matrix which significantly reduces the temperature increase in the pulpal chamber compared with a vacuum formed polypropylene matrix.

**Robinson FG, Haywood VB, Meyers M (1997)**<sup>30</sup> studied the effect of Night Guard Vital Bleaching [NGVB] solution containing 10 percent carbamide peroxide on colour stability of provisional restoration materials. They observed an orange discoloration with provisional materials that contained methacrylate, when they were exposed to 10 percent carbamide bleaching solutions.

**Jemt T (1999)**<sup>31</sup> conducted a study on provisional implant crowns placed after single implant treatment in 55 patients with single implant restorations. The results indicated that the use of provisional crowns may restore soft tissue contour better than healing abutments alone.

**Jaffin RA, kumar A and Berman CL (2000)**<sup>32</sup> conducted a clinical study of immediate loading of dental implants in edentulous and partially edentulous jaws and found that success rate was found similar to those in delayed loaded cases. They advised the immediate loading of implants.

**Lane DA and Rosalin (2003)**<sup>33</sup> did clinical trial to compare double arch and complete arch impression technique in the provisional indirect restoration. They concluded that the double arch impressions were found to take less time, use of less material and also same accuracy.

**Rodrigus AH and Morgano SM (2003)**<sup>34</sup> advocated a clinical and laboratory technique of preparation of restorations for immediate loading of implants on the edentulous mandible with the use of a laboratory processed provisional, screw-retained, implant supported fixed complete denture that incorporates cast metal reinforcement. This method is consistent with reported biologic and clinical requirements for achieving successful results with immediate and early loaded implants. This technique offers advantage compared with a prefabricated provisional prosthesis: it is efficient, uncomplicated and cost effective.

**Sham ASK and Chu FCS (2004)**<sup>35</sup> conducted a study and said that bis-acryl methacrylate resins were more colour stable than methyl/ethyl methacrylate based resins in water at 60° for 20 days. On the other hand, the bis-acryl methacrylate resin showed significantly higher discoloration in coffee. After exposure to UV light, the 2 bis-acryl methacrylate based provisional materials showed significantly less colour change than any of the methyl/ethyl methacrylate based provisional materials. If provisional

restorations have to be used for long period, bis-aryl methacrylate is preferred over methyl /ethyl methacrylate based resins. However, when bis-acryl methacrylate resin is used as a provisional material, patients should be advised of the propensity of such materials to staining by coffee.

**Bohnekamp DM and Gracia LT (2004)<sup>36</sup>** described the effective procedure for use of light polymerized flowable composite resin for intraoral repair of bis-acryl provisional restorations.

**Hamza TA and Rosenstiel SF, Elliosary MM and Ibraheem RM (2004)<sup>37</sup>** conducted a study on fiber reinforcement, fracture toughness and flexible strength of provisional restorative resin using Construct, Fiberstick, Ribbond normal, Ribbond THM, Ribbond triaxinal and concluded that fiber reinforcement increases both fracture toughness and flexible strength.

**Eskitascioglu G, Eskitascioglu A and Belli S (2004)<sup>3</sup>** advocated use of polyethylene ribbon to create a provisional fixed partial denture after immediate implant placement for bonding natural lateral incisors to the adjacent teeth with an acceptable esthetic outcome.

**Haselton DR, Diaz-Arnold AM and Dawson DV (2005)<sup>39</sup>** conducted a clinical study to evaluate the colour stability of provisional crown and fixed partial denture resins. The purpose of this study was to measure the colour

change of 12 provisional prosthodontic material after immersion in artificial saliva and artificial saliva coffee solutions for 1, 2 and 4 weeks. Under the condition of this study they demonstrated varying tendency to discolor over a range time periods when immersed in artificial saliva and artificial saliva coffee solutions. This study showed colour stability to be material specific without improved stability of newer bis-acryl products. Patient should be warned to expect colour shift towards yellow within a relatively short period of time dependent upon dietary habits.

**Swall BW (2005)<sup>40</sup>** stressed the importance of wax up for provisional restorations for cases of all kinds ranging from a single tooth to full mouth constructions and considered it an important factor in restorative success.

**Begum Turker S, Kocak A, Esra A (2006)<sup>41</sup>** studied the effect of coffee, tea, coca-cola, orange juice and red wine on the color stability of acrylic and composite based provisional materials. They concluded that red wine and tea caused the most significant color changes and orange juice showed the least significant colour change.

## DISCUSSION

Provisional restorations in fixed partial dentures are an essential part of fixed Prosthodontic treatment. Patient must be provided with an interim restoration from initial tooth preparation until the definitive prosthesis is placed. A provisional restoration is defined as "a fixed or removable prosthesis, designed to enhance esthetics, stabilization or function for a limited period of time, after which it is to be replaced by definitive prosthesis". Often such prosthesis is used to assist in determination of the therapeutic effectiveness of a specific treatment plan or the form and function of the planned definitive prosthesis. The word 'interim prosthesis' is often used as a synonym for "provisional" prosthesis. Even though a definitive restoration may be placed as quickly as 2 weeks after tooth preparation, a provisional restoration must satisfy important needs of the patient and the dentist. Unfortunately, temporary usually connotes laxity and this may imply that requirements pertaining to the more permanent condition are ignored. If this connotation becomes a philosophy governing the provisional phase of treatment, the dentist will needlessly be reducing clinical efficiency and treatment quality. Experience has repeatedly shown that the time and effort expended in fulfilling the requisites of provisional restorations are well spent.

Because of unforeseen events (e.g., laboratory delays or patient unavailability), a provisional restoration may have to function for an extended period. On the other hand, a delay in placing the definitive restoration may be deliberate. Whatever the intended length of time of treatment, a provisional will have to be adequate to maintain patient health. Thus, it should not be casually fabricated on the basis of expected short-term use.

Provisional procedures also must be efficiently performed, because they are done while the patient is in the operatory and during the same appointment that the teeth are prepared. Costly chairside time should be used efficiently with the practitioner producing an acceptable restoration. Failure to do so will result in the eventual loss of more time than was initially thought to be saved. For example, an inadequate restoration may lead to unnecessary repairs or the need to treat gingival inflammation and remake the impression. Such problems can be avoided if one thoroughly understands what the requirement of provisional restoration is and make the efforts to meet these requirements.

➤ **Requirements of provisional restorations:**

The requirements of a provisional restoration are same as for the definitive restoration, with exception of longevity and possibly the

sophistication of colour.

The basic requirement of an interim restoration is to provide pulpal protection, positional stability, and maintenance of occlusal function, cleansability, strength, retention and esthetics. The requirement can be subdivided into biologic, mechanical and esthetic categories.

### **I) Biologic requirements:**

#### ***a) Pulp Protection-***

A provisional restoration must seal and insulate the prepared tooth surface from the oral environment to prevent sensitivity and further irritation to the pulp. Because of the sectioning of dentinal tubules, a certain degree of pulp trauma is inevitable during tooth preparation. When healthy, each dentinal tubule contains the cytoplasmic process of a cell body (Odontoblast), whose nucleus is in the pulp cavity. Unless the environment around the exposed dentin is carefully controlled, adverse pulp effects can be expected. In addition, the pulp health of a tooth requiring a cast restoration is likely to be compromised before and after preparation. In severe situations, leakage can cause irreversible pulpitis and resulting in need for root canal treatment.

### **b) Periodontal Health-**

To facilitate plaque removal, a provisional restoration must have good marginal fit, proper contour, and a smooth surface. This is particularly important when the crown margin will be placed apical to the free gingival margin. If the provisional restoration is inadequate and plaque control is impaired, gingival health will deteriorate. The maintenance of good gingival health is always desirable, but it has special practical significance when fixed prosthodontics is undertaken. Inflamed or hemorrhagic gingival tissues make subsequent procedures (e.g., impression making and cementation) very difficult. The longer the provisional restoration must serve, the more significant become any deficiencies in its fit and contour. When gingival tissue is impinged upon, ischemia is likely. This can be detected initially as tissue blanching; else a localized inflammation or necrosis will develop.

### **c) Occlusal Compatibility and Tooth Position-**

The provisional restoration should establish or maintain proper contacts with adjacent and opposing teeth. Inadequate contacts allow supraeruption and horizontal movement. Supraeruption is detected at try-in when the definitive restoration makes premature contact. Correcting this in the operatory is possible, but the effort is time consuming and often leads to a restoration with poor occlusal form and function. Horizontal movement

results in excessive or deficient proximal contacts. The former requires tedious chair-side adjustment; the latter involves a laboratory procedure to add metal or ceramic to the deficient site. This often results in a compromised proximal contour. This along with root proximity impairs oral hygiene measures.

**d) Prevention of Enamel fracture-**

The provisional restoration should protect prepared crown margins. This is particularly true with partial-coverage designs in which the margin of the preparation is close to the occlusal surface of the tooth and could be damaged during chewing. Even a small chip of enamel will make the definitive restoration unsatisfactory and necessitate a time consuming remark.

**II) Mechanical Requirements**

Provisional restorations should be able to withstand the functional forces of mastication without fracture or displacement. They should maintain the position of the prepared teeth and stability of inter-arch and intra-arch relationship through establishment of optimal proximal and occlusal contacts. The requirements can be grouped under following headings:

**a) Function-**

The greatest stresses in a provisional restoration are likely to occur during mastication. Unless the patient avoids contacting of the prosthesis when eating, internal stresses will be similar to those occurring in the definitive restoration. The strength of poly (methyl methacrylate) resin is about one-twentieth that of metal ceramic alloys making fracture of the provisional restoration much more likely. Fracture is not usually a problem with a complete crown as long as the tooth has been adequately reduced. Breakage occurs more frequently with partial-coverage restorations and fixed partial dentures. Partial-coverage restorations are inherently weaker because they do not completely encircle the tooth.

An FPD must function as a beam in which substantial occlusal forces are transmitted to the abutments. This creates high stresses in the connectors which are often the site of fracture. To reduce the risk of fracture, connector size must be increased in the provisional compared to the definitive restoration. Greater strength is achieved by reducing the depth and sharpness of the embrasures. This increases the cross-sectional area of the connectors<sup>43</sup>, while reducing the stress concentration associated with internal line angles. The biologic and sometimes the esthetic requirements place limits on just how much larger connectors can be made. To avoid jeopardizing periodontal

health, they should not be over contoured near the gingiva. Good access for plaque control must have high priority. In some instances, high-strength provisional restoration (e.g., cast metal, fiber reinforced or heat-processed resin) can spare the practitioner and patient inconvenience, lost time and the expense of remaking a restoration.

***b) Displacement-***

To avoid irritation to pulp and tooth movement, a displaced provisional must be recemented promptly. An additional office visit is usually required, resulting in considerable inconvenience to the patient and the dentist. Displacement is best prevented through proper tooth preparation and a provisional with closely adapted internal surface. Excessive space between the restoration and the tooth places greater demands on the luting agent which has lower strength than regular cement and thus cannot tolerate the added force. For this and biologic reasons, unlined preformed provisional should be avoided.

***c) Removal for Reuse:***

Provisional restorations often need to be reused and therefore should not be damaged when removed from the teeth. In most instances, if the cement is sufficiently weak and the provisional has been well fabricated, it will not break when removed.

### **III) ESTHETIC REQUIREMENTS:**

The appearance of a provisional restoration is particularly important for incisors, canines, and sometimes premolars. Although it may not be possible to duplicate exactly the appearance of an unrestored natural tooth; tooth contour, color, translucency and texture are essential attributes. When conditions require it, esthetic enhancement procedures are available to create personalized details; however, these are not routinely called for.

The degree to which a material matches the color of adjacent teeth initially is an essential requirement of prosthodontics. However, colour stability can govern the selection of materials when a long period of service is anticipated, because some resins discolor after several months in the mouth.<sup>44</sup> The propensity for discoloration due to stain accumulation or secondary to home bleaching procedures<sup>30</sup> differs according to resin composition.

The provisional is often used as a guide to achieve optimum esthetics in the definitive restoration. In complete denture prosthodontics, it is customary to have a wax try-in so the patient can respond to the dentist's esthetic interpretation before the denture is processed. Many dentists consider this essential because of the frequency of patient's request for changes and the ease with which such changes can be made. When fixed

prosthodontics is being performed in the anterior oral cavity, it greatly influences appearance; the patient should be given an opportunity to voice an opinion. Beauty and personal appearance are highly subjective and difficult to communicate verbally, and a facsimile prosthesis can play a vital role in the patient's consideration of esthetics and the impact that the prosthesis will have on self-image. Obtaining the opinion of others, whose judgment is valued is also important. An accurate provisional is a practical way of obtaining specific feedback for the design of a definitive restoration. Verbal descriptions are often too vague and frequently cause overcorrection, which are difficult to reverse in the definitive restoration. The provisional restoration is shaped and modified until its appearance is mutually acceptable to the dentist and the patient. When this is achieved, an impression is made of the provisional and a cast is poured. This cast accompanies the fixed prosthodontic working cast to the laboratory, where the contours are duplicated. This process is more efficient when it begins with diagnostic waxing procedure. Involving the patient in decision making results in greater patient satisfaction.

➤ **Summary of rationale and requirements:**

**Rationale of provisional restorations-**<sup>3, 11, 19</sup>

1. Protect pulpal tissues and sedate prepared abutments
2. Protect teeth from dental caries.
3. Provide comfort and function.
4. Evaluate parallelism of abutments.
5. Provide method for immediately replacing missing teeth.
6. Prevent migration of abutments.
7. Improve esthetics.
8. Provide an environment conducive to periodontal health.
9. Evaluate and reinforce the patient's oral home care.
10. Assist with the periodontal therapy by providing visibility and access to surgical sites when removed.
11. Stabilize mobile teeth during periodontal therapy and evaluation.
12. Provide anchorage for orthodontic brackets during tooth movements.
13. Aid in developing and evaluating an occlusal scheme before definitive treatment.
14. Allow evaluation of vertical dimension, phonetics, and masticatory function.

15. Assist in determining the prognosis of questionable abutments during prosthodontic treatment planning.

**Requirements of provisional restorations-<sup>3,11,19</sup>**

1. Good marginal adaptation, should adapt well to a tooth and matrix surface.
2. Adequate retention and resistance to dislodgement during normal masticatory function.
3. Strong, durable and hard.
4. Nonirritating to pulp and other tissues; low exothermicity.
5. Nonporous and dimensionally stable.
6. Comfortable.
7. Esthetically acceptable shade selection; translucent tooth like appearance.
8. Colour stable.
9. Physiologic contours and embrassures.
10. Easy to mix and load in matrix, fabricate, reline and repair; relatively short setting time.
11. Physiological occlusion.
12. Conductive to routine oral home care cleaning procedures.
13. Finishes to a highly polished, plaque and stain-resistant surface.

14. Easy to remove and recement by the dentist.
15. Relatively inexpensive.
16. Low incidence of localized allergic reactions.

➤ **Materials and procedures:**

Many procedures using a wide variety of materials are available to make satisfactory provisional restorations. As new materials are introduced, associated techniques are reported, creating even more variety. Particularly helpful thing is the fact that all the procedures have in common the formation of a mold cavity into which a plastic material is poured or packed. Furthermore, the mold cavity is created by two correlated parts: one forms the external contour of the crown or fixed partial denture, and other forms the prepared tooth surfaces and (when present) the edentulous ridge contact area. The terms external surface form (ESF) and tissue surface form (TSF) are suggested for these mold parts. This terminology will be used in the ensuing discussions.

➤ **External surface form (ESF)-**

There are two general categories of external surface forms: custom and preformed.

*A) Custom:* A custom ESF is a negative reproduction of either the patient's teeth before preparation or a modified diagnostic cast. It may be obtained directly with any impression material. Impression made in a quadrant tray with irreversible hydrocolloid or silicone rubber is convenient. The higher cost of silicone rubber may be offset by its ability to be retained for possible reuse at any future appointment. Accurate representing of the ESF is easier and the mold cavity produces better results if thin areas of impression material (as may be found inter-proximally or around the gingival margin) are trimmed away. Moldable putty materials are popular because they can be used without a tray and can be easily trimmed to minimum size with a sharp knife. In addition, their flexibility facilitates subsequent removal of the polymerized resin.

A custom ESF can be produced from thermoplastic sheets, which are heated and adapted to a stone cast with vacuum or air pressure while the material is still pliable. This produces a transparent form with thin walls, which makes it advantageous in the direct technique because of its minimum interference with the occlusion. It is filled with resin, placed in the mouth, and fully seated as the patient closes into maximum intercuspation. Little additional effort is required to adjust the occlusal contacts. The thinness of the material may also be a disadvantage in the direct technique, however.

The material is a poor dissipater of the heat released during resin polymerization,<sup>45</sup> so care must be taken to remove it from the mouth before injury can occur. A thermoplastic ESF has other uses in fixed prosthodontic treatment, in both clinical and laboratory phases; for example, it can help evaluate the adequacy of tooth reduction.

Transparent sheets are available in cellulose acetate or polypropylene and come in various sizes and thicknesses; a 125 X 125 mm sheet of 0.5 thickness is recommended for provisional restorations. Polypropylene is preferred because it produces better surface detail and is more tear resistant. Better tear resistance makes initial removal from the forming cast less tedious and enables ESF to be used more than once.

Although thermoplastic sheets have a number of advantages, a wide variety of other materials and methods can be used successfully. For example, some practitioners favor baseplate wax because it is convenient and economical.

**B) Preformed:** A variety of preformed crowns are available commercially. On their own, they rarely satisfy the requirements of a provisional restoration, but can be thought of as ESFs rather than as finished restorations and therefore must be lined with auto-polymerizing resin. Most

crown forms need some modification (e.g., internal axial recontouring, and occlusal adjustment) in addition to the lining procedure. When extensive modification is required a custom ESF is superior because it is less time consuming. Preformed crowns are generally limited to single restorations, since using them as pontics for fixed partial dentures is not feasible.

Materials from which preformed ESF's are made include polycarbonate, cellulose acetate, aluminum, tin-silver and nickel-chromium. These are available in a variety of tooth types and sizes.

- 1. Polycarbonate:** Polycarbonate has the most natural appearance of all the preformed materials. When properly selected and modified, its appearance reveals a well-executed porcelain restoration and is a very color-stable resin. Although it is available in only one shade, this can be modified to a limited extent by the shade of the lining resin. Polycarbonate ESF's are supplied in incisor, canine and premolar tooth types.
- 2. Cellulose Acetate:** Cellulose acetate is a thin (0.2 to 0.3 mm) transparent material available in all tooth types and a range of sizes. Shades are entirely dependent on the autopolymerizing resin. The resin does not chemically or mechanically bond to the inside surface of the shell, so after polymerization the shell is peeled off and discarded to prevent

staining at the interface. However, removing the shell requires the addition of resin to reestablish proximal contacts.

**3. Aluminum and Tin-silver:** Aluminum and tin-silver are suitable for posterior teeth. The most elaborate crown forms have anatomically shaped occlusal and axial surfaces. The most basic and least expensive forms are merely cylindrical shells resembling a tin can. Non-anatomic cylindrical shells are inexpensive but require modification to achieve acceptable occlusal and axial surfaces. Using crowns that have been preformed as individual maxillary and mandibular posterior teeth is more efficient. Care must also be taken to avoid fracturing the delicate cavosurface margin of the tooth preparation when fitting a metal crown form. This risk is greater if adaptation is carried out directly by having the patient forcefully occlude on the crown shell. The edge of the shell can engage the margin and fracture it under biting pressure. An even greater risk occurs when the crown has a constricted cervical contour. Tin-silver crowns are deliberately designed this way. This highly ductile alloy allows the crown cervix to be stretched to fit the tooth closely. Direct stretching on the tooth is practical only where feathered edge margins are used. For other margin designs, cervical enlargement should be

performed indirectly on a swaging block, which is supplied with the crown kit.

**4. Nickel-chromium:** Nickel-chromium shells are used primarily for children with extensively damaged primary teeth. In application, they are not lined with resin but are trimmed adapted with contouring pliers and luted with high-strength cement. They may be applied to permanent teeth but are more suitable for primary teeth. Nickel-chromium alloy is very hard and therefore can be used for long term provisional restorations.

➤ **Tissue surface form (TSF)-**

There are two primary categories of tissue surface forms: indirect; and direct and the third category, indirect-direct results from the sequential application of these two forms.

**A) Indirect Procedure:** An impression is made of the prepared teeth and ridge tissue and is poured in quick setting gypsum or polyvinyl siloxane.<sup>3</sup> The provisional restoration is fabricated outside the mouth.

This technique has the following advantages over direct procedures:

1. There is no contact of free monomer with the prepared tooth or gingiva, which might cause tissue damage and an allergic reaction or sensitization.

One group of investigators reported a 20% incidence of allergic sensitivity in subjects previously exposed to a monomer patch test. The risk of sensitization in patients who are not allergic to monomer increases with the frequency of exposure. In allergic patients, an exposure to even small amounts of monomer usually causes painful ulceration and Stomatitis.

2. The procedure avoids subjecting a prepared tooth to the heat created from polymerizing resin. Clinical simulation experiments<sup>46</sup> have shown peak temperature increase of approximately 10° C in the pulp chambers of prepared teeth upon which the direct provisional restorations had been made. This amount of temperature elevation is capable of causing irreversible pulp damage. The simulation experiment also indicates that an increase in temperature depends directly on the type and volume of resin present. Therefore, a directly made restoration with a large pontic is more likely to cause injury than one for a single crown (especially if the tooth is prepared conservatively). These studies also demonstrate that the heat-conducting properties of the ESF's significantly influence the maximum temperature reached. However, it is important to note that peak temperatures were not reached until 7 to 9 minutes had elapsed.<sup>46</sup> For this reason and also because it must be drawn through the undercuts of adjacent proximal tooth surfaces, the resin should be removed at the rubbery stage of polymerization, which

typically occurs 2 to 3 minutes after insertion in the mouth. The temperature increase is negligible at 3 minutes, suggesting that thermal injury is easily avoidable.

**3.** The marginal fit of provisional restorations that have been polymerized undisturbed on stone casts is significantly better than that of provisionals that have been removed from the mouth before becoming rigid.<sup>20,47</sup> This is because

(a) the stone restricts resin shrinkage during polymerization and

(b) separating the resin from the tooth causes distortion.

Directly made long-span or multi-abutment FPDs are likely to have unacceptable marginal discrepancies caused by shrinkage and distortion.

**4.** When a dimensionally stable elastomer impression is made to form the TSF, it can be retained for possible reuse with the ESF. This allows replacement restorations to be made without having the patient present. For example, if a patient calls to report a lost interim FPD, a replacement can be made at the dentist's convenience before the patient arrives. This minimizes disruption of the office schedule and earns the patient's appreciation. It is not known whether using an elastomer TSF results in margins that fit as well as those obtained with gypsum TSF. The elastomer may not resist polymerization shrinkage as effectively as the gypsum.

5. This technique gives the patient a chance to rest and let the dentist perform other tasks, provided an assistant is trained to carry out the laboratory procedures.

**B) Direct Procedure:** The patient's prepared teeth and gingival tissues (in the case of FPD) directly provide the tissue surface form, so the intermediate steps of the indirect technique are eliminated. This is convenient when assistant training and office laboratory facilities are inadequate for efficiently producing an indirect restoration.

However, the direct technique has significant disadvantages:

- potential tissue trauma from the polymerizing resin and
- inherently poorer marginal fit.

Therefore, the routine use of directly formed provisional restorations is not recommended when indirect techniques are feasible.

**C) Indirect-direct Procedure:** In this technique, the indirect component produces a "custom-made preformed ESF" similar to a preformed polycarbonate crown. In most cases, the practitioner uses a custom ESF with an under prepared diagnostic cast as the TSF. The resulting mold forms a shell that is lined with additional resin after tooth preparation (using the patient for the TSF). This last step is the direct component of

the procedure. Another method of creating the shell eliminates the need for an indirect TSF. It is accomplished by painting monomer liquid into the ESF and carefully sprinkling or blowing resin powder on it. The thickness of the resin shell is difficult to control with this technique however and may result in time-consuming corrective grinding.

The indirect-direct approach offers these advantages:

1. Chairside time is reduced. Most of the procedures are completed before the patient's visit.
2. Less heat is generated in the mouth. The volume of resin used during lining is comparatively small.
3. Contact between the resin monomer and soft tissues is minimized compared to the direct procedure. Because pontic ridge areas do not normally require lining, there is a reduced risk of allergic reaction.

➤ **Provisional restorative materials:**

Interim treatment promotes numerous adjunct benefits to definitive prosthodontic treatment. The materials and techniques used for these purposes must reflect these variable treatment demands and requirements. Consistent with nearly all areas of dental management where material science plays such a significant role, there is presently no ideal provisional

material suitable for all clinical conditions; however, there are many materials that have been used successfully for this purpose.

The requirements needed for provisional treatments are already stated above. Many of these requirements such as appropriate marginal adaptation, low thermal conductivity, non irritating reaction to the dental pulp and gingival tissue, ease of cleaning, ease of contour, ease of alterability and repair are extremely important to the success or failure of treatment outcomes.

While in a fluid state, the provisional restorative material fills the cavity formed by external and tissue surface forms; they then solidify, producing a rigid restoration.

➤ **Ideal Properties:** An ideal provisional material has the following characteristics:

1. Convenient handling- adequate working time, easy moldability and rapid setting time.
2. Biocompatibility- non-toxic, non-allergenic and non-exothermic.
3. Dimensional stability during solidification.
4. Ease of contouring and polishing.
5. Adequate strength and abrasion resistance.

6. Good appearance- translucency, color controllable, color stable.
7. Good patient acceptance- non-irritating, odorless.
8. Ease of adding to or repairing.
9. Chemical compatibility with provisional luting agents.

➤ **Currently Available Materials:**

The ideal provisional material has not yet been developed. A major problem still to be solved is dimensional change during solidification. These materials shrink during polymerization, which causes marginal discrepancy<sup>20,47,49</sup> especially when the direct technique is used. In addition, the resins currently used are exothermic and not entirely biocompatible.

Provisional material selection should be based on the strength and weakness of a given material relative to clinical mandate for specific treatments. Differing clinical techniques such as indirect interim fabrication may be required to accommodate certain situations, finally among the differing proprietary material brands exhibiting similar chemical composition and physical properties, experience and personal preference is an important consideration on material selection.

Mechanical, physical handling properties, as well as biocompatibility, will influence material selection in fabricating provisional restorations. A

material should be easy to handle, provide adequate working time and be nontoxic. Treatment complications such as chemical injury from the presence of monomer residue, thermal injury from exothermic polymerization shrinkage must be considered. Likewise, after fabrication, considerations such as preventing repairs and remakes often continue to be a direct reflection of the physical properties of a provisional material. Interim restorations are fabricated using 1 of 2 techniques: (1) Custom fabrication; or (2) fabrication with preformed materials. Additionally both of these procedures can be accomplished with direct clinical, indirect laboratory, or combination techniques. Indirect technique may result in an increased cost of the fabrication and may require special equipment and increased non clinical time for fabrication.<sup>49</sup>

**A) Custom fabricated materials:**

Custom fabrication represents one of the best choices for provisional restorative treatment.<sup>50</sup> The technique allows for intimate contact between a provisional restoration and prepared tooth. It provides a continuous mechanism for a variety of alterations during treatment such as marginal adaptation, contour change, shade adjustment, occlusal modification and repair.

Provisional materials have been divided into the following categories based on how they are converted from plastic to solid-elastic masses:

- (1) Chemically activated auto-polymerizing acrylic resins;
- (2) Heat activated acrylic resins;
- (3) Light-activated acrylic resins;
- (4) "Dual" light and chemically activated acrylic resins; and
- (5) Others (alloys).

The most common materials used for custom interim fixed restorations are acrylic resins. Generally, acrylic resins used for provisional restoration are brittle, but their great advantage is the ease with which they can be altered by additions and subtractions. Several types of acrylic resin materials are available for interim restorative treatment. They are:

- (1) Polymethylmethacrylate resins;
- (2) Polyethylmethacrylate resins;
- (3) Other types or combinations of unfilled methacrylate resins and composites. A comparison of physical properties associated with a variety of provisional unfilled methacrylate resins; and
- (4) Composite.

## 1. Methacrylate resins:

Autopolymerizing polymethylmethacrylate (PMMA) first appeared around 1940 and remains the most frequently used material for fabrication of interim restorations.<sup>2</sup> Plant et al found that the intra-pulpal temperature rise associated with the polymerization of methyl methacrylate materials could be up to 5 times that associated with the normal consumption of thermally hot liquid. The literature indicates that polymethylmethacrylate is the preferred material when provisional restorations are made using indirect techniques.

Ethyl methacrylate, introduced in the 1960's<sup>51</sup> has a number of advantages and disadvantages relative to methyl methacrylate. One study<sup>52</sup> however, showed the highest value of fracture resistance with an ethyl methacrylate material relative to methyl methacrylate and bis-acryl materials. Ethyl methacrylate may be a better selection for direct interim prosthesis fabrication and is best suited for short-term use relative to methyl methacrylate.<sup>50</sup> Two other chemically similar materials, Vinylethyl and butylmethacrylate display comparable clinical behavior to polyethylmethacrylate.

### **Methyl Methacrylate-**

The monomer methyl methacrylate is of considerable importance in dentistry. Methyl methacrylate is a transparent liquid at room temperature with the following physical properties:

- Molecular weight= 100
- Melting point =  $-48^{\circ}\text{C}$
- Boiling point =  $100.8^{\circ}\text{C}$  (note how close this is to the boiling point of water).
- Density = 0.945 g/ml at  $20^{\circ}\text{C}$
- Heat of polymerization = 12.9 kcal/mol

Methyl methacrylate exhibits a high vapor pressure and is an excellent organic solvent. Although the polymerization of methyl methacrylate can be initiated by visible light, ultraviolet light or heat; it is commonly polymerized in dentistry by the use of a chemical initiator.

The conditions for the polymerization of methyl methacrylate are not critical provided that the reaction is not carried out too rapidly. The degree of polymerization varies with the conditions of polymerization, such as temperature, method of activation, type of initiator, initiator concentration, purity of chemicals and similar factors. Because they polymerize readily under the conditions of use, the methacrylate monomers are particularly

useful in dentistry. Many other resin systems do not polymerize at room temperature in the presence of air. Volume shrinkage of 21% occurs during the polymerization of the pure methyl methacrylate monomer.

### **Poly (methyl methacrylate)-**

Poly (methyl methacrylate) is a transparent resin of remarkable clarity; it transmits light in the ultraviolet range to a wavelength of 250 nm. It is a hard resin with a Knoop hardness number of 18 to 20. It has a tensile strength approximately 60 MPa, a density of 1.19 g/ cm<sup>3</sup> and a modulus of elasticity of approximately 2400 MPa.

This polymer is extremely stable. It does not discolor in ultraviolet light and it exhibits remarkable aging properties. It is chemically stable to heat and softens at 125°C and it can be molded as a thermoplastic material. Between 125° and 200°C de-polymerization takes place. At approximately 450° C, 90% of the polymer depolymerizes to form the monomer. Poly (methyl methacrylate) of high molecular weight degrades to a lower polymer at the same time that it converts to the monomer.

Like all acrylic resins, poly (methylmethacrylate) exhibits a tendency to absorb water by a process of imbibition. Its non-crystalline structure possesses a high internal energy. Thus molecular diffusion can occur in the resin, because less activation energy is required. Furthermore, the polar

carboxyl group, even though esterified, can form a hydrogen bridge to a limited extent with water. Because poly (methyl methacrylate) is a linear polymer, it is soluble in a number of organic solvents that may be found in a dental laboratory or operatory, such as chloroform and acetone.

## **2. Multifunctional Methacrylate and Acrylate resins:**

The backbone of the molecule formed in this system can have any shape, but methacrylate groups are found at the end of the branching chains. One of the first multifunctional methacrylate used in dentistry was Bowen's resin or bis-GMA. The bis-GMA resin can be described as an aromatic ester of a dimethacrylate, synthesized from an epoxy resin (ethylene glycol of bis-phenol A) and methyl methacrylate. Because bis-GMA has two -OH groups which form hydrogen bond between the monomers, it is extremely viscous. A low viscosity dimethacrylate, such as triethyleneglycol dimethacrylate (TEDMA), is blended with it to reduce viscosity.

The rigid central core of two aromatic groups reduces the ability of bis-GMA molecules to rotate during polymerization and thereby to participate efficiently in the polymerization process. Therefore, one of the methacrylate groups reacts often, whereas the other does not. This process results in a bis-GMA molecule that forms a branch or pendant group, along the polymer chain. Some of these branches crosslink with adjacent chains

and some do not. To quantify the efficiency of polymerization and cross-linking, the clinician determines the ratio, 'R' of unreacted methacrylate groups before and after polymerization. The degree of conversion, expressed in percentage of consumed methyl methacrylate groups, can be determined from the formula:

$$(1 - R) \times 100 = \text{degree of conversion}$$

Various dimethacrylate resin combinations have been explored through the years in attempts to reduce viscosity and to increase the degree of conversion. One resin group that has shown promise is urethane dimethacrylate (UDMA). This UDMA group can be described as any monomer chain containing one or more urethane groups and two methacrylate end groups.

In addition to the dimethacrylates mentioned previously, other multifunctional resins have been introduced to dentistry during the last few years. For example, in some dentin bonding agents a monomer called dipentaerythriol penta-acrylate monophosphate (PENTA-P) is used. As seen from the PENTA-P formula, this monomer contains as many as five acrylate groups per monomer molecule.

Another multifunctional resin that has been used extensively during the last few years is poly(acrylic acid), to which hydroxyethyl methacrylate

(HEMA) has been grafted. Such a modified poly (acrylic acid) (PAA) is used in light-curable glass ionomer cements. During light exposure, free radical polymerization is initiated, causing the methacrylate groups to react. The reaction that cross-links the PAA molecules constitutes the initial setting reaction. After this reaction, the carboxylate groups continue to react with the glass particles through an acid-base reaction. During this reaction, the PAA releases the hydrogen ions and the PAA chains become negatively charged.

These negative charges, however, are balanced by cations leached from the glass. These cations, such as  $\text{Ca}^{2+}$  and  $\text{Al}^{3+}$  form ionic bonds between the chains that now also become ionically cross-linked. In addition, the negatively charged PAA chains also form bond to tooth tissues containing cations such as  $\text{Ca}^{2+}$ .

By observing this modified PAA molecule, you can see that as the number of methacrylate group increases, the number of carboxylate group decreases. This is important because fewer carboxylate groups reduce the extent of acid base reaction and weaken the enamel-dentin interaction.

### **3. Composites:**

Composite provisional materials encompass a fairly variable category by virtue of the fact that they are chemically comprised of a combination of

two or more types of material. Most of these materials use bis-acryl resins, a hydrophobic material that is similar to bis-GMA. When this resin is mixed with inorganic, radiopaque filler it combines to provide an interim treatment material that is similar to composite restorative materials. Typically these materials use a variety of multifunctional acrylic resin monomers that provide high-density cross linking during polymerization. Consequently they exhibit a unique rubbery stage during the polymerization process. These materials are available as autopolymerized, dual- (auto /visible light) polymerized or visible light polymerized forms.

Most of the composite materials are now available with an auto-mix delivery system similar to polyvinylsiloxane impression materials. This makes them quick and easy to use, but expensive. Diaz-Amold et al<sup>53</sup> showed a general decrease in hardness over time for 2 out of 3 composite materials tested. This is consistent with studies conducted by Ireland et al who showed that the bis-acryl materials exhibited higher flexural elastic moduli and moduli of rupture values at 24 hours but exhibited the greatest decrease in these values over time.

Varnish materials designed to coat provisional restorations and produce a smoother surface are commercially available but are not advisable. Bis-acryl materials are compatible with other composite materials, but

alterations for repairs and addition are difficult. In fact, Koumjian and Nimmo<sup>51</sup> showed an 85% decrease in transverse strength after repair of a bis-acryl material. They suggested that it might be more advantageous to make a new provisional restoration than repair this material. Young et al<sup>54</sup> compared bis-acryl and polymethylmethacrylate materials in terms of occlusion, contour, marginal fidelity and finish. For both anterior and posterior teeth, they found the bis-acryl materials significantly superior to PMMA in all categories. Another report makes similar comments.

Some practitioners find bis-acryl materials difficult to manipulate before setting because of difficult handling properties.<sup>34</sup> Conversely, it has also been reported that dual-polymerized materials provide a more rigid rubbery stage where considerable adjustment and evaluation can be made before the final photo-polymerization.

Two other studies have discouraged the use of dual polymerizing materials because of technique sensitivity.<sup>1,29</sup> Luthardt et al<sup>1</sup> compared the clinical performance of autopolymerizing, dual-polymerizing and visible light-polymerizing bis-acryl materials. They concluded that the light- and dual-polymerizing materials did not offer a clinical benefit relative to autopolymerizing material. Reduced flexibility of the partially polymerized materials made them difficult to handle, which lead to complications with the

integrity of provisional restorations. Tjan et al<sup>44</sup> stated that handling techniques might contribute to problems with marginal accuracy.

#### **4. Visible light-polymerized resin:**

The visible light polymerized (VLC) material, first introduced in the 1980's<sup>51</sup> requires the addition of urethane dimethacrylate, a resin whose polymerization is catalyzed with visible light energy and a camphoroquinone/amine photo initiator. These materials usually incorporate filler such as microfine silica to improve physical properties such as reduced polymerization shrinkage. Unlike methacrylate resins, they do not produce residual free monomers after polymerization, which explains why they exhibit significantly decreased tissue toxicity relative to methacrylate resins.<sup>55</sup> Haddix<sup>56</sup> indicated that VLC materials could produce provisional restorations with quality similar to heat-polymerized, laboratory-processed restorations, but with less time and expense. Dual-polymerizing composite materials generally incorporate both chemically polymerized bis-acryl and light-polymerized urethane dimethacrylate resins in variable product-specific combinations.

### ***B) Preformed Materials:***

Preformed provisional crowns or matrices usually consist of tooth-shaped shells of plastic, cellulose acetate, or metal. They are commonly relined with acrylic resin to provide a more custom fit before cementation, but the plastic and metal crown shells can also be cemented directly onto prepared teeth using a stiff luting material following adjustment. They are commercially available in various tooth sizes and are usually selected for a particular tooth anatomy. Nonetheless, available sizes and contours are finite which makes the selection process important for clinical success. Compared with custom fabricated restorations, this treatment method is quick to perform but is more subject to abuse and inadequate treatment outcome. This can result in improper fit, contour or occlusal contact for a provisional restoration.<sup>50</sup>

#### **1. Polycarbonate resin:**

Poly carbonate resin is commonly used for preformed crowns and possesses a number of superior properties relative to polymethyl methacrylate materials.<sup>3,57</sup> These crowns combine micro glass fibers with a polycarbonate plastic material. Practitioners commonly use polycarbonate resin shell crowns as a matrix material around a prepared tooth that is relined with acrylic resin to customize the fit.<sup>3</sup> This material possesses high impact

strength, abrasion resistance, hardness and a good bond with methyl-methacrylate resin.<sup>57</sup>

## **2. Metal crowns:**

Metal provisional materials are generally esthetically limited to posterior restorations. Aluminum shells provide quick tooth adaptation due to the softness and ductility of the material, but this same positive quality can also promote rapid wear that results in perforation in function and/or extrusion of teeth. An unpleasant taste is sometimes associated with aluminum materials. Iso-Form Crowns (3M Dental Products, St. Paul, Minn) are manufactured with high-purity tin-silver and tin-bismuth alloys. Like aluminum, they possess reasonable ductility and can be contoured quickly, but the occlusal table is reinforced, so they are more resistant to wear related failure. For longer-term use, nickel-chrome and stainless steel crowns are available but may be more difficult to adapt to a prepared tooth. Commercially available preformed materials are listed as Preformed materials along with manufacturer's details:

<b>Material classification</b>	<b>Product name</b>	<b>Manufacturer</b>
Polycarbonate resin	B-Crowns	Harry Bosworth, Skokie, III
	Polycarbonate crown	3M Dental, St. Paul, Minn.
	Molar B-Crowns	Harry J. Bosworth, Skokie
Nylon fiber reinforced	Iso-form Crowns ( Ti/silver alloy)	3M Dental, St. Paul, Minn
	Gold Anodized Crowns (gold anodized)	3M Dental, St. Paul, Minn
	Stainless Steel Crowns (nickel chrome)	3M Dental, St. Paul, Minn

➤ **Influence of material properties on treatment outcome:**

*1. Marginal accuracy*

Accurate marginal adaptation of resinous provisional restorations to the finish line of a prepared tooth assists in protecting the pulp from thermal, bacterial, and chemical insults.<sup>58</sup> Barghi and Simmons<sup>22</sup> indicated from their

qualitative assessment that autopolymerizing acrylic resin provisional restorations routinely did not have adequate marginal adaptation. The accuracy could be significantly improved by relining the restoration after the initial polymerization. Furthermore, they found that because of hydraulic pressure, 80% of restorations did not fully reseat after the reline procedure. They suggested that this problem could be improved by venting a provisional restoration before reline.

Crispin et al<sup>47</sup> evaluated marginal accuracy with direct and indirect techniques. They reported that indirect fabrication provided significant improvements in marginal fit relative to direct methods when methyl and vinyl ethyl methacrylate resins are used. They demonstrated that the marginal fit of polymethylmethacrylate restorations could be improved by up to 70% with an indirect technique. Other reports showed similar results.<sup>20</sup>

A number of studies have focused on the effects of thermocycling on provisional crown margins<sup>59,60,61,62,64</sup> They reported that:

1. Acrylic resin provisional crowns demonstrated dimensional degeneration and enlarged marginal gaps resulting from thermocycling and occlusal loading;
2. Marginal gap changes were greater after hot thermocycling than cold thermocycling;

3. Improved marginal accuracy of PMMA provisional restorations occurred when a shoulder finish line was used compared with a chamfer marginal design;
4. In addition to improved initial accuracy, provisional resin restorations that were relined had smaller marginal changes after thermocycling and occlusal loading; and
5. Light-polymerized materials provided significantly improved marginal accuracy relative to autopolymerizing PMMA resin after thermocycling.

Koumjian and Holmes<sup>64</sup> examined a variety of resinous provisional materials and reported that they all demonstrated continued polymerization shrinkage after storage in air for 1 week. When stored in water for 1 week, water absorption compensated for polymerization shrinkage in all of the materials except for polyvinyl ethyl methacrylate and bis-acryl materials. The water storage environment was the most clinically relevant in this study and produced significantly lower marginal discrepancies with the PMMA and ethyl methacrylate materials.

Lepe et al<sup>65</sup> reported that polymerization shrinkage of acrylic resin would play an important role in the fit of provisional restorations. Volumetric polymerization shrinkage for polymethylmethacrylate is 6% compared with 1% to 2% for composite materials. They speculated that

composite materials would provide a better marginal fit relative to unfilled polymethylmethacrylate because of less polymerization contraction, but the authors also pointed out that marginal fit is not the only factor affecting the overall retentive quality of provisional restorations. They found a nearly 20% improvement in the retention of interim crowns made with polymethylmethacrylate compared to those fabricated with composite materials. They concluded that polymerization shrinkage occurring with polymethylmethacrylate material might have allowed for a tighter fit of the restoration on the prepared tooth, which had a direct influence on improved retentive quality.

## **2. Color stability:**

In esthetically critical areas it is desirable for provisional restorations to provide an initial accurate color shade match and then to remain color-stable over the course of provisional treatment. Discoloration of provisional materials can produce serious esthetic complications, especially when long-term provisional treatment is required. Modern provisional materials use stabilizers that decrease chemically induced color changes, but these materials are susceptible to other factors that will promote staining. Most provisional materials are subject to sorption, a process of absorption and adsorption of liquids that occurs relative to environmental conditions. When

provisional material contact pigmented solutions such as coffee or tea, discoloration is possible. Porosity and surface quality of provisional restorations, as well as oral hygiene habits, can also influence color changes.

Crispin and Caputo<sup>52</sup> studied the color stability of provisional materials. They found that methyl methacrylate materials exhibited the least darkening, followed by ethyl methacrylate and vinyl-ethyl methacrylate materials. They also reported that increase in surface roughness has induced increase in material darkening; and pressure polymerizing did not influence discoloration relative to air polymerizing. Koumjian et al<sup>57</sup> included a visible light-polymerized material in their investigation. They placed test materials into the flanges of complete dentures and concluded that for short time periods of 5 weeks or less, all materials demonstrated acceptable color stability. They stated, however, that the Triad VLC material exhibited more adverse color change relative to other materials at the end of 9 weeks.

Yannikakis et al<sup>63</sup> immersed provisional materials in various staining solutions for up to 1 month. They reported that all materials showed perceptible color changes after 1 week. After 1 month, the methyl methacrylate materials exhibited the best color stability and bis-acryl materials the worst.

Robinson et al<sup>30</sup> reported the effect of vital tooth bleaching on

provisional restorative materials. They prepared disks of polymethyl, polyethyl, polybutyl methacrylate, and bis-acryl composite materials. Polycarbonate crowns were studied. Specimens of each type of provisional material were placed into varied proprietary dental bleaching agents and soaked for up to 14 days. They concluded that an orange discoloration occurred throughout the specimens representing all methacrylate materials. The bis-acryl and polycarbonate crowns showed no difference relative to the control group. Another study confirmed the color stability of composite materials during vital bleaching treatment.<sup>69</sup>

Monaghan et al found that vital bleaching produced visibly lighter composite restorations. They reported that in some situations composite restorations might lighten along with natural teeth that are simultaneously bleached.

### ***3. Gingival response:***

Inflammation and recession of the free gingival margin associated with provisional treatment is a common occurrence.<sup>17, 71</sup>

Donaldson<sup>71</sup> reported the following observations regarding gingival recession:

a) The presence of a provisional restoration lead to at least some recession at about 80% of the free gingival margin sites evaluated;

- b) The degree of recession was time dependant;
- c) Placement of the definitive treatment commonly leads to gingival recovery;
- d) 10% of subjects demonstrated recession in excess of 1 mm; and
- e) In the presence of gingival recession, only one third of subjects demonstrated complete gingival recovery.

In a separate report, Donaldson<sup>71</sup> indicated that the occurrence of gingival recession before provisional treatment was directly linked to further recession observed after the completion of definitive Prosthodontic treatment. A history of bone loss and subsequent gingival recession would suggest that a patient would have an adverse reaction to provisional fixed prosthodontic treatment. He also found a direct relation between the degree of pressure applied by a provisional restoration and gingival recession. An anatomically contoured provisional restoration caused less recession than did a nonanatomically contoured one.

In contrast, MacEntee et al,<sup>72</sup> in a histologic evaluation of tissue response, reported no detectable change in gingival tissue associated with provisional restorative treatment over a 3 week period. Waerhaug and Zander<sup>33</sup> found that in the presence of mechanical irritation such as poor restorative contours, provisional treatment did not negatively alter gingival

tissue response. Rather, they implicated the presence and accumulation of necrotic tissue and plaque material in areas associated with poor marginal adaptation and surface roughness of interim restorations as a constant source of inflammation to the gingival tissues leading to diminished gingival health. Garvin et al<sup>17</sup> concluded that periodontal inflammation associated with provisional treatment could be expected to be a reversible process provided that the amount of gingival irritation is minimal and provisional treatment occurs over a short time span.

#### ***4. Pulpal response:***

Dental pulp inflammation can be caused by either thermal or chemical insult resulting from materials used to produce direct provisional restorations.

Tjan et al<sup>44</sup> studied the dental pulp chamber temperature rise associated with the direct fabrication of provisional restorations. In this in-vitro study, a thermocouple probe was placed into the pulp chamber of specimen teeth to measure the exothermic reaction associated with the direct contact polymerization of methyl methacrylate, ethyl methacrylate, vinyl ethyl methacrylate and bis-acryl materials. Although the bis-acryl material produced the lowest temperature increase, no significant differences were found among the 4 types of materials tested. The results of this study suggest

the possibility of thermal damage to dental pulp tissue and odontoblasts during direct provisional fabrication, but the authors also indicated that actual damage could only be accurately assessed by use of histological studies. They suggested that by use of air and water coolants, as well as by use of a matrix material, that can dissipate heat rapidly, the pulp temperature rise might be reduced. Additionally, the amount of heat rise is dependent on the quantity of provisional restorative material used.

Other studies have found comparable results with similar methods.<sup>74</sup> Moulding and Teplitsky<sup>78</sup> reported that intra-pulpal temperature rise was dependent on the type of acrylic resin and the type of matrix used to retain the material on the tooth during polymerization. Temperature rise was greatest with polymethylmethacrylate and vacuum adapted templates; least with bis-acryl and relined resin shells; and intermediate temperature increases were recorded with polyethyl methacrylate materials and either irreversible hydrocolloid or polyvinylsiloxane impression materials used as a matrix for holding acrylic resin provisional material against a tooth. The authors also identified that fixed partial denture provisional restorations produced a greater temperature rise than did single-unit provisional restorations.

Grajower et al<sup>74</sup> showed that faster polymerizing acrylic resin materials could generate higher temperatures than slower polymerizing resins. They indicated that external heat dissipation might be enhanced with a water spray or by polymerization of restorations in silicone impressions. Additionally, this external heat dissipation caused retardation in the polymerization, which further decreased heat production. The retardation resulted from the cooling effect of the spray and not the water itself, since moisture quickens the polymerization of autopolymerizing acrylic resins that contain tertiary amine accelerators. The authors concluded that:

- a) Provisional acrylic resin restorations might be fully polymerized on prepared teeth by appropriate methods such as in impressions or with external cooling, without causing excessive heating of the dental pulp;
- b) Removal of a provisional restoration before complete polymerization, leading to potential deformation of the acrylic resin material, is therefore unnecessary; and
- c) A thin insulating layer should be applied to a prepared tooth before contact with non-polymerized acrylic resin to avoid chemical injury.

### ***5. Hypersensitivity:***

Hypersensitivity from provisional materials has been reported but appears to be rare. Autopolymerizing methacrylate materials have greater

potential for producing allergic contact stomatitis than similar heat-polymerized materials. The residual monomer in the material has been implicated as the causative factor. One report showed that the residual monomer content in heat-polymerized acrylic resin ranges from 0.045% to 0.103%. Autopolymerized acrylic resin has a residual monomer content of 0.185%. Over time residual monomer is gradually leached out, leaving a fraction that is tightly bound to the resin material.

Allergic reaction to provisional materials will demonstrate the following features:

- a) The patient had previous exposure to the provisional material;
- b) The reaction conforms to a known allergic pattern, such as redness, necrosis or ulceration;
- c) The reaction resolves when a provisional restoration is removed;
- d) Reaction recurs when a provisional restoration is replaced; and
- e) A patch test for the material is positive.

Patch testing has demonstrated less response with light-polymerized materials relative to autopolymerizing acrylic resin. Indirect material processing methods are recommended for individual showing evidence of hypersensitivity.<sup>77,79</sup> After complete polymerization, the polymerized acrylic

resin usually does not induce allergic reactions. Unpolymerized monomer can be substantially removed by placing an autopolymerized provisional restoration in a pressure pot with warm water for 20 minutes.

➤ **Strengthening provisional materials:**

The literature clearly favors acrylic resin as the material of choice for provisional restorations. Most resins used for provisional restorations are brittle. Repairing and replacing fractured provisional restoration is a concern for both clinician and patient because of additional cost and time associated with these complications. Failure often occurs suddenly and probably as a result of a crack propagating from a surface flaw. The strength and serviceability of any acrylic resin, especially in long span interim restorations, is determined by the material's resistance to crack propagation. Crack propagation and fracture failure may occur with these materials because of inadequate transverse strength, impact strength, or fatigue resistance.

Physical properties of strength, density, and hardness may predict the longevity of provisional restorations. Donovan et al<sup>13</sup> examined methods to improve the longevity of these restorations using variable indirect polymerization techniques. They compared methyl methacrylate material

strength, porosity and hardness under the following polymerization conditions:

- (1) In air;
- (2) Under water;
- (3) Under air pressure; and
- (4) Under water and air pressure.

They found that polymerization with a pressure vessel with air and water had the greatest influence on increasing strength and reducing porosity. There was no difference in hardness for the 4 conditions tested. A similar study, however, evaluated the fracture toughness of provisional resins and found that the use of a pressure vessel during polymerization did not significantly increase the fracture toughness for the resins tested. Convey et al<sup>135</sup> found that oven heat treatments at 120°C for 7 minutes could significantly increase the tensile strength for both chemical and light-polymerized composite materials.

Heat-polymerization of acrylic resin materials can be used when provisional restorative treatment will be required for extended periods of time or when additional strength is required. This indirect laboratory process results in materials that are denser, stronger, more wear resistant, more color stable, and more resistant to fracture than their autopolymerizing

counterparts.

Metal castings and swaged metal substructures in combination with resin materials have been incorporated into provisional restorations and have been reported as especially useful with long-term or long-span interim treatment.<sup>3</sup> Both heat polymerized acrylic resin and metal provisional restorations should last longer than autopolymerized restoration, but the expense and time required for indirect fabrication can make them less cost effective for routine use.

Reinforcing frameworks reduce flexure, increase retention, and increase structural integrity. Attempts have been made to strengthen acrylic resin materials by reinforcement with either chemical modification with grafted co-polymers and stronger cross linkage or by inclusion of various organic and inorganic reinforcing fibers. Materials used for fiber reinforcement have included metal, glass, carbon graphite, loo sapphire, Kevlar (Du Pont, Wilmington, Del), polyester, and rigid polyethylene. Most of these materials have had little or no success in increasing resin strength.

Investigations on fiber reinforcement have favored the use of long continuous fibers, with strand alignment placed perpendicular to the direction of applied loads.<sup>80</sup> Samadzadeh et al<sup>80</sup> studied the effects of plasma-treated woven polyethylene fiber (Ribbon Inc, Seattle, Wash) on the

fracture strength of methyl methacrylate and bisacryl materials. Fracture strength was increased for the bis-acryl material. Ribbond fibers did not increase the fracture strength of PMMA prostheses, but complete catastrophic fracture was avoided.

Emtiaz and Tarnow,<sup>51</sup> Davidoff,<sup>49</sup> and others<sup>81,82</sup> have described various methods of adding metal reinforcing structures to acrylic resin provisional restorations; castings, spot welded stainless steel matrix bands, and precut stainless mesh have been used. Generally margins are not reproduced in the cast alloy. Yuodelis and Faucher<sup>82</sup> described using stainless steel wire material while Hazelton and Brudvik reported the benefits of stainless steel orthodontic band material adapted around abutment teeth, removed, welded, and fitted inside acrylic resin shell crowns to reinforce autopolymerizing acrylic resin materials. Similarly, Greenburg recommended ultra thin stainless steel bands. Spot-welded stainless steel band reinforced acrylic resin provisional restorations are stiffer and more resistant to cement degradation and loss of cement seal from deformation. Fabrication of a reinforcing metal framework is guided by a diagnostic wax-up that generates the desired contours for the finished provisional.<sup>54</sup>

In a study describing a negative influence on the strength of provisional materials, Chee et al<sup>45</sup> studied the effect of chilled monomer on

the working time for 3 autopolymerizing acrylic resins. They found that the working and setting times increased by up to 4 minutes when chilled monomer was used, but the transverse strength for the materials were decreased by 17%.

➤ **Provisional luting materials:**

Provisional luting agents should possess good mechanical properties, low solubility, and tooth adhesion to resist bacterial and molecular penetration.<sup>46</sup> The most important function of these materials is to provide an adequate seal between the provisional restoration and prepared tooth. This is necessary to prevent marginal leakage and pulpal irritation.<sup>46</sup> There are a variety of luting materials used for interim purposes. The most common ones include:

- (1) calcium hydroxide;
- (2) zinc-oxide eugenol;
- (3) noneugenol materials<sup>46</sup>

Generally, all of these possess poor mechanical properties that likely worsen over time. This can have a negative influence on marginal leakage but also provides an advantage by allowing easier dislodgment and removal of provisional restorations from teeth.<sup>16</sup>

The retentive requirements for provisional luting materials are that they be strong enough to retain a provisional restoration during the course of treatment but allow easy restoration removal when required. This paradoxical necessity for good retentive and sealing quality and easy restoration retrieval may lead to a compromise in material behavior, particularly regarding mechanical properties.<sup>45</sup> Baldissara et al<sup>50</sup> recommended that interim restorations be frequently evaluated and used for only short periods of time. Literature reports advise that if provisional treatment is required over a protracted time period, it is best to remove and replace the provisional luting agent on a regular basis.<sup>74</sup>

Some of the most commonly used cements with provisional prostheses are those containing zinc-oxide and eugenol.<sup>36</sup> They provide sedative effects that reduce dentin hypersensitivity and possess antibacterial properties.<sup>46</sup> Unfortunately, free radical production necessary for polymerization of methacrylate materials can be significantly hampered by the presence of eugenol found in eugenol based provisional luting materials. This can interfere with the acrylic resin polymerization and hardening process.<sup>21</sup> They can also be incompatible with some resin-based definitive luting agents for the same reason.<sup>46</sup>

Eugenol-free provisional luting materials are commercially available and have gained popularity due to the absence of resin-softening characteristics.<sup>21</sup> Gegauff and Rosenstiel<sup>36</sup> however, reported that Temp-Bond (Kerr Dental, Orange, Calif) a zinc oxide and eugenol based cement did not appear to have a significant adverse effect on the polymerization of acrylic resins. They postulated that the softening effect of eugenol on acrylic resin is dependent on the presence of unreacted eugenol, which may be minimal in Temp-Bond cement.

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## **CLINICAL CONSIDERATIONS FOR PROVISIONAL TREATMENT INVOLVING NATURAL TEETH**

The literature describing the fabrication of provisional restorations is extensive but largely anecdotal. Virtually all teeth receiving cast restorations require provisional restorations. Properly executed provisional restorative treatment rarely fails and dislodgment or fracture usually indicates that their form is unacceptable or that a tooth preparation is inadequate. Provisional restorations should be smooth, highly polished, and alterable and for this reason custom made provisional restorations most consistently meet the biological, functional and esthetic needs of a patient. The brand of provisional material and method of fabrication are not as important as the devotion, skill and attention to detail of the dentist.

### **➤ Provisional restorations as a part of comprehensive treatment:**

Provisional restorations are not devoid of interactions with other modes of therapy. Patients often have periodontal, endodontic, orthodontic or surgical needs in conjunction with their prosthodontic treatment. Provisional restorations produce outcomes that range from microscopic tissue effects to psychological factors that change the patient's behavior. Provisional restorations can provide patients with increased confidence in treatment.

➤ **Diagnostic provisional treatment:**

In the simplest situations, complete oral and extra oral clinical examination, as well as radiographic evaluation may be all that is necessary before commencing prosthodontic treatment. In more complex treatments, however, provisional restorations provide a means of designing, improving and assessing the occlusion, esthetics and contours for definitive restorations, as well as to determine their effects on gingival health, phonetics and patient's adaptability before the initiation of the definitive treatment.<sup>87</sup>

Provisional restorations fit into 2 categories:

- (1) Those that fit within an arch of fundamentally intact teeth that provide reference for their occlusion, contours and esthetics; and
- (2) Those that become the reference for the entire prosthesis. Provisional treatment for patients with more complex prosthodontic needs demand the fabrication and articulation of diagnostic casts and completion of a diagnostic wax-up in the maxilla-mandibular relationship in which definitive treatment is to be performed.

➤ **Occlusal diagnosis and treatment:**

Casts of provisional restorations mounted to opposite definitive casts transfer contours, clinical crown dimensions and maxilla-mandibular relationship from a patient to a dental laboratory for developing occlusal

factors, especially anterior guidance for fixed prosthodontic treatment.<sup>3,59</sup> Sometimes treatment feasibility can only be tested via full-arch provisional restorations and occlusal problems are best diagnosed during a functional testing period with provisional treatment.

➤ **Esthetic and phonetic diagnosis and treatment:**

Provisional restorations assist development and assessment of esthetic and phonetic values of the planned fixed prosthesis.<sup>18</sup> Zinner et al<sup>4</sup> proposed use of guidelines to test anterior contours. They recommended that the maxillary anterior incisal edges follow the contour of the lower lip, the "smile line" and all 6 maxillary anterior teeth should be in contact with their antagonists in maximum intercuspation. Evaluation of labiodental ("F" and "V") and sibilant ("S" and "CH") sounds are useful methods of ascertaining the lengths of maxillary incisors. Matrixes created from a diagnostic waxing or from casts of provisional restorations are useful tools for producing specific contours in a definitive prosthesis or communicating those concepts to the dental laboratory.<sup>9,50</sup>

In certain situations phonetics and esthetics of a planned prosthesis can be assessed before tooth preparation by use of vacuum or pressure-formed matrixes that hold auto polymerizing acrylic resin between unprepared teeth

and proposed tooth contours to provide intraoral treatment simulation.

➤ **Periodontal treatment and maintenance:**

Periodontal treatment is commonly the part of comprehensive prosthodontic care. These provisional restorations provide a matrix against which the tissue heals, guiding the generation of correct soft tissue architecture.<sup>72</sup> According to Shave<sup>12</sup>, tooth preparations and provisional restorations should be completed with retraction cord in place. Patients should be seen weekly for evaluation and the provisional restorations are judged successful only when the gingival tissue reflects good general health. It has been recommended that when the duration of the periodontal treatment is less than 6 months, the use of acrylic resin provisional restorations should be adequate.<sup>82</sup> For longer treatment periods, gold-band and acrylic-resin restorations are more appropriate. A provisional restoration also guides preparation of teeth that require periodontal surgery. Poorly fabricated provisional restorations have consequences for fixed prosthodontic treatment including: gingival recession; difficulty making impressions; difficulty fitting the definitive restorations; soft tissue damage; and inefficient use of time at prosthesis insertion.<sup>2</sup> Provisional restorations play a role in long-term periodontal therapy as well. Chlorhexidine used in conjunction with

provisional treatment has been shown to reduce plaque levels and improve gingival indexes.<sup>75</sup>

Slightly convex facial and lingual contours of provisional restorations and a flat emergence profile are effective in promoting gingival health. Good periodontal health can be created by developing the appropriate contour, good gingival adaptation and embrasure space of the prosthesis for the particular situation. Embrasure spaces that are too broad can cause food impaction and blunting of the papilla.

➤ **Orthodontic conjoint treatment:**

It is generally better to avoid crown preparation before orthodontic treatment because after tooth movement; a tooth may be incorrectly prepared. However, in conjunction with tooth movement procedures, carefully planned provisional restorations can-

1. Replace hopeless or missing teeth to improve esthetics;
2. Achieve occlusal stability with missing posterior teeth and maintain vertical dimension of occlusion;
3. Retain teeth in proper position;
4. Allow maturation of investing tissues;
5. Allow evaluation of questionable teeth; and

6. Provide anchorage where only a few teeth remain.

➤ **Provisional fixed prosthesis fabrication:**

**A) General concepts:** Provisional fabrication involves 2 segments:

- (1) "supragingival construction," the basic form providing abutment protection, stabilization, and function; and
- (2) "intrasulcular extension," marginal fit and correct contours to promote soft tissue health.

Central to this is the use of a matrix to produce the external form and adaptation of material replicating the contour of the prepared tooth or teeth. Provisional restorations are often made clinically, though they may also be fabricated indirectly in the laboratory. In contemporary practice, the majority of provisional restorations are made wholly or in part with autopolymerizing acrylic resin.<sup>2</sup> Lubricants applied to teeth or casts with indirect methodology are often recommended during fabrication of provisional restorations.

**B) Adaptation to a prepared tooth:** Adaptation is done either directly on a tooth or indirectly on a plaster, stone, polyvinylsiloxane, or other replica of a prepared tooth.<sup>2,3</sup> Representation of the internal surface adaptation, or intaglio is typically accomplished by adapting a plastic material such as

acrylic resin or occasionally a cement, such as zinc oxide eugenol to a tooth or tooth replica with an external shell or custom-made matrix. The internal surface adaptation is evaluated much like the surface of an impression.<sup>2</sup>

**C) Cavosurface adaptation:** Provisional restorations must be made of a material, which is alterable and can be precisely adapted to prevent excessive cement film thickness. A marginal gap usually exists at the interface between tooth, provisional restoration, and cement allowing plaque to accumulate and compromise cementation. Relining provisional restoration margins produces the best adaptation as long as potential trauma from monomer and the exothermic heat of reaction is controlled with methods such as external water spray. Exposure of margins by placement of retraction cord, not by electrosurgery is recommended during fabrication directly on the teeth. Burnished copper or gold bands adapted to the cervical one third of a prepared tooth and incorporated into a provisional restoration are reported to improve margin adaptation, physiological contours and hygiene however; at least one report asserts that acrylic resin margins can be as good as metal band margins.

Posterior crown preparations can expose 1-2 million dentinal tubules if all the enamel is removed. Dentin conditioners used with dentin bonding

systems have been shown to increase fluid flow through the dentin. Although dentin-sealing agents have demonstrated a reduction in dentinal tubule fluid flow, numerous sealants have a significant film thickness at the margin area, some as thick as  $263\mu\text{m}$ .

*Form:* Provisional restorations should have cervical concavities and proper emergence profile. It has been suggested that pontics should be designed for hygiene on the mandibular arch and hygiene and esthetics on the maxillary arch. The convex, "bullet-shaped," pontic has been suggested to be easiest to keep clean.<sup>2</sup>

Liebenberg<sup>83</sup> advocated avoiding splinted acrylic resin restorations whenever possible to promote better hygiene, cement removal, and reuse. Others advocate splinting adjacent provisional restorations together even if the definitive treatment plan calls for individual definitive restorations. Burnished metal bands incorporated in the provisional reportedly improve contours.

#### **D) Clinical Methods:**

*Matrices:* Numerous references have appeared in the literature since 1970 describing clinical fabrication methods. A matrix planned for provisional fabrication may copy existing tooth contours from the mouth with a diagnostic cast<sup>18</sup> or produce customized contours created by a diagnostic

waxing. It is further suggested that, when possible this matrix should extend onto at least 1 tooth adjacent to the tooth being restored. The addition of acrylic resin, VLC resin or even elastomer impression materials can add contour to select areas of cast to correct extensively damaged teeth before making the matrix.<sup>53,54</sup>

Transparent thermoplastic materials may be vacuum<sup>13, 29, 41, 55, 56</sup> or pressure adapted to a dental stone cast creating a matrix or external surface form. Transparent matrices can be used for provisional fabrication, to guide tooth preparation, as a laboratory aid and can become a part of the patient's record.<sup>56</sup>

Impression materials are useful for provisional matrices. Polyvinylsiloxane and irreversible hydrocolloid matrices serve functions other than providing an external surface form for the provisional restorations in that they can limit thermal insults to pulpal tissues.<sup>74</sup> A disadvantage of Polyvinylsiloxane as a matrix material is its high cost. Other materials such as baseplate wax have also been used for matrices.

**1. Direct fabrication:** For selected patients, a denture tooth secured in position with typical class III composite restorations and orthodontic wire may be a suitable provisional restoration for a missing mandibular incisor<sup>37</sup> For urgent situations, in the absence of any matrix or opportunity to create a

matrix, a provisional restoration can be fabricated by adapting a block of freshly mixed acrylic resin directly to a tooth. After the acrylic resin block has polymerized, the tooth contours can be carved with acrylic resin burs of choice and the restorative margins perfected intraorally.

Most patients, however, require a more conventional approach. Fabricating provisional restorations directly on teeth using the "direct method" is suitable for single units and up to 4-unit fixed partial denture provisional restorations, according to a report. Three techniques encompass virtually all of the literature on direct provisional restorations:

1. Use of a premanufactured provisional shell.<sup>2,11,19,28</sup>
2. Use of an impression material<sup>24,54,68,69,74,77</sup> or pressure or vacuum formed translucent matrix; and
3. Use of a custom, prefabricated acrylic resin shell.<sup>21,23,29</sup>

Prefabricated shell crowns are constructed from a variety of materials including aluminum, silver-tin, tin-bismuth, polycarbonate resin, celluloid, stainless steel and nickel-chrome and can be used as matrices for direct fabrication.<sup>2,19</sup>

Much more common in the literature is the use of impression materials or thermoplastic materials as shell matrices. Direct provisional restorations

made particularly of PMMA and to a lesser degree, poly-ethyl methacrylate (PEMA) must be cooled if the material is allowed to polymerize completely on a tooth; polymethylmethacrylate can increase pulpal temperatures as much as 7°C.<sup>45</sup> Cooling the material during polymerization by its removal at initial polymerization and allowing complete polymerization to be completed while it is off the tooth, cooling with air-water spray, periodic removal, and flushing with water and use of a "heat sink" matrix material such as alginate will limit temperature increases to less than 4°C, minimizing the exothermic risk. Larger masses of exothermic materials, such as with FPD provisional restorations produce greater pulpal temperature increase.

Visible light polymerized materials produce smaller pulpal temperature increase and have extended working time compared with PMMA or PEMA.<sup>45</sup> One author recommended softening Triad material in 120°F to 150°F water, creating a "hollow" in the center of the softened material mass with a blunt instrument before seating and lubricating the tooth as a method for reducing the viscosity of material and promoting tooth adaptation. The adaptation was then evaluated extraorally before polymerization. External colorants can be applied either as autopolymerizing pigments or as suspensions within light polymerized unfilled acrylic resins. A number of reports<sup>62</sup> have recommended hybrid visible light-polymerized

composite/PMMA direct provisional restorations. Fehling<sup>14</sup> stated that this combination decreased occlusal and proximal wear and recommended placing 3 coats of copal cavity varnish to protect the tooth from "deleterious effects" of free monomer.

**2. Indirect fabrication:** The indirect method has been indicated to fabricate multiple unit provisional restorations to-

- (1) Avoid exposure of a patient to adverse properties of provisional acrylic resins;
- (2) Optimize the properties of provisional acrylic resins;
- (3) Allow the use of materials that are difficult to polymerize intraorally;
- (4) Make significant contour or occlusal changes; and
- (5) Provide for the fabrication of hybrid provisional restorations.

A variety of methods of creating an acrylic resin shell customized for a patient's occlusion or contours have been published.<sup>81,56</sup> Many authors describe indirect methods.<sup>24,48,51,61,73,78</sup> Indirect techniques generally use either approximate tooth preparations made on a duplicate cast or a cast of the actual tooth preparations made after the clinical procedure has been accomplished. A matrix made from a diagnostic wax-up of planned treatment tooth contours can be placed over the tooth preparations on the cast. Autopolymerizing acrylic resin can be packed into a matrix and fitted

over the prepared tooth cast or a diagnostic wax-up can be invested and boiled out so that tooth-colored, heat polymerized acrylic resin can be packed and processed.<sup>49</sup> One advantage of the indirect technique is that it can be allocated to auxiliary personnel.

Fabricating a provisional restoration wholly or in part using an indirect method reduces exposure of oral tissues to monomer, heat, shrinkage<sup>10,71</sup> and reduces the volume of volatile hydrocarbons inhaled by a patient. Creating an indirect acrylic resin shell of an unprepared tooth that is later relined intraorally is one method of reducing patient exposure. Extensive shell matrices designed for adaptation and margin relining in the mouth can be initially fabricated of polycarbonate or visible light polymerized polymers.<sup>57</sup>

It has been reported that provisional restorations fabricated indirectly have superior margins to those from direct techniques because the acrylic resin polymerizes in an undisturbed manner.<sup>10</sup> Polymerizing auto polymerizing acrylic resin under heat and pressure improves the physical properties of the material. Reinforcing the vacuum or pressure formed matrix allows it to be secured to the cast on which the provisional shell is polymerized.<sup>24, 81</sup>

➤ **Provisional treatment for all ceramic veneer restorations:**

All-ceramic restorations including laminate, veneers have become a large part of dental practice. Most of what has been published regarding provisional treatment for veneers has focused on technical procedures. Provisional veneers are indicated when-

- (1) Esthetics and intelligible speech are important;
- (2) Mandibular incisors are veneered;
- (3) Dentin is exposed;
- (4) Proximal contacts are broken;
- (5) Maxillary teeth are inverted lingually and the veneer surface affects occlusion;
- (6) The preparation margin invades the gingival sulcus; and
- (7) The final veneer is dependent on patient approval of form, color, contour and position.

Sheets stated that patients were happier with provisional veneers but recommended that provisional restorations not be luted. Provisional restorations allow patients to have a trial period for making notes about esthetics so that their desires can be taken into account with the definitive veneer treatment. Provisional veneers may be cemented,<sup>9,15,16</sup> bonded<sup>44,45</sup> or left unluted.<sup>48</sup>

In contrast to preparations for conventional cast restorations, preparations for porcelain veneers may not have mechanical retentive features and thus one concern regarding a provisional restoration's tooth attachment while avoiding irreversible contamination or alteration of the luting surface of a prepared tooth. Elledge<sup>6</sup> advocated placing 2 small dimples on opposing surfaces of the preparation to provide mechanical retention for the provisional veneer that is luted with a cement of the clinician's choice. One method that avoids excess cement while sealing the margin area is the "peripheral seal technique" that uses a 3-second etch of the preparation periphery and then bonding a provisional restoration primarily at the etched periphery. Similarly, a colored luting resin may facilitate removal of excess resin and reduce contamination of a tooth surface. After a provisional restoration is removed, 1 report indicated that a tooth could be satisfactorily cleaned of all residues with a micro-etcher (Danville Engineering, San Ramon, Calif).<sup>27</sup>

Another technique known as the "spot etch" method incorporates provisional restorations that are luted with light polymerized acrylic resin to an etched spot near the center of the preparation. In an in vitro study of surface contamination associated with provisional bonding, a polyurethane isocyanate surface treatment left the cleanest tooth structure whereas non

eugenol provisional cement left significant but removable residue; dual polymerizing resin cement left tenacious residue that could only be removed with a bur.<sup>75</sup>

A variety of methods for fabrication of veneer provisional restorations have been reported and are not unlike the methods advocated for conventional provisional restorations including a removable "splint,"<sup>48</sup> with hand formed visible light polymerized materials, polycarbonate provisional crowns,<sup>14</sup> acrylic resin shells<sup>9</sup> and splinting together adjacent provisional veneers.

➤ **Esthetics:**

Patients may be highly motivated by esthetics and instant improvement can be achieved through provisional restorations. Custom colored provisional restorations made with mixtures of acrylic resin powders creating an incisal polymer, a body polymer, and a cervical blend are easier to fabricate with an indirect method.<sup>24</sup> Esthetically enhanced provisional restorations can be fabricated with visible light polymerized labial veneers or denture tooth facings conjunction with acrylic resin.<sup>3,51,55</sup>

Gingival architecture and tissue contour are among the many factors other than materials that influence esthetics. Anterior provisional restorations should provide the following esthetic benefits:

- (1) Optimal periodontal health;
- (2) Visualization of the anticipated treatment Outcome;
- (3) Ability to test the incisal edge position and cervical emergence;
- (4) Development of appropriate anterior guidance;
- (5) Determination of need for periodontal surgery.

Methods for improving or customizing colors also include coloring provisional luting cements<sup>15</sup> and coloring provisional restoration with porcelain stains and visible light cure acrylic resins. Custom colored restorations have also been recommended.<sup>16,17</sup>

**CLINICAL CONSIDERATIONS FOR  
PROVISIONAL TREATMENT INVOLVING  
DENTAL IMPLANTS**

Provisional prosthesis design for dental implant patients can vary widely, ranging from a removable acrylic resin complete denture, to an implant supported fixed prosthesis with several different potential designs that promote esthetics, convenience, loading of implants, tissue contour control, material strength and interim prosthesis durability. Although several removable prosthodontic provisional treatment modalities are available in conjunction with implant treatment, this discussion is primarily limited to fixed provisional prosthodontic treatment and specific materials. Manufacturers are indicated when available in the original reference. Generally, the literature related to implant provisionalization is dominated by anecdotal information and clinical observation. Information related to implant fixed provisionalization is therefore limited and is generally a carryover from natural tooth provisional treatment techniques.

A provisional restoration in combination with an implant-retained restoration provides many of the same benefits derived when treating non-implant retained fixed restorations. However, implant-retained treatment can

require an extended period of time and provisional treatment can present a challenge. When the implant retained prosthesis is located in an esthetic region, the need and desire for an interim prosthesis increases. In this respect, the transition from tooth-related fixed prosthodontics to implant-retained prosthodontic treatment has evolved from experience with conventional treatment. Restorative techniques are often the same and management of a patient can simulate conventional fixed prosthodontic treatment. Nonetheless, the significance of provisionalization with implant prosthodontics cannot be overstated.

Provisional fixed prosthodontic treatment options for an implant patient that may vary depending on:

- (1) The number, position or location of the implants;
- (2) The number of natural teeth remaining in the treatment arch;
- (3) Opposing occlusion;
- (4) Whether teeth adjacent to the implant site(s) can serve as abutment teeth for a provisional restoration; and
- (5) The desired protocol for provisional treatment at either first or second-stage surgery.

Historically, most endosseous implant systems have used a 2-stage surgical procedure. The surgical stages were separated by a 4- to 6-month

period to allow tissue integration. When necessary, a removable interim prosthesis was used. This protocol evolved from treatment of an edentulous patient to treating a partially edentulous patient. The use of a removable provisional prosthesis, however, in some situations has been less popular when treating a partially edentulous patient. Several factors have been proposed suggesting why this protocol has been challenged. When treating a partially edentulous patient, acceptance of a removable interim prosthesis may be objectionable and great lengths may be taken to fabricate a fixed provisional restoration to transition a patient through the implant integration period.

A reduction of micro-movement of an implant due to the potential stability obtained from adjacent teeth as well as a rigid implant connection when treating both partially and completely edentulous patients may lead to successes when providing provisional treatment at first stage surgery. As a result, early or rapid loading of several implant systems has been tested; however, routine immediate or rapid loading of dental implants is still controversial. The use of transitional implants has also been explored for support of a fixed implant-retained provisional prosthesis. Of course when the adjacent teeth can be used as abutments supporting a fixed interim restoration, this treatment option may be more easily accommodated

throughout the implant integration time period.

➤ **Single-tooth implant provisional treatment:**

One of the most challenging restorative treatment scenarios involves restoration of a single tooth implant. The demand for optimal esthetics and a natural appearance to a definitive restoration dictates a comprehensive diagnosis and treatment plan. Depending on the location of an implant, an interim prosthesis may or may not be necessary. For example, providing a provisional restoration in the posterior region during the implant integration period may be avoided if esthetic demands from the patient are low. On the other hand, in an esthetic region, great lengths may be taken to replace the edentulous area with a provisional restoration thereby providing a more socially acceptable interim treatment before a definitive restoration.

Techniques related to replacing a single tooth with an implant prosthesis embrace both first and second stage surgical protocols. Provisional treatment options are also related to treatment history of the adjacent abutment teeth.<sup>26</sup>

➤ **Provisional treatment at first-stage surgery: single-tooth, implant-retained:**

The placement of interim implant-retained fixed restorations at first-stage surgery provide benefits related to the time involved and the multi-step process in dental implant therapy, as a result, provisional fixed implant supported restorations have gained in popularity. Fixed implant-retained provisional treatment at first-stage surgery eliminates a removable interim prosthesis and the need to involve adjacent natural teeth. Although many reports advocate or explore this protocol, implant provisionalization techniques are, in most respects, a carryover from conventional natural tooth provisionalization. The literature is comprised of technique information with little or no scientific or evidence-based information presented.

Several studies have questioned or evaluated the potential to restore an implant fixed prosthesis using earlier or more rapid occlusal loading thereby incorporating a fixed provisional restoration early in the implant restorative procedure. Kupeyan and Ma described a technique in which the 2-stage Branemark implant system (Nobel Biocare, Yorba Linda, Calif) was used in a I-stage, non-submerged surgical procedure with placement of an interim fixed single crown restoration at stage-I surgery. The authors modified

Branemark healing abutments (5.5 or 7.5 mm in length) in laboratory before the surgical date for fabrication of provisional restorations. The authors also fabricated acrylic resin coping to fit the modified healing abutments, with an autopolymerizing acrylic resin (Jet Acrylic, Lang Dental Mfg. Co, Chicago, Ill) in the appropriate patient shade. A provisional crown was fabricated from either a polycarboxylate material or a polystyrene reformed provisional shell that was filled with autopolymerizing methylmethacrylate of an appropriate shade. After surgical implant placement, an interim restoration was fabricated by fitting the resin coping to the modified implant healing abutment and uniting crown to the coping with a small amount of autopolymerizing resin. Final finishing of the margins of provisional restoration was accomplished extraorally. The provisional restoration was luted with provisional cement.

Chee and Donovan<sup>84</sup> also described provisional restorative treatment of a single implant-retained crown at both first- and second-stage surgery. At second-stage surgery, the authors advocated recontouring the soft tissue cuff with a coarse diamond and placement of a provisional restoration with ideal axial contours. They also described fabrication of a provisional crown before second-stage surgery with the technique described by Hochwal<sup>54</sup> in which an impression is made at first stage surgery by use of surgical guide. The

resultant cast allowed fabrication of a provisional restoration before uncovering the implant.

A technique for fabricating a provisional, screw-retained restoration for immediate loading of single implants was presented by Proussaefs and Lozada.<sup>126</sup> A provisional restoration was fabricated for a maxillary first premolar extraorally during the surgical appointment. The usual preparatory phase of treatment was done before the surgical procedure: (1) diagnostic casts; (2) diagnostic waxing (Sculpturing Wax; Williams Co, Amherst, Mass); (3) duplication of diagnostic waxing with an impression (Coe Alginate; GC America Inc, Alsip, Ill); and (4) generation of a gypsum cast (Microstone; Whip Mix Corp, Louisville, Ky). A vacuum formed matrix (Ultradent Products Inc, South Jordan, Utah) was also fabricated. The authors fabricated a light-polymerized acrylic resin template (Triad; Dentsply International, York, Pa) on the duplicate cast that was used as a surgical guide during implant placement and also registered the implant position at time of surgery by applying autopolymerizing resin between the access hole of the template and the implant (Pattern Resin; GC Co, Tokyo, Japan). After polymerization, the template was removed, an implant analog was attached to the guide, and the template was positioned on the original diagnostic cast that had been modified to allow placement of the implant

analog. The analog was incorporated into the cast with autopolymerizing acrylic resin (Pattern Resin; GC America). A "temporary" hexed abutment (Replace; Nobel Biocare) was placed on the implant analog and, after verifying the appropriate occlusal height and position of the abutment with a clear vacuum formed matrix, a screw-retained provisional was fabricated with matrix and autopolymerizing acrylic resin (Alike; GC America). The provisional restoration was trimmed in the laboratory and adjusted intraorally. Gomes et al also described this technique in which the provisional restoration was fabricated in the laboratory before the surgical placement of the implant.

➤ **Provisional treatment at first-stage surgery: partially edentulous and edentulous implant retained-**

Published reports have advocated immediate loading of multiple implants in an edentulous or partially edentulous patient to avoid a removable interim prosthesis. In most articles, authors did not describe the material and methods involved with provisional fabrication therefore details are limited.

Horiuchi et al<sup>37</sup> reported the immediate loading of Branemark implants after placement in edentulous patients and treatment with fixed interim restorations. The authors fabricated heat-polymerized acrylic resin provisional restorations reinforced with chromium-cobalt castings. At the time of stage-1 surgery, implants were immediately loaded and incorporated within the provisional restoration using "temporary" cylinders. Jaffin et al<sup>33</sup> also evaluated the immediate loading of implants in partially and completely edentulous patients. Rigid fixation and the use of a metal reinforced, passively fitting provisional restoration were factors proposed for successful use of this protocol.

Kinsel and Lamb<sup>36</sup> described gingival esthetics related to treatment of an edentulous patient with an immediately loaded single-stage, implant-supported fixed prosthesis. The authors fabricated heat-polymerized acrylic resin provisional restorations from diagnostic casts. These provisional restorations were relined intraorally at the time of implant placement. The authors also described treatment in which retention from sufficient teeth to support a transitional fixed prosthesis and ovate pontics were created within the extraction sites to be used to maintain facial prominence and interdental papillae surrounding the extracted teeth. After implant integration, the

remaining abutment teeth were extracted, and the provisional prosthesis was converted to a solely implant-supported provisional prosthesis.

In a preliminary report, Balshi and Wolfinger<sup>30</sup> evaluated the immediate loading of Branemark implants placed in the mandibular arches of 10 edentulous patients. The design involved 4 widely distributed implants that were immediately loaded with an interim, fixed, implant-retained prosthesis at first-stage surgery. The authors used additional implants in a conventional manner to provide sufficient support for a definitive fixed prosthesis, even if all the immediately loaded implants failed.

Balshi and Wolfinger<sup>30</sup> also described the "conversion prosthesis," one that at second-stage surgery was converted from a complete denture to a fixed interim prosthesis. The technique involved incorporation of modified screw-retained impression copings (as opposed to more costly gold cylinders) within a wire-reinforced complete denture. Advantages suggested by the authors were as follow:

- 1) A fixed prosthesis with improved function, stability, and distribution of load was provided immediately following second-stage surgery;
- 2) The prosthesis protected the mucosa;
- 3) It served as a prototype for definitive prosthesis;
- 4) It could be used as a verification jig;

- 5) The original vertical dimension of occlusion was preserved;
- 6) The provisional restoration aided in obtaining and transferring interocclusal records;
- 7) It assisted long-term patient maintenance and reduced the number of treatment visits.

Cibirka and Linebaugh<sup>36</sup> described modification of an existing conventional complete denture to a fixed/ detachable interim prosthesis 10 to 14 days after second stage surgery. The authors modified an existing mandibular complete denture by attaching Branemark "temporary" cylinders (Nobel Biocare) with an autopolymerizing acrylic resin using a closed-mouth technique. Once polymerization was complete and the fit verified, the denture base flanges were modified with the provisional prosthesis removed to resemble the definitive prosthesis. After polishing, the prosthesis was attached to transmucosal abutments and the screw access holes were sealed with Cavit (ESPE). The authors suggested advantages of this interim treatment technique stating that the procedure was accomplished in 1 appointment, it was convenient for a patient and the prosthesis served as a template for a definitive Prosthesis. Berglin also presented conversion of a patient's existing complete denture by fitting gold cylinders to a prosthesis (DCA-072 or 073; Nobelphanna USA, Inc) with acrylic resin (Coe-reet; Coe

Laboratories).

Aparicio<sup>32</sup> outlined the importance of passively fitting provisional implant retained prostheses in a technical report. He emphasized that interim treatment offers the possibility of evaluating or creating the following:

- (1) A proper emergence profile;
- (2) Peri-implant health;
- (3) Occlusion; and
- (4) Esthetics, phonetics and hygiene.

This also facilitates progressive loading of implants during the bone maturation period. Modified gold cylinders for Estheti Cone abutments (Nobel Biocare) were used so that a provisional prosthesis could be luted to the cylinders in the mouth with a provisional luting cement (Kulzer Microfilm Pontic Cement; Heraeus Kulzer , Wehrheim, Germany). This provided a circumferential fit between the prosthesis and gold cylinders and easy retrievability.

➤ **Tooth-retained provisional treatment at or before first-stage surgery:**

When teeth adjacent to an implant are not to be restored with a fixed prosthesis, a resin-bonded fixed partial denture (RBFDP) may provide an

interim treatment option, avoiding or eliminating a removable prosthesis. Breeding and Dixon<sup>32</sup> described the fabrication and use of a resin-bonded prosthesis with orthodontic retainers (Bond-A-Splint; TP Orthodontics, Inc, La Port, Ind) and a light-polymerizing restorative material (Triad VLC Provisional Material; Dentsply). After surgery, the interim prosthesis is bonded to adjacent natural teeth.

Hannon et al<sup>18</sup> described bonding an extracted or denture tooth to adjacent natural teeth as a means of providing provisional treatment for an edentulous space. This technique offers fixed, reversible provisional treatment ultimately leading to an implant-supported restoration.

Zinner et al<sup>68</sup> presented 2 RBFPD techniques as a means of eliminating a removable provisional prosthesis in a partially edentulous patient. Both used cast -metal frameworks with denture teeth processed to the framework before cementation, but only one method involved longer span requiring preparation of abutment teeth.

A provisional fixed prosthesis can be placed before or at the time of implant placement surgery when the adjacent teeth either need full coverage restorations or might be extracted after integration of the implants. The advantages of this treatment compared to a provisional removable prosthesis have been described.

A multifunctional provisional implant-retained FPD described by Tung et al<sup>38</sup> was a modification of a previously reported metal-reinforced FPD.<sup>1</sup> The authors incorporated matrix-patrix plastic patterns as an integral part of the metal framework (Rexillum III; Jeneric/ Pentron Inc, Wallingford, Conn). The matrix was fabricated as part of a cast metal framework and cast matrix was later incorporated into the removable pontic section. The pontic section was initially used as a radiographic and surgical guide and was subsequently modified and provisionally cemented (Temp-Bond; Kerr Corp) until second-stage surgery, when the pontic section was again modified and cemented as an implant supported prosthesis. A disadvantage noted by the authors was cost; however, they stated that the long-term cost-effectiveness and benefit of the prosthesis outweighed the disadvantage of increased cost.

Zinner et al<sup>11</sup> advocated use of a cantilever provisional restoration when no maxillary molars and posterior implants are planned. If the premolar(s) are to be restored with complete crowns, 1- or 2-unit, metal-reinforced, acrylic resin cantilever provisional pontics may meet the esthetic requirements of a patient; the pontics are left out of occlusion to reduce torquing forces applied to the provisional prosthesis and abutment teeth. After implant integration, a screw retained acrylic resin provisional can be

fabricated with titanium provisional abutments (Implant Innovations, Inc, West Palm Beach, Fla). The authors supported the advantages of second-stage provisional treatment by citing anecdotal references involving incremental and progressive loading and clinical criteria related to the control of occlusal and restorative contours.

➤ **Implant-retained provisional treatment at second-stage surgery:**

Several advantages have been purportedly related to fixed provisional restorations after second-stage surgery:

- (1) Improved tissue contours related to emergence profile;
- (2) Development of inter-dental or inter-implant papillae;
- (3) Potential avoidance of a third surgical operation;
- (4) Fixation of the prosthesis; and
- (5) Customization during the healing process to form an esthetically contoured prosthesis.

Dumbrigue et al<sup>19</sup> described options for fabrication of provisional restorations for an ITI solid abutment (Straumann, USA, Cambridge, Mass). The uses of an ITI plastic (burn-out) coping, fabrication of an acrylic resin coping on a brass ITI practice solid abutment, with the ITI impression cap for solid abutment as a core and fabrication of a provisional restoration with

the ITI cementable Protective Cap were presented.

Techniques for incremental loading can be employed either directly or indirectly after second-stage surgery. Others have described similar techniques involving tissue contour development and esthetic concerns<sup>6, 19</sup>

The use of interim restorations to influence or maintain soft tissue contours before fabrication of a definitive prosthesis has been suggested as a key function of an interim implant restoration.<sup>28, 73</sup>

Jemt<sup>11</sup> reported that although provisional crowns may accelerate soft tissue contour development compared with healing abutments, the papillae adjacent to single implant definitive restorations developed similar tissue volume in both modalities after 2 years in function. The author recommended the need for more scientific data to evaluate different clinical procedures for optimizing esthetic results in implant dentistry.

Stein and Nevins<sup>10</sup> outlined the relationship of the guided gingival contour to a provisional crown for a single implant restoration. Submergence profile (the vertical discrepancy between an implant platform and an adjacent tooth's cemento-enamel junction), the potential guided gingival growth, and the relationship of titanium provisional abutment gingival surfaces to the healing tissue were explained. The authors propose that the greater this discrepancy, the more unpredictable the guided gingival growth. Other

aspects of guided gingival growth include

- (1) Keratinized gingival tissues;
- (2) Titanium provisional abutments;
- (3) A non-traumatic provisional treatment; and
- (4) A goal of achieving a realistic 1 mm to 4 mm increase in gingival growth.

Although these techniques and guidelines may lead to successful treatment, no scientific data were presented. Biggs and Litvak<sup>12</sup> advocated making impressions at first-stage surgery to fabricate casts incorporating implant analogs for single-tooth replacement. They used interim cylinders (Implant Innovations Inc.) to fabricate autopolymerized, screw-retained, acrylic resin provisional restorations that were placed at second-stage surgery. The authors recommended screw-retained provisional restorations suggesting that elimination of cement aided tissue healing, that the highly polished surface of the abutment would not be damaged by cement removal and the ability to remove a provisional restoration helped facilitate adjustments to perfect contours of both the provisional restoration and soft tissues.

In a clinical report describing the adverse axial inclination of a single tooth implant, author used a single interim abutment (Nobel Biocare) to

provide a matrix for a provisional restoration. The abutment was evaluated so that the portion that protruded beyond the proposed provisional crown contour was marked. The abutment was removed from the implant, adjusted extraorally to create the proper profile, reinserted, and an acrylic resin provisional restoration (Myerson acrylic resin; Nobelpharma USA Inc) was fabricated directly by use of a vacuum formed matrix. The desired emergence profile was created extraorally and the provisional restoration was luted with provisional cement (Temp- Bond; Kerr Mfg. Co). The provisional restoration could also be screw retained.

➤ **The immediate fixed transitional restoration:**

Another means of eliminating a potentially unstable removable provisional prosthesis that might interfere with soft tissue healing was proposed that used immediate transitional implants supporting a fixed provisional prosthesis at just after first stage surgery.

➤ **Dental implant provisional treatment: Materials and Methods**

Several methods of implant provisional restoration fabrication have been described in the literature.<sup>19,21</sup> Chaimattayompol<sup>23</sup> described the use of square impression copings for wide diameter implants at the implant level

when fabricating a provisional implant supported prosthesis, advocating improved precision of fit, healthier peri-implant tissue because of high polished metal surface and cost effectiveness of the procedure.

Fabrication of an autopolymerizing acrylic resin cylinder was also described and advantages such as simplicity, lack of special equipment required, improved resin bonding, ease of modification and potential color improvement were noted.

Balshi and Volfinger<sup>14</sup> presented a technique for fabricating autopolymerizing acrylic resin copings for CeraOne abutments. Jet Acrylic was allowed to flow onto the lubricated abutment and was manually adapted as it polymerized. After polymerization of the resin, the coping was removed, trimmed and polished. The acrylic resin coping could then be placed on the abutment at time of connection and a polycarbonate resin provisional tooth form (Ion; 3M Dental Products) was relined onto the coping. The authors pointed out that this procedure provided a chemical bond of resin to resin which they explained was lacking when a manufactured healing coping or the provisional coping components were used. Other benefits included increased patient satisfaction and reduced chair time for repairs.

Another use for the fixed interim partial denture in preliminary phase of implant treatment was presented by Stellino et al.<sup>15</sup> A dual purpose

implant guide was described where the author fabricated abutment- retained FPD incorporating gutta-percha in locations where implant placement is desired. The cemented provisional restoration, therefore, served as a radiographic guide and was also use later as a surgical guide. After implant placement, the gutta-percha was replaced with autopolymerizing acrylic resin.

➤ **Material strength and provisional prosthesis durability in relation to dental implants:**

The necessity for long-term provisional treatment of an implant-restored patient follows provisional techniques used in traditional fixed restorative treatment. Longer spans, longer treatment times and the necessity for addressing tissue contour issues before definitive treatment dictate techniques that would provide more durability. Management involving indirect fabrication of acrylic resin provisional restorations for increased polymerization and reinforcement with assorted types of methods and materials has been described.

Fabrication of a heat-polymerized provisional implant-supported fixed partial denture was advocated by allal and Morgano<sup>16</sup>. The authors sighted increased resin strength and durability as advantages when longer healing times are necessary for the patient treated

with implants.

➤ **Procedures:**

✓ **Technique for Prefabricated Provisional Restorations:**

The requirements for a good provisional restoration are most easily and completely met by a custom indirect restoration. But clinical situations will arise in which it may not be possible or desirable to make a custom acrylic resin provisional crown. Prefabricated polycarbonate crowns are easily adapted to produce esthetic provisional crowns in expeditious manner on prepared single anterior teeth in most patients.<sup>17</sup> The patient may present with an emergency situation in which a posterior tooth has fractured and there is no time available for a definitive tooth preparation and a custom provisional crown. In those cases, a preformed anatomic metal crown form can be employed to protect the tooth and the patient made comfortable until sufficient time can be arranged for completing the treatment.

○ **Anterior Polycarbonate Crown:**

A suitable provisional restoration can be made for single anterior teeth by use of polycarbonate crowns. However, they frequently will require extensive alterations, correct morphologic discrepancies and improper contours. If they are not carefully contoured, they will have horizontal overhangs that will be damaging to the gingiva; to accomplish recontouring

that is required and to provide the necessary retention. The tooth-colored crown must be relined with a resin. This can be accomplished with greatest accuracy by doing the reline on a quick-set plaster cast of the prepared tooth.

○ **Armamentarium:**

1. Anterior sectional impression tray (one only)
2. Alginate
3. Rubber bowl
4. Spatula
5. Quick-set plaster
6. Polycarbonate crown kit
7. Pencil
8. Straight hand piece
9. Acrylic bur
10. Coarse garnet disc on Moore mandrel
11. Burlew disc on mandrel
12. Large camel-hair brush
13. Cement spatula
14. Dappen dish
15. IPPA plastic instrument
16. Separating medium

17. Monomer and polymer
18. Medicine dropper
19. Muslin rag wheel
20. White polishing compound
21. Miller forceps
22. Articulating paper
23. Zinc oxide – eugenol cement
24. Explorer
25. Mouth mirror
26. Dental floss

When the tooth preparation has been completed, make an alginate impression of the prepared tooth, using an anterior sextant tray. Apply alginate around the prepared tooth with the tip of the index finger. After the impression has been removed from the mouth, pour it up with a thin mix of fast-setting plaster. Separate the cast from the impression as soon as a fingernail cannot score the cast.

Use the mold guide provided with the kit being utilized to determine proper mesiodistal size for crown form. Remove the corresponding size of crown from its compartment in the kit and place it on the prepared tooth on

the cast or in the mouth. With a pencil, make a mark on the gingival portion of the labial surface. The distance from the pencil mark to the margin should equal the length discrepancy between the incisal edge of the crown form and the incisal edges of the adjacent teeth.

The excess gingival length is trimmed away with a large carborundum stone or an acrylic bur, using the pencil line as a reference mark. Try the shortened crown back onto the prepared tooth. If it is too tight interproximally adjust it.

Paint the cast of the prepared tooth and the surrounding area with liberal amounts of a "tin foil substitute" separating medium (Alcote). Accelerate the drying with an air syringe and make sure that the cast is dry before starting to mix the resin.

Place four drops of monomer into a dappen dish and add tooth-colored polymer. While polycarbonate crowns are available in only one shade, it is possible to modify that shade somewhat by shade of acrylic resin used to reline it. Fill the crown form with resin applied with an IPPA plastic instrument. When the acrylic resin just begins to lose its gloss, seat the crown forth on the plaster cast, slowly expressing all the excess resin around the margins. Make sure that it is seated completely, and place it in a bowl of hot tap water to accelerate polymerization.

When the resin has polymerized completely, remove the provisional crown from cast, breaking the cast if necessary. A coarse garnet disc on the straight handpiece is used to trim away the excess at the margins. In many cases this will mean that part of the original polycarbonate crown will be cut into and recontoured. Do not leave any sharp ledges or abrupt contour changes near the margin. If necessary, recontour the gingival half of the axial contours. Only in this way will it be possible to obtain a satisfactory provisional restoration by this technique.

If the tooth is non-vital or if a resin other than poly (methyl methacrylate) is used, the crown can be relined on the prepared tooth in the mouth. The preparation is coated with petrolatum and crown must be removed before the resin has polymerized to a stiffness that locks it into interproximal undercuts. Cut off as much of the rubbery excess as possible with a pair of curved scissors. Keep reseating and removing the crown until the relining resin has completely polymerized.

Place the crown on prepared tooth in mouth and check the occlusion with articulating paper. Adjust any high spots with a non-dentate bur after removing the crown from the tooth. Smooth out the rough abraded areas in the lingual and incisal areas, as well as those surfaces recontoured near the margin, with a Burlew wheel in the straight handpiece.

Polish all surfaces of the provisional restoration with polishing compound (Yellow Diamond Polish Compound, Matchless Metal Polish Co) on a muslin wheel. It is possible to return the crown to its original luster by this means. Coat the outer surface of the crown with petrolatum to prevent the cement from sticking to it. Cement the restoration with zinc oxide-eugenol cement. Make certain that all cement has been removed from the gingival crevice by using an explorer. Use dental floss interproximally to remove any cement left there.

✓ **Technique for custom provisional restoration:**

○ **Over impression fabricated provisional crown:**

The use of alginate over impression remains a popular technique, because it is always readily available in the dental operator. It is easily adapted to intraoral use in the event that the proposed restoration of a tooth with amalgam is unexpectedly re-planned as a cast restoration.

○ **Over impression Armamentarium:**

1. Diagnostic cast
2. Utility wax
3. No.7 wax spatula

4. Quadrant impression trays (two, same side)
5. Alginate
6. Rubber bowl
7. Spatula
8. Quick-set plaster
9. Laboratory knife with no. 25 blade
10. Heavy-duty laboratory knife
11. Large camel-hair brush
12. Cement spatula
13. Dappen dish
14. Separating medium
15. Monomer and polymer
16. Medicine dropper
17. Heavy rubber band
18. Straight handpiece
19. Acrylic burs
20. Abrasive discs and Moore mandrel

The over impression, frequently is made in the patient's mouth while waiting for the anesthetic to take effect. However, if the tooth to be restored has any obvious defects, the over impression should be made from the

diagnostic cast, after immersed in a plaster bowl of water for 5 minutes. Wetting the cast in this manner will keep the alginate from adhering to it.

When the alginate has set, the over impression is removed from the diagnostic cast and checked for completeness. A laboratory knife with a no. 25 blade is used to trim off all excess alginate. Thin flashes of impression material that replicate the gingival crevice are removed to insure that there will be no impediments to the complete seating of cast into the over impression later. The impression is wrapped in a wet paper towel and placed in a ziplock plastic bag for later use.

When the tooth preparation is completed, another quadrant impression is made in alginate. This impression is poured up with a thin mix of quick-setting plaster. Excess material should be trimmed off on a model trimmer when the plaster has set. The trimmed cast should have at least one tooth on either side of the prepared tooth, if possible. Areas of the cast that duplicate the soft tissues should be reduced as much as possible.

Check the occlusal surfaces and gingival crevices for any plaster nodules that will prevent complete seating. Then try the trimmed quick-set plaster cast in the over impression to make sure that it will seat completely. Coat the prepared tooth and adjacent areas of the cast liberally with a "tin

foil substitute" separating medium (Alcote). Allow the material to dry before mixing the acrylic resin. Drying can be accelerated by use of an air syringe.

Mix tooth-colored acrylic resin in a dappen dish with a cement spatula. Use 12 drops of monomer for each tooth being restored. Place resin in the over impression so that it completely fills the crown area of the tooth for which the provisional restoration is being made.

Seat the cast into over impression, making sure that teeth on the cast are accurately aligned with the tooth impression. The force used to seat the cast into alginate impression is critical.<sup>12</sup> Excessive force can overseat the cast and uneven force can torque the cast, either of which will affect the restoration.

Once the cast has been firmly seated and the excess resin has been expressed, hold the cast in place with a large rubber band. It is important that the cast be oriented securely in an upright position so that the space between the cast and the impression that is filled with the resin forming the provisional restoration will not be distorted. If the cast is torqued to one side by the rubber band, the cast may be forced through the soft resin in some areas, resulting in a provisional restoration that may be thin in those areas and thicker than desirable in others. If the cast is seated with too much force, or if rubber band is wrapped around the assembly too many times, the cast

may be forced through the resin occlusally, resulting in a provisional restoration with an occlusal surface that is too thin.

Place the over impression plaster cast assembly in a plaster bowl full of hot tap water for approximately 5 minutes or into a pressure pot if one is available. Allowing a poly (methyl methacrylate) provisional restoration to polymerize in a pressure pot less than 20 psi will decrease porosity and increase the transverse strength of restoration by 28%.<sup>18</sup>

When the resin has polymerized, remove the rubber band to disassemble quick-set plaster cast from the over impression. If the restoration is not easily removed from the cast, break the tooth off the plaster cast with a heavy-bladed laboratory knife. Use the sharp end of a thin-bladed knife or some other small, pointed instrument to remove any plaster that remains in the provisional restoration. Ease of removal is one of the advantages of using weak, quick-set plaster.

Acrylic burs or coarse Moore discs are used to trim excess resin from the provisional restoration. Before attempting to seat the restoration on tooth, be sure to remove all resin extending beyond the preparation finish line into undercut areas. Smooth the axial surfaces near the margins of restoration with a fine sandpaper disc.

○ **Cementation Armamentarium :**

1. Articulating paper
2. Miller forceps
3. Straight handpiece
4. High-speed handpiece
5. No. 171 L FG bur
6. Muslin rag wheel
7. Pumice
8. Cement spatula
9. Paper pad
10. Zinc oxide-eugenol cement
11. Petrolatum
12. Explorer
13. Mouth mirror
14. Dental floss

Seat the provisional restoration on the tooth in mouth. Check the occlusion with thin articulating paper. Remove restoration from the tooth and adjust the occlusal prematurities with a non-dentate bur. When the occlusion has been adjusted to make the patient comfortable, polish the restoration first with pumice and then polishing compound on muslin rag wheel. Besides

making the provisional restoration easier to clean and more comfortable for patient, polished materials are much less likely to discolor.<sup>79</sup>

To fit a provisional crown with an existing removable partial denture, under contour the crown so it does not touch any rests or clasps on that tooth. Add resin to outside of the crown and while the resin is still soft, seat the crown on tooth. To form the rest seat and guide planes on the crown, lubricate the partial denture with petrolatum and seat it over the provisional crown. Pump the partial denture up and down several times to insure that it is not locked into any undercuts. Remove the crown from the tooth, smooth any rough areas and polish the crown.

The restoration should be cemented with a temporary cement of moderate strength. After zinc oxide-eugenol cement has been mixed to a thick, creamy consistency, an amount of petrolatum equal to 5% to 10% of the cement volume is incorporated to slightly reduce the strength of cement. This will facilitate removal of the provisional restoration at a subsequent appointment. If the preparation is short or otherwise lacking in retention, the petrolatum should not be added.

It is not necessary to keep zinc oxide-eugenol cement dry while it is setting. In fact, moisture will accelerate the hardening. Coating the outside of the restoration with a thin film of petrolatum prior to cementation will aid in

the removal of excess cement. After the cement has hardened, all excess must be removed from the gingival crevice. Use an explorer in accessible areas and dental floss inter-proximally.

✓ ***Template-Fabricated Provisional Fixed Partial Denture:***

When a fixed partial denture is to be made for a patient, the provisional restoration should also be in the form of a fixed partial denture rather than individual crowns. In the anterior region it will provide a better cosmetic result. However, even in the posterior region a provisional fixed partial denture will better stabilize the teeth and will afford the patient the opportunity to become accustomed to having a tooth in the edentulous space again.

○ **Template Armamentarium:**

1. Diagnostic cast
2. Mor-"Tight strand
3. N0.7 wax spatula
4. Denture tooth
5. Crown form
6. Vacuum forming machine
7. Coping material or temporary splint material

8. Quadrant impression trays
9. Silicone Putty
10. Wire frame
11. Bunsen burner
12. Scissors
13. Laboratory knife with no. 25 blade
14. Heavy-duty laboratory knife
15. Large camel-hair brush
16. Cement spatula
17. Dappen dish
18. Separating medium
19. Monomer and polymer
20. Medicine dropper
21. Heavy rubber band
22. Straight handpiece
23. Acrylic burs
24. Abrasive discs and Moore mandrel.

To make a template, place the metal crown form or denture tooth in edentulous space on the diagnostic cast. All of the embrasures should be filled with putty to eliminate undercuts during adaptation of the resin

template.

To facilitate removal of the template, a thin strand of putty can be placed around the periphery and on the lingual surface of the cast, apical to the teeth. Use a large acrylic bur to cut through the middle of the cast (mid palatal or mid lingual). Place a 5 x 5 inch sheet of 0.020 inch thick resin in the frame of vacuum forming machine with the shiny surface down. If temporary splint material is used, both sides will be shiny. Turn on the heating element of the machine and swing it into position over the plastic sheet.

As the resin sheet is heated to the proper temperature, it will droop or sag about 1.0 inch in the frame. If you are using coping material, it will lose its cloudy appearance and become completely clear. The cast should be in position in the center of the perforated stage of vacuum forming machine. Turn on the vacuum.

Grasping the handles on the frame that holds the heated coping material, forcefully lower the frame over perforated stage. Turn off the heating element and swing it off to the side. After approximately 30 seconds, turn off the vacuum and release resin sheet from the holding frame. After removing the resin sheet from the frame, use a laboratory knife with a sharp blade (no. 25) to cut through resin over the Mor-'Tight strand.

If a vacuum forming machine is not available, it is still possible to fabricate a template for a provisional restoration. Fill a quadrant impression tray with soft silicone putty available in most variety or toy stores. Cut a sheet of coping material in half and insert it, shiny side down into a wire frame bent from a coat hanger. Heat the resin sheet over a bunsen burner flame until it sags and becomes clear, which usually occurs in about 10 seconds.

Place the softened sheet over the cast. Forcefully seat the tray of silicone putty over the coping material. To accelerate cooling, blow compressed air on the plastic sheet and the impression tray. After about a minute, snap the tray off the cast. If the silicone putty sticks to resin sheet, the putty can be easily removed by pulling it off in quick jerks. Rapid separation causes the silicone putty to exhibit brittleness that will result in easy removal. Replace the putty in its original container for later reuse. Separate the template from the diagnostic cast.

Trim the template (however it was fabricated) with a pair of scissor. It should extend at least one tooth on either side of the prepared teeth. Save those portions not needed for possible later use.

Upon completion of the preparations, make an alginate impression of them and pour it in fast-setting plaster. The plaster cast will include replicas

of soft tissue and teeth that are not needed. Trim the cast so that it includes only one tooth on either side of the prepared teeth. Try on the template to verify its fit.

Coat the cast with Alcoté separating medium and allow it to dry. Mix the acrylic resin in a dappen dish and place some on protected areas of the cast, such as interproximal spaces and in grooves and boxes. As the resin begins to lose its surface gloss and becomes slightly dull, fill the area for which the provisional fixed partial denture is being made. Place some extra bulk in the portion that will serve as the pontic.

Wrap rubber bands around the template and cast, being careful not to place them over the abutment preparations, lest they cause the template to collapse in that area. Place the cast in a pressure pot if one is available. Otherwise, place it in warm (not hot) tap water to hasten polymerization. Hot water causes the monomer to boil, increasing porosity. Wait for about 5 minutes. Pry off the template and save it in case it is needed again. Before removing the provisional restoration from the cast, add resin to any voids or thin spots and place the cast back in warm water. Do not replace the template for this correction. Placing the unpolymerized resin back into water will prevent evaporation of monomer and formation of a granulated, "frosted" surface.

Remove the fixed partial denture from the cast. Do not hesitate to break the cast if necessary. Trim off the excess acrylic resin. Use discs to trim the axial surfaces down to the margins. The pontic should be trimmed with discs and burs to open up the proximal embrasures. Remove the saddle configuration that was created by the crown form in the edentulous space. The pontic should have same shape that the pontic on the permanent prosthesis will have. This will ensure that the patient will be comfortable and satisfied with the pontic from before the completed fixed partial denture is inserted.

✓ **Template-Fabricated VLC Provisional Restoration:**

A transparent template is essential to the use of a visible light-cured (VLC) resin because clear matrix allows the light access to the resin to initiate polymerization.

○ **Template- VLC armamentarium:**

1. Items in template armamentarium
2. Silicone impression putty
3. Triad resin
4. Model release agent (MRA)
5. Air barrier coating material (ABC)

6. Triad curing unit
7. Straight handpiece
8. Acrylic burs
9. Abrasive discs and Moore mandrel
10. Items in cementation armamentarium

Fabricate a template on the diagnostic cast. If the restoration is to be a fixed partial denture, set a metal crown form or denture tooth in Mor- Tight putty in the edentulous space. If a diagnostic wax-up has been made, soak the cast for 5 minutes and duplicate it with an alginate impression. Pour the impression in quick-set plaster.

Produce a template from a resin sheet on the vacuum forming machine. Trim the template and replace it on the cast. Mix a scoop of silicone impression putty with accelerator and mold it around the template on the cast. This is needed to reinforce the unsupported template and prevent displacement by the highly viscous resin later. Quickset plaster also can be used to make this reinforcing index. Set the template and the index aside until the teeth have been prepared.

Make an alginate impression of the prepared abutment teeth and pour a cast of quick-set plaster. Coat the cast with a layer of model release agent,

which is part of the resin system. Then place some of the Triad resin around the finish lines of the abutment preparation. Lay a strand of resin inside the clear template. "Enamel" resin can be placed in the incisal or occlusal portion of the template first to enhance esthetics.

Use fine pressure to seat the loaded template on the quick-set plaster cast of the prepared abutments. Compress the silicone putty index over the template to ensure complete seating of template and an even thickness of resin in the provisional restoration. In an alternative technique, the template can be seated into the silicone putty index before the resin is loaded into the template. Remove the putty index from the cast, leaving the resin and template in position on the cast.

Place the cast in the Triad curing unit to polymerize the resin in the template for 4 minutes. Carefully remove the template and then provisional restoration from the cast. Paint all surfaces of the restoration with air barrier coating material. Place the provisional restoration back in the curing unit, tissue side up, for an additional 6 minutes. Retrieve the restoration from the curing unit and remove all of the coating material with a brush and water.

Trim as much excess material as possible with a pair of curved scissors. Finish trimming the axial surfaces to the margins with discs. Open the embrasures around the pontic with discs and burs. Be sure to remove the

saddle form produced by the template. Polish the restoration with pumice and a high-shine polishing material.

Another technique has been described in which the restoration is started in a template on the prepared teeth in the mouth. Polymerization of the restoration is initiated by a 10-second application of a hand-held curing light. After the restoration is "frozen" in this manner, it is removed from the mouth and further exposed to the high intensity curing light in the laboratory.

✓ ***Shell-Fabricated Provisional Restoration:***

A thin shell crown or fixed partial denture can be made from any of the acrylic resins and then that shell can be relined indirectly on a quick-set plaster cast. It also can be relined directly in the mouth. If the reline is done directly, a methacrylate other than poly (methyl) should be used. This technique can save chair time because the restoration is partially fabricated prior to the preparation appointment.

Care must be taken not to make the shell too thick. If too thick, the shell will not seat completely over the prepared teeth and it will need to be trimmed internally. This can be time-consuming and defeats any advantage gained by making it before the preparation appointment.

○ **Shell Fabrication Armamentarium:**

1. Items in over impression armamentarium
2. Items in cementation armamentarium
3. Liquid applicator
4. Powder blower

An over impression is made from a diagnostic wax-up before the preparation appointment. Check it for completeness. Trim off thin flashes of impression material created by the gingival crevice to produce an extra bulk of resin near the margins. Use a plastic squeeze bottle with a fine tip (Liquid Applicator, Prairie Village Prosthetics, Prairie Village, KS) to deposit one drop of monomer on the facial and one drop on the lingual surface of the imprint of each tooth to be restored.<sup>19</sup> Keep the monomer near the gingival portion of the impression to prevent excess from accumulating in the incisal or occlusal area. Extend the coverage by the resin to one tooth imprint on either side of the teeth being restored.

With an insufflator (Powder Blower, Prairie Village Prosthetics), gently spray enough polymer onto the surface of the impression to absorb the monomer.<sup>19</sup> Repeat the process four times, inverting the impression frequently to allow the material to run down to the margins rather than

puddling in the incisal or occlusal areas of the impression. Gently remove the shell from the impression after 4 minutes. Trim the flash from the gingival area and open gingival embrasures with an abrasive disc.

When the teeth have been prepared, make a quadrant alginate impression and pour it with a thin mix of quick setting plaster. Trim off excess plaster on a model trimmer. Save one tooth on either side of the prepared tooth, if possible. Remove areas of the cast that duplicate soft tissues. Examine the cast for nodules that would prevent complete seating.

Try the shell gently on the cast to make sure it seats completely without binding. If it does bind, relieve the inner surfaces of the shells until the restoration seats completely and passively. Liberally coat the tooth preparations on the cast with separating medium and make sure it is dry before mixing the acrylic resin.

Monomer and polymer can be added directly to the shell and mixed there. The resin also can be mixed in a dappen dish and then transferred to the shell, completely filling each tooth. Seat the shell onto the prepared teeth on the cast. Wrap a rubber band around the shell and cast and place them in a plaster bowl full of hot water for approximately 5 minutes, preferably in a pressure pot. The uses of a pressure pot will significantly increase the

strength of the restoration.

If the direct technique is employed, seat the shell on the prepared teeth in the mouth. When the resin becomes rubbery, elevate the restoration 2.0 mm and flush the teeth under it with water.<sup>84</sup> Pump the restoration up and down several times to eliminate undercuts. Then remove the restoration from the mouth and place it in warm water.

When the resin has polymerized, remove the rubber band and disassemble the shell from the plaster cast. If the restoration resists removal from the plaster cast, break the teeth off with a heavy-bladed laboratory knife. Use a small pointed instrument to remove any plaster left in the provisional restoration. Trim excess resin from the provisional restoration with acrylic burs or coarse Moore discs. Smooth the axial surfaces of the restoration with a fine sandpaper disc, followed by pumice and polishing compound on a muslin rag wheel.

#### ✓ **Over impression Fabricated Bis-acryl Composite Crown:**

Bis-acryl composite resin can be used to fabricate a provisional restoration on a quick-set plaster cast. Its polymerization produces very little heat and it has minimal toxic effect on soft tissues and pulp. It is probably as well suited as any resin for use in a direct technique, based on the study

materials by Wang et al.

Alginate makes a satisfactory over impression, but this discussion will focus on the use of an elastomeric impression material, polyvinyl siloxane, for the sake of presenting as many techniques as possible. A heavy bodied elastomeric material has the advantages of being very stable and difficult to distort. Its disadvantages include greater expense and extra time required for the impression material to polymerize.

Load a disposable aluminum sextant tray with impression material and make over impression while waiting for anesthesia. Trim the excess from the borders of the impression to facilitate accurate placement back in the mouth. Remove the webs of material between the imprints of individual teeth in the impression. These could interfere with complete reseating of the over-impression.

The margins of a provisional restoration may be thin or deficient because the over-impression was not seated straight, or because the thickness required for a resin restoration is greater than that needed for a metal restoration. To avoid this problem, use a no. 8 round bur to cut a trough in the gingival area of the facial and lingual surfaces of the tooth imprint(s) in which the restoration will be fabricated. This will produce a bead of material parallel with the margin of resulting restoration. This ensures adequate

material in the margin and excess can be trimmed off during finishing.

After the tooth preparation has been completed, begin the provisional restoration. Check that the plastic catch is engaged in the vertical groove on the threaded plunger in the ratchet at the back end of the large blue syringe containing the ProtempII base material. To extrude one full measure of base paste onto a mixing pad, give the thumbscrew at the end of the threaded plunger one complete turn clockwise until it clicks. Check the simple ratchet on the threaded center plunger of the smaller white, double-barreled catalyst paste syringe to see that it is in place. Express an equal amount of each of the "two catalyst pastes onto the same pad by twisting the single threaded shaft one full revolution or "click".

Mix the catalyst paste and the base material with a cement spatula for approximately 30 seconds. Use the spatula to load the back end of a frosted plastic syringe.

Place the resin in the over impression with the syringe as suggested by von Krammer<sup>10</sup>. Keep the syringe tip buried in resin and fill the cusp tip or incisal edge areas from the bottom up to prevent voids in the completed provisional restoration. The use of an application syringe will frequently require a second unit of resin, but it greatly reduces the possibility of

creating bothersome voids in the restoration.

Lubricate the prepared teeth with petrolatum and position the impression tray on them no later than 2 minutes from the start of mixing. Allow the resin to polymerize in the mouth for approximately 2 minutes. Check excess resin around the border of the tray for consistency. Do not rely on material left on the mixing pad as an indication of polymerization, because the reaction in the oral cavity at body temperature and 100% humidity will proceed more rapidly than on a mixing pad at room temperature. When the resin becomes elastic, it is ready for removal. That should occur no later than 6 minutes from the start of the mix.

Tease the restoration from the tooth or from the impression. Remove as much excess as possible with scissors. Replace the provisional restoration on the tooth and ask the patient to close down on it several times. Then pump it several times to ensure removability. Remove the restoration no later than 7 minutes from the start of mixing. Wipe off the air-inhibited, upset resin with an alcohol sponge. If there are voids or other defects, they can be repaired by mixing another batch of resin and applying it to the affected area with an instrument. Repairs also can be affected by using VLC composite resins and a light.

Remove excess near the margins (including the intentional bead, if used) with fine abrasive discs. Place the restoration back on tooth in the mouth. Test and adjust the occlusion if necessary. Polish the outer surfaces of the restoration with pumice and polishing compound. Seat the restoration with temporary cement.

✓ **Provisional Crown for an Endodontically Treated Tooth:**

It is often difficult to fabricate a provisional restoration for a tooth that has been prepared for a dowel core because there is so little intact supragingival tooth structure. This can be accommodated for in the use of a standard polycarbonate crown by placing a piece of paper clip or other stiff wire into the canal and placing the resin filled crown down over that.

✓ **Preformed Anatomic Metal Crown:**

Emergency cases involving fractured molars are one of the best indications for the use of preformed metal crowns. Zinc oxide eugenol alone will not adhere to the tooth and there is rarely enough time at the emergency appointment to fabricate a custom acrylic resin provisional crown. By using the preformed anatomic metal crown, it is possible to provide the patient with temporary coverage to protect the fractured tooth and prevent irritation of tongue and mucosa.

There are several systems available for this purpose, utilizing the same general principles. The procedure consists of:

1. Minimal tooth preparation
2. Measurement and selection of crown
3. Trimming and adaptation of gingival margin
4. Occlusal adjustment
5. Cementation

○ **Armamentarium:**

1. High speed handpiece
2. No. 170L or 171L bur
3. Measuring gauge
4. Crown forms
5. Stretching block
6. Crown and bridge scissors
7. Contouring pliers
8. Straight handpiece
9. Sandpaper disc on Moore mandrel
10. Articulating paper
11. Miller forceps

12. Cement spatula
13. Paper pad
14. Zinc oxide eugenol cement
15. Petrolatum
16. LL6-7 curved burnisher
17. Explorer
18. Mouth mirror
19. Dental floss

The maxillary molar with a lingual cusp fractured off is not an uncommon dental emergency. It is most easily protected on a short-term basis with a preformed metal crown (Iso-Form Temporary Crown, 3M Dental Products, St Paul, MN).

The tooth must be prepared minimally to create space for the restoration. The initial step is occlusal reduction, which follows the inclined planes of the occlusal surface. The depth will be 1.0 mm on the nonfunctional cusps and 1.5 mm on the functional cusps. A functional cusp bevel (on the lingual incline of the maxillary lingual cusp) is placed to a depth of 1.5 mm to complete the occlusal reduction.

Only enough proximal reduction is done to permit the seating of the crown. If an MOD amalgam restoration is present in the tooth, the proximal

reduction is most easily accomplished by removing the amalgam in the boxes. The boxes are cut with a no. 170L or 171L bur. All caries is removed at this time. No effort is made to remove all of the existing restoration, or to provide permanent bases or a completed preparation.

Each of the three measuring heads in the metal crown form kit has converging blades that measure a 1.0-mm range: 9 to 10 mm, 10 to 11 mm, and 11 to 12 mm. Hold the gauge in line with the contact points, resting it on the occlusal surfaces of the other teeth in the arch. Slide the blades until they wedge between the contacts of the teeth on either side of the preparation. The point at which blades wedge indicates the dimension to be used for selection of the proper crown form.

The crown is tried on the tooth. If the gingival collar is too tight, the crown is placed on the appropriate post of the stretching block. There is a tapered post corresponding to each of the maxillary and mandibular molars, left and right. Flaring the margins is also required when there is a shoulder finish line. The crown is pushed down on the post until an adequate amount of gingival flare is obtained.

The crown is placed on the tooth to evaluate its occlusogingival length. Compare the height of each marginal ridge of the crown with that of the adjacent tooth. Use crown and bridge scissors to remove an amount at the

gingival margin equal to the marginal ridge height discrepancy. Festoon the margin to follow the contours of the gingival tissue.

Smooth rough spots and any irregularities in the gingival margin with sandpaper disc. Use no. 114 contouring pliers to produce a slightly convex contour occlusal to the margins. The margin will be slightly constricted as a result.

Place the crown on the tooth and check the occlusion with articulating paper. Remove the crown and burnish areas on the occlusal surface that are in hyper-occlusion. Open proximal contacts can be corrected by burnishing the proximal area from the inside of the crown.

Coat the outside of the crown with petrolatum to facilitate the removal of excess cement later. Mix zinc oxide eugenol to a thick creamy consistency on a paper pad. Fill the crown with cement and seat it on the prepared tooth with finger pressure.

Burnish the margins of the crown with an LL 6-7 curved burnisher before the cement hardens. Run dental floss through the proximal contacts to remove hardened cement from the interproximal areas. Use an explorer to remove all remaining subgingival cement. Make a final check of the margins to ensure that they are not impinging on the gingiva.

### ✓ **Techniques for Provisional restorations for implants:**

Implant dentistry provide unique and predictable methods for the replacement of missing teeth. This is especially important in esthetic regions. A challenge exists for the restorative dentist when planning and providing treatment for the patient before surgical phases are complete. The provisional restoration can be the restorative dentist's most important diagnostic tool and is a key factor in communication, tissue management and patient management prior to finalizing restorative treatment. Although implant-supported provisional restorations are usually fabricated in the laboratory, there are some clinical situations that demand the direct fabrication of provisional restorations, especially when there is a high esthetic demand.

Provisional restorations are generally necessary to restore lost function and esthetics during the implant integration period. Different techniques are suggested by different authors for provisionally restoring implants. A few techniques are discussed below.

- **A technique for fabricating a fixed provisional prosthesis on osseointegrated fixtures:**

The Branemark technique (and others) of osseointegration involves a second surgical phase consisting of exposing the fixtures, removing the

healing caps and placement of the cylindrical abutments. This technique describes a method of altering the existing denture, allows for direct placement onto the fixture abutments. The modification provides a trial period of adjustment while the final prosthesis is being made and increases the patient's comfort, confidence and expectations.

◦ **Technique** <sup>36</sup>

1. Tighten the abutment on a fixture and remove existing plaque and calculus.
2. Relieve the existing denture generally to permit adequate clearance when repositioning over the abutments. The distal extension bases are not altered
3. Load the anterior region of the denture with a polyether or similar type of impression material.
4. Inject impression material around the abutments, seat the denture and instruct the patient to close lightly into occlusion.
5. After removing the completed impression from the mouth, place the access hole in the denture with a Pindex machine by aligning the beam of light with center of each abutment.
6. Remove the impression from access holes and enlarge the opening with

an acrylic trimming bur.

7. Tighten gold cylinders to at least three abutments with 10mm or 15 mm guide pins.

8. Place the denture over the guide pins and inject denture repair acrylic resin beneath the relieved denture around the guide pins and gold cylinders by using a standard impression syringe. Stabilize the distal extension base while acrylic resin is setting.

9. Upon set of the resin, remove guide pins from the denture. The cylinders are secured within the denture by the resin. Fill the voids and porosities using fine brush. Inspect carefully to ensure that acrylic resin is not present on the cylinder-abutment interface.

10. Mark the distal extension bases 11 to 12 mm from most distal abutment and section the prosthesis.

11. Place the modified prosthesis clinically and verify that it is supported by implant only.

12. Polish, disinfect, and insert the interim prosthesis using the gold mounting screws through the prepared access openings.

13. Fill the access filling with a temporary sealing material and adjust occlusion as necessary.

14. Give the patient complete oral hygiene instructions.

**A) The modification of interim cylinders for the fabrication of cement - retained implant-supported provisional restorations:**

This describes a technique for modification of metal interim cylinders and their use in the fabrication of cement retained implant-supported provisional restorations. This chairside technique allows for direct provisionalization of single or multiple implants during or after second-stage surgery, especially when there is a high esthetic demand.

✓ **TECHNIQUE** <sup>9</sup>

○ **Laboratory phase: Modification of interim metal cylinders:**

1. Place an interim metal cylinder onto an implant analog with a guide pin or laboratory waxing screw and pour dental stone up to the neck of the analog to fabricate a stable stone base.
2. Make 3 notches with a bur in a low-speed handpiece on the stone base as a repositioning index and place a layer of baseplate wax around the wall of metal cylinder.
3. Pour polyvinylsiloxane duplicating material into a container to make a mold for fabrication of modified interim abutments.
4. Attach a new metal cylinder onto the implant analog in the stone base, fill with light-polymerizing composite and polymerize incrementally into

the space of silicone mold.

5. Repeat this procedure to make a number of modified interim abutments for different diameters of implant platforms.

- **Clinical phase:** Chairside use of the modified interim abutment for fabrication of a provisional restoration.

1. Unscrew the healing abutment after second stage implant surgery. Place one of the modified interim abutments with an abutment screw into the implant and check the accuracy of fit with a radiograph.

2. Prepare the supragingival portion of the interim abutment intraorally with diamond burs at high speed with copious amounts of water. Remove the abutment from the mouth and adjust subgingival form and contour of the interim abutment to develop proper emergence profile. Screw the completed interim custom abutment back into the implant.

3. Select a denture tooth or a polycarbonate crown of appropriate size and trim it to the proper form and contour. Reline the provisional restoration with autopolymerizing acrylic resin on the interim customized abutment, polish and stain to match the adjacent teeth. Cement the completed provisional crown to the interim customized abutment with provisional cement.

4. Transfer the information gathered during this procedure, along with photographs and impressions, to the laboratory technician for predictable fabrication of an esthetic definitive restoration.

This technique makes use of readily available materials for the direct fabrication of implant provisional restorations without use of impression procedures or a dental laboratory for situations in which there is a high esthetic demand. This method may be useful for patients who present with restorations bonded to adjacent teeth at the implant sites or an interim acrylic removable prosthesis that must be replaced during or immediately after implant second-stage surgery.

This technique also allows for control of soft tissues and emergence profile in the esthetic zone at the provisional restoration stage. Simple modification of the interim custom abutment provides proper peri-implant tissue contours that mimic natural teeth. Several techniques for the reproduction of tissue contours on the definitive cast have been suggested in literature. Adding autopolymerizing acrylic resin or flowable composite to impression coping up to the height of peri-implant tissue level prevents collapse of the soft tissue around the implant during the impression procedure. This transfer procedure assists the laboratory technician in achieving esthetic custom abutments and definitive restorations.

**B) Use of polyethylene ribbon to create a provisional fixed partial denture after immediate implant placement:**

This technique describes an esthetic and economic bonded provisional fixed partial denture used in immediate implant situations. The extracted incisors of the patient can be used as pontics and fixed partial denture can be fabricated using a bondable reinforcement fiber.

○ **Technique**<sup>37</sup>

1. Extract the incisors; remove their roots using a high speed diamond bur under water cooling. Pulp is removed; coronal pulp chamber is irrigated and restored with composite.
2. Place hydroxyapatite coated, 15x 3.75-mm, threaded implants immediately to anterior region.
3. Trim the lingual surface of the crowns as a pontic, covered with composite and polished with polishing discs.
4. Prepare a groove on the lingual surface of teeth for Ribbon
5. Burnish a 2mm aluminum foil into lingual surface of abutment teeth to determine the length of Ribbon required. With the hand instrument, the foil was placed interproximally so that it is closely adapted to contours of the teeth. The measured length of Ribbon was cut and then kept on a clean

pad until ready for use.

6. Etch the lingual and interproximal enamel surfaces for 45 seconds. Cover the etched surfaces with a layer of unfilled bonding resin. Gently air thin and polymerize for 20 sec.

7. Apply a thin layer of flowable composite to etched lingual and interproximal surfaces of the teeth using a syringe, but don't polymerize the material.

8. Wet the ribbon with a light coating of unfilled bonding adhesive and remove the excess with a hand instrument.

9. Press the ribbon into unpolymerized flowable composite and place interproximally and keep between interproximal contacts of the abutment teeth. Polymerize for 20 sec.

10. Prepare lingual surface of the pontic for bonding by acid etching and apply a thin layer of flowable composite and cure for 20 sec.

11. Apply a thin layer of flowable composite into the grooves prepared on palatal surfaces, place the pontics on to second ribbon in the desired position and polymerize for 40 sec.

12. Remove the excess and polish the restoration.

## SUMMARY

Provisional fixed prosthodontic treatment involves a multifaceted array of clinical activities, special knowledge, material selection and management. Contemporary treatment incorporates both natural teeth and dental implants. Although provisional restorations are usually intended for short term use and then discarded, they can be made to provide pleasing esthetics, adequate support and good protection for teeth while maintaining periodontal health. They may be fabricated in the dental office from any of several commercially available materials and a number of practical methods. The success of fixed prosthodontics often depends on the care with which the provisional restoration is designed and fabricated.

Dentistry continues to struggle with the limitations of existing materials available for fixed prosthodontic provisional treatment. Clinical techniques and indications are reasonably well characterized, but future research activities will need to focus on technological advances to provide improved materials that demonstrate improved biocompatibility, ease of use and modification and physical properties.

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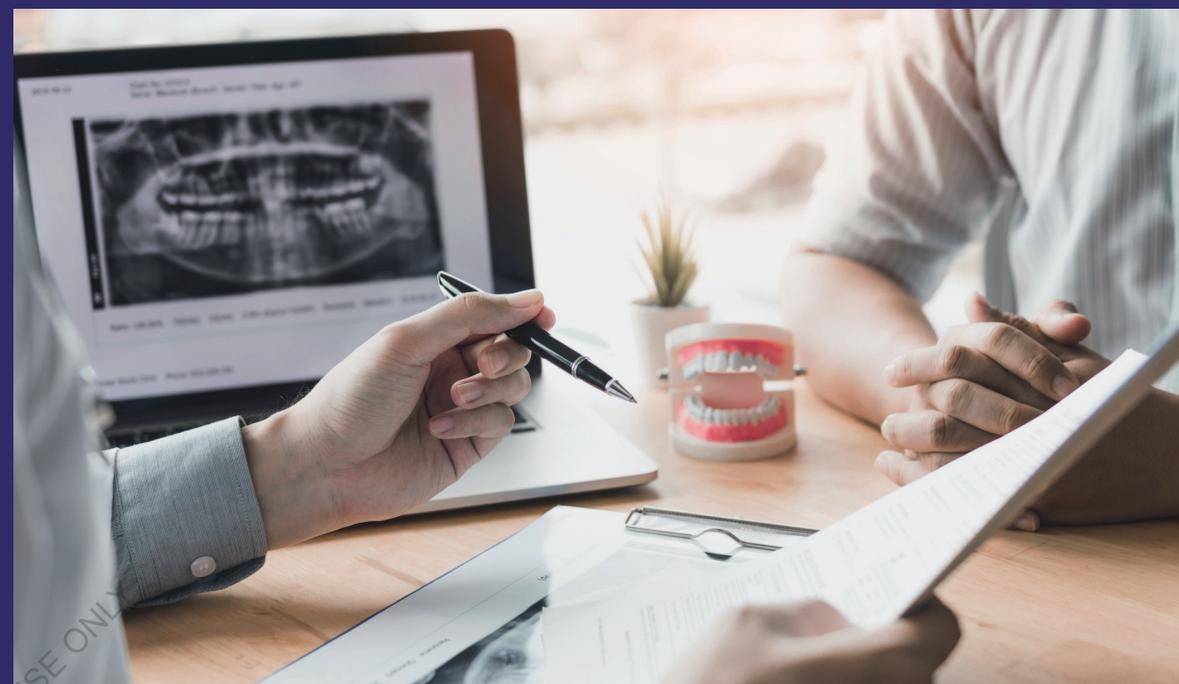
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This textbook documents about the advancements that has taken place in the prosthetic aspect of implant dentistry. Since traditional tooth replacements has taken a backstage because of an immense impact followed by an appreciable and commentable results in implantology, where the key lies in updation of technology in tandem with latest research prospects which brings about new clinical methodologies and materials for better patient satisfaction and long term predictable results.

The content deals with the advances in changes in concepts in biomaterials, loading protocols and restorative aspects followed by usefulness and implications of the most modern diagnostic aids.

It also deals with the precision and use of implant components and the changes to it in due course of time. With the advent of most modern ultra precise machinery and armamentarium the components has achieved predictable and long lasting efficacy and new design in form of various systems in the market.

Thus the textbook highlights the evolution of implant dentistry which deals with changes in techniques and approach to a brighter future.

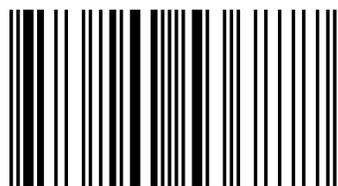


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# Advancements in Dental Implants

A glimpse into changing thought process and paraphernalia in implant dentistry

Dr. Adarsh Varma R is currently a post graduate student specializing in Prosthodontics, Crown, Bridge and Implantology in Viswanath Katti Institute of Dental Sciences, KLE University, Belagavi, Karnataka, India. He completed his undergraduate degree from Manipal College Of Dental Sciences, Mangalore, Manipal University, Manipal, India.



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# **ADVANCEMENTS IN DENTAL IMPLANTS**

## **GLOSSARY**

<b>1)<u>INTRODUCTION</u></b>	2
<b>2)<u>HISTORY</u></b>	3
<b>3)<u>DISCUSSION</u></b>	6
<b>I. <u>Advances As Related To Changes In Concept</u></b>	6
<b>A. Occlusal/Restorative Material</b>	
<b>B. Submerged and Non Submerged Implants</b>	
<b>C. Occlusal Load/Overload/Progressive Load</b>	
<b>D. Progressive Loading</b>	
<b>E. Immediate Loading</b>	
<b>F. Passivity of Prosthesis Fit</b>	
<b>G. Screw-Retained Versus Cemented Implant Restoration.</b>	
<b>H. Use of Implants as Overdenture Abutments</b>	
<b>I. Number of Implants Needed To Support A Restoration</b>	
<b>J. Connecting Implants to Natural Teeth</b>	
<b>II. <u>Advances As Related To Changes In Diagnostic Aids</u></b>	14
<b>A Ridge Mapping</b>	
<b>B. Resonance Frequency Analysis</b>	
<b>C. Computed Tomography</b>	
<b>D. Cone Beam Radiography</b>	
<b>E. Cone Beam versus Conventional CT</b>	
<b>F. Magnetic Resonance Imaging</b>	
<b>G. Tuned Aperture Computed Tomography</b>	

### III. Advances As Related To Implant Component 25

#### A. Implant Biomaterials

#### B. Implant design and surface coatings

##### Implant Body Geometry

##### Wide- And Narrow-Diameter Implants and Platforms

##### Small-Diameter implants

##### Transitional Implants

##### Implant Surface and Coatings

##### Thread Design

#### C. The Abutment Connection

#### D. A Critical look at the Implant/Abutment Interface

#### E Abutment Screw Design

#### F Various Osseointegrated Implant System.

### 4) SUMMARY 91

### 5) REFERENCES 93

## INTRODUCTION

Dental implants are the fastest-developing technology in dentistry today. Implants are used for anchoring replacement of artificial teeth with bone-anchored systems. Archeological findings showed that ancient civilizations in Egypt and South America had already experimented with re-implanting lost teeth with hand-shaped ivory or wood replacements. Developing artificial tooth replacements has been an elusive aim for over 1500 years. A small, dark stone, shaped like a tooth was found implanted in Mayan skull in Central America from 600AD and implant attempts were recorded in ancient Egypt and Middle East .

Dr. P-I Branemark's coincidental discovery of tenacious association between living bone and titanium oxides, called osseointegration, launched dentistry into a new age of reconstructive dentistry. Originally, the basic principles for obtaining osseointegration prescribed atraumatic insertion of a titanium screw into a viable bone and extended, undisturbed healing time. In the 35 years since osseointegration was first applied to human patients, many advances have been made during recognizing and applying implant dentistry as a means of replacing missing teeth.

Osseointegration as first identified by Branemark is a scientific achievement that delineates a sense of separation from the old in implant dentistry. Osseointegration has always changed the way dentists view their choices when dealing with a patient needing tooth replacement. The effectiveness and predictability of osseointegrated implants no longer pose problems<sup>2</sup>.

In the initial years, research focused on developing surgical techniques and grafting procedures. Finally, the focus turned to a number of technical and esthetic problems that remained problem-solved. The efficacy and predictability of osseointegrated implants are no longer issues. During the initial years, research focused on refinements in surgical techniques and grafting procedures. Eventually the emphasis shifted to a variety of mechanical and esthetic challenges that remained problematic and unresolved<sup>2</sup>.

With the increasing esthetic and mechanical challenges as mentioned before, the advancements in the implant dentistry is quite remarkable and noteworthy. It not only increased the prognosis of the treatment plan but as well increases the longevity of prosthesis and predictability of the treatment planning. The advancements are not just confined to a single factor, it has taken place in various aspects including even the concepts in treatment delivery<sup>2</sup>.

In due course of time the evolution has brought about changes to the implant components like the abutment connection, thread design, thread pitch, screw design, implant body geometry etc with the aid of superior machining, which to the liking of clinicians and patients offering them with wide array of treatment options<sup>2</sup>.

## **HISTORY**

The search for natural teeth has fascinated mankind since ancient times. Although many models were used with great success to replace human teeth by using crowns and bridges, the ability to substitute and support given by the natural tooth remained elusive until the recent past. Across history, several physicians have tried to treat dental edentulism, but sadly their work has resulted in failure. Nonetheless, without the early work to build on, we wouldn't appreciate the success we show today. Implant designs are traceable to early Egyptians and societies of South Central America and have developed into implant designs that are now experiencing explosive popularity. The earliest dental

implants were pre-Common Era stone and ivory cited in archeological records of China and Egypt. Dental implants were used in the 16th and 17th centuries. The early 20th century created metal implants of gold, lead, iridium, tantalum, stainless steel and cobalt alloy<sup>3</sup>.

### **ANCIENT IMPLANTS:**

Since ancient times, man has tried to solve problems associated with failed dentition. Ancient Egyptians, in 2500 B.C., sought to strengthen periodontally damaged teeth using gold ligature wire. Implanted animal teeth made with ivory are the earliest examples of ancient implantology. From about 500 B.C. the Etruscan people used golden bands incorporating animal teeth to restore chewing capacity. In the same period, the Phoenician people used gold wire to protect damaged teeth. They created a fixed bridge replacement in 300 A.D, using carved ivory teeth, supported by gold wire<sup>4</sup>.

The Harvard University Museum has a pre-Columbian-era skull in which an artificial tooth made from dark stone replaced a lower left lateral incisor. It is unlikely that any of these early attempts on raw materials and coarse methods enjoyed sufficient durability.

In 1700, John Hunter suggested the possibility of transplanting teeth from one person to another. To support this theory, he performed an experiment in which he inserted an incompletely formed tooth into a rooster comb, he observed the tooth being firmly rooted in the comb that the blood vessel of the rooster expanded directly into the tooth pulp<sup>4</sup>.

### **EARLY IMPLANTS**

In 1809, in a fresh extraction site just above the gingiva, Maggiolo inserted a single tooth-size gold implant without a crown. Healing removed the crown. Inserting these gold sources immediately followed by intense pain and gingival inflammation.

Edmunds placed a porcelain crown on a root-shaped platinum shell with lead; a porcelain crown followed on a platinum frame. In 1913, Greenfield used a two-piece hollow basket made of 24-gauge iridium soldered 24-karat gold. This was the predecessor to today's hollow basket design<sup>5</sup>.

In 1911, Greenfield identified endosseous implant manufacturing and insertion. A 24-karat-gold iridium post was placed into the prepared area.

Current implant dentistry was delineated from mid-1930's to present. During this time, one begins to see the emergence of implant technologies evolving into the most advanced and popularly

used systems. In 1939, Strock identified a method of inserting a vitalium screw to secure a missing tooth. Formiggium engineered a spiral implant in the mid-1940s, folding a stainless steel wire on itself<sup>5</sup>.

Gustav Dahl first proposed the implant sub-periosteal type in 1943. In 1948, Goldberg and Gershkoff developed a sub-periosteal implant structure extending to the outer oblique ridge. In the mid-1950s, Lee pioneered the use of an endosseous implant with a central part and circumferential extensions. In the 1960s, Chercheve engineered a Co-Cr double-helical spiral implant. He put the spirals deep into the prepared site with a long post that would act as the transmucosal abutment. Scialom identified a tripod endosseous pin arrangement. It was anchorage for a single crown as permanent fixed bridges. Linkow created vent implants in the same time<sup>5</sup>.

By the mid-1960s, Linkow developed the blade vent implant. Originally designed for use in the knife edge ridge, this blade form of endosseous implant. He later adapted this implant's model for most medical conditions<sup>5</sup>.

Roberts and Roberts developed endosseous implant Ramus knife. It was constructed using surgical grade 316 stainless steel, this blade type of implant was placed to attach distantly between the cortical plates in the mandible ramus bilaterally and in the mandibular symphysis region. This endosseous implant obtained stabilization from its anchorage. A one-stage procedure was followed to immediately reinforce the full mandibular denture against a complete maxillary denture<sup>5</sup>.

Early 1970s animal studies started using non-metallic forms of endosseous implants. Aluminum oxide implant was one of human-placed varieties.

Small's Mandibular Staple Implant is developed to rehabilitate the atrophic, edentulous mandible.

Grenoble first mounted vitreous carbon implants.

Weiss and Judy popularized Intra mucosal implants to maintain flexible maxillary prosthesis.

In the early 1980s, Tatum launched the Omni R implant. This is a root-form titanium alloy implant with horizontal pins. Niznick introduced the core ventimplant. This is a hollow basket implant with a threaded bone portion. Use the latest guideline in the posterior mandible<sup>5</sup>.

Screw-Vent implants an endosseous implant are later added by the same agency. It's mainly used in the previous jaw. The core vent company produces a microvent implant that incorporates the mixture of anterior and post-machine tapping / screw style hydroxyapatite coated implant<sup>5</sup>.

Such implants were made in both titanium alloy and hydroxyapatite coated versions. Driskells launched stryker root form endosseous implants. There are two unique features of the Kirsell IMZ implant. Firstly, a titanium plasma spray covered the surface and increases the surface area. Secondly, the intramobile portion was installed in an abutment to mimic natural teeth's flexibility<sup>5</sup>.

In 1985 the company launched an integrated implant system with the launch of a hydroxyapatite-coated cylindrical pin, titanium alloy implant, and the production and marketing of its synthesis-based polycrystalline ceramic hydroxylates, calcitite. Implamex developed cylindrical plasma spraying with titanium and cylindrical hydroxyapatitecoated implants. Screw Titanium Implants with external hexagonal heads were also added<sup>5</sup>.

Denar has launched root type sequence of endosseous implants. These have implants coated with hydroxyapatite and implants lined with titanium. The plasma screws and scooters were designed to be used in one-stop operations.

The ITI implant invented by Straumann in 1985 is special. Around 1983–87, the number of dentists implanting and the number of implants implanted was increased by 10%<sup>6</sup>.

## **DISCUSSION**

### **ADVANCES IN DENTAL IMPLANT IS DIVIDED INTO**

**Advances As Related To Changes In Concept**

**Advances As Related To Changes In Diagnostic Aids**

**Advances As Related To Implant Component**

#### **I. ADVANCES AS RELATED TO CHANGES IN CONCEPT**

**A. Occlusal/Restorative Material**

**B. Submerged and Non Submerged Implants**

**C. Occlusal Load/Overload/Progressive Load**

**D. Progressive Loading**

**E Immediate Loading**

**F Passivity of Prosthesis Fit**

**G Screw-Retained Versus Cemented Implant Restoration.**

**H Use of Implants as Overdenture Abutments**

**I Number of Implants Needed To Support A Restoration**

**J Connecting Implants to Natural Teeth**

#### **A. OCCLUSAL/RESTORATIVE MATERIAL**

One of the fundamental principles of restoring tooth implants was to secure the implant against the occlusal effect or the parafunction shock. Within key articles, Skalak outlined this concept in detail. It was widely assumed that the avoidance of ceramic or metal occlusal surfaces was important. An effective implant system is designed on the basis of the presumed need to protect the implant from occlusal damage and the ability to mimic the damping effect of the periodontal ligament in the natural teeth. The understanding of osseointegration and its dependence on this damping effect resulted in repeated restoration problems with implant-supported protheses<sup>7</sup>.

In the mid to late eighties, as osseointegrated dental implants increasingly were utilized to solve the lack of the single denture and in edentulous situations. Ample resinous material was quickly found to be insufficient in the back of the mouth, especially when it was used in the opposite way to natural teeth. Most practitioners were persuaded of the risk of osseointegrated interface being compromised of repair and maintenance issues, which could be minimized by regular repair and replacement demands due to high wear levels. Patient requests for esthetic implant help restore implants with more natural and durable materials such as porcelain often required restoration. It took a relatively short time to move from resin to porcelain<sup>7</sup>.

The transition was almost completed by the end of the 1980s and implant manufacturers introduced new elements onto the market that made the transition even easier. Distinguished from the literature is mainly concerned with the need to protect dental implants from painful shock from occlusal surfaces. The implant-supported restoration standards today covers the application of ceramic occlusal materials. The most widely used material for the manufacture of implant superstructures remains precious metal alloys. The use of base metal alloys has not been common since the corrosion potentials between different metals are one of the reasons cited for the avoidance of base metals in implant restorations. While in a system that includes other metals there is a risk of pitting or crevice corrosion, corrosion of precious metals with titanium is supposed to be less than that of base metals, and a byproduct in the process of corrosion is believed to be less harmful or hazardous than its base metals equivalents. A field of additional research is needed to evaluate the potential for corrosion between commercially pure titanium and traditional titanium alloys and different metals<sup>7</sup>.

The advent of machining and laser soldering of titanium as a replacement for the more conventional lost-wax grinding methods used for the manufacture of implants superstructure resulted in potential problems associated with metal casting engineering and materials. The prothesis that are correctly produced with this technology are solid and offer long-term success potential. While the laser produced superstructures are certain to provide improvements in comparison with cast metal superstructures, the medical gain was not shown or even tested in a manner monitored. For some time to come, laser soldered and computerized titanium superstructures will probably remain state of the art<sup>7</sup>.

The feasibility of fully metal-free implant-supported prothesis is being explored in several centres for the first time. A possible alternative to more conventional metal-based prothesis is the use of ceramic and/or plastic abutments and fiber-reinforced composites. Nonmetallic prostheses work is now in its early stage, but it is possibly advancing quickly as the material for conventional prothesis that are assisted by tooth becomes more and more common<sup>7</sup>.

## **B. SUBMERGED AND NON SUBMERGED IMPLANTS**

There was challenge to the need for full coverage of soft tissue and long healing times. Studies have shown that non-submerged implants have received similar soft and hard tissue reactions and have performed comparably in submerging implants.

Immediate removal sites can be used for implants. For incremental or immediate mounting, non-submerged implants may be used<sup>7</sup>.

## **C. OCCLUSAL LOAD/OVERLOAD/ PROGRESSIVE LOAD**

Much has been written about the effect of occlusal forces on osseointegrated dental implants. Unfortunately, very little of what has been written is based on scientific evidence, and the need for fundamental research into these issues is important from the long-term perspective as it relates to the survival and function of implant-supported prostheses<sup>7</sup>.

Avoidance of non-axial loading of dental implants is one example of a clinical concern that is not based on evidence. Many authors have warned of the hazards of non-axial loading of dental implants, but there is no scientific evidence that the osseointegrated interface between living host and non living implant responds differently to compressive forces than it does to tensile or shear forces of similar magnitude. In fact, each of these types of stress transfer is present on the surface of every loaded implant because of the very geometry of the implant and the chemical micromechanical nature of the bond between implant and tissue. The few animal studies that have attempted to examine this issue, in fact, shown that non-axial loading is not detrimental to the integration of the implant, even when non-axial occlusal forces are greatly exaggerated. One exception is a work reported by Isidor that did show evidence of non-axial load destroying implant integration, but only after the magnitude of load was elevated to catastrophic levels; in that report, forces generated appeared to be far beyond the range of clinical reality and were likely heavy enough to cause substantial deformation of the implant body itself, thereby precipitating bone loss. The facts that, to date, experimental evidence does not substantiate the concern regarding non axial loading and implant success makes this an area where much research is needed to permit an understanding of the mechanism of load transfer through the implant to the surrounding bone<sup>7</sup>.

When the issue of nonaxial loading is extended to include the restorative component of dental implants, the concern may well be justified. Screw-retained components of implant systems seem much less able to withstand non-axial forces than those within the long axis of the implant pillar. Tolerances between mechanical components permit relative motion across interfaces, and flexure fatigue becomes an important consideration of long-term prosthesis and implant survival. The potential for non-axial loading to cause plastic deformation (swaging), wear, or fatigue failure of implant restorative components is clearly design and material-dependent, and research is needed to determine the best design(s) for components to resist off-axis loads over extended periods of time<sup>7</sup>.

As with non axial loading, the literature on the use of cantilevers in implant-supported prostheses is largely anecdotal, and evidence from clinical data is lacking. Nevertheless, many authors have given their recommendations as to when cantilever prostheses are acceptable, what limits of length are permissible, and how many implants are necessary to support a cantilever<sup>7</sup>.

The work of Branemark and colleagues demonstrated the feasibility of fixed, cantilevered prostheses to treat the edentulous mandible, particularly when opposed by a conventional complete denture. Other authors have made empirical recommendations for length of cantilever as a function of implant position (A-P spread), arch form and length, cantilever location (maxilla or mandible), and opposing occlusion<sup>7</sup>.

While these recommendations may have been successful when followed, the evidence to support them is lacking. Similarly, cantilever extensions on prostheses in the posterior part of the mouth are dictated by implant position and convenience, rather than by sound principles of design that have resulted from scientific evidence. Cantilever extensions in the posterior mouth are likely to be at higher risk of mechanical failure because of increased occlusal load, fewer implants, and implant position in a straight line along the arch<sup>7</sup>.

As it is difficult to imagine clinical trials gathering sufficient data to make sound recommendations on cantilever length, guidelines based on anecdotal experience and the principle that the shorter cantilevers are kept the better. They will serve to minimize the problem of cantilever overload. Some clinicians have advocated placing; more implants, in particular, posterior to the mental foramina in edentulous patients and eliminating cantilever extensions on these complete-arch restorations<sup>7</sup>.

The concept of a fixed, cantilever prosthesis supported only by implants anterior to the mental foramina, as described by Branemark and coworkers, was based upon several important factors. Placement of implants anterior to the mental foramina allowed the inferior cortex to be engaged by the tip of the implant, increasing primary stability and improving chances that osseointegration would occur. By avoiding more posterior placement, the risk of damage to the mental branch of the inferior alveolar nerve was minimized. Finally, by avoiding the posterior segments as sites for implants, the potential complication of stress shielding related to mandibular flexure could be avoided. The fact that the fixed cantilever concept has been so successful prompts a question: why would clinicians feel it necessary to extend implant placement into the posterior mandible? The increased number of implants necessary and the increased risks associated with the concept makes it difficult to justify from the standpoint of increased patient benefit<sup>7</sup>.

The use of tripod implant placement in the posterior part of the mouth is a concept that makes sense geometrically but has not been demonstrated clinically. The ability to support a prosthesis on a tripod requires that at least 3 implants be present. Sufficient ridge width to allow a bodily offset of 1 implant is frequently not available, and a slight tip in the angulation of 1 implant to give the appearance of an offset or tripod at the level of the occlusal plane is not likely to provide the expected support. To counteract moments generated by occlusal forces in a buccolingual direction, the implants must be bodily offset at the level of the ridge crest, rather than merely being tipped<sup>7</sup>.

The advantage of tripodding 3 implants in the posterior part of the mouth, while one assumes that it is likely to improve longevity of prosthesis and possibly the supporting implants has not been demonstrated in a prospective manner to be superior to a more conventional design utilizing 2 implants and a 3- or 4-unit fixed partial denture. One implant manufacturer, in fact, recommends that 2 implants and a 3- to 4-unit fixed partial denture are sufficient to withstand occlusal function over time. This recommendation is based on retrospective data demonstrating a low rate of complication with such a design<sup>7</sup>.

Anatomic characteristics of the occlusal scheme that should be placed on restorations supported by dental implants have once again been described many times in an empirical manner but have not been examined scientifically. Cusp height, angulation, type of excursive contact, occlusal table width, and other considerations have all been described extensively but have not been examined scientifically. The variety of recommendations only confuses the clinician, providing little substance for guidance and disagreement as to what scheme or design is appropriate for a given situation in such a complicated and elusive area<sup>7</sup>.

#### **D. PROGRESSIVE LOADING**

The implant is left submerged after successful atraumatic placement and left undisturbed for the osseointegration to take place. After successful osseointegration has occurred provisional restoration is progressively loaded<sup>7</sup>.

Progressive loading has been put forward as a necessary and carefully engineered phase of implant restoration. The methods used to gradually increase the functional load on a new implant are well described and justified by their proponents. Unfortunately once again, the scientific literature does not support the clinical practice of progressive loading. No trial has been reported wherein parts of the subjects were treated with progressive loading and the other group provided with definitive restorations as the initial and only restoration. Lack of evidence does not by itself condemn the practice, but what little literature is an available point to progressive loading as unnecessary<sup>7</sup>.

Another concern about progressive loading is that there is no evidence that it can even be done in a controlled manner. The argument that provisional restorations made of polymethyl methacrylate or a similar resinous material will transmit less force to an underlying implant than a ceramic occlusal surface would transmit is not consistent with the physics of occlusal function. The load transmitted to an implant is dependent upon the force of contraction of the elevator muscles of the mandible. If a force of 1 kg is generated by the muscles, that force must be transmitted through the restoration, regardless of material, to the implant and its surrounding bone. The damping effect described by Skalak concerning implant occlusion does not affect the total force transmitted and would have an effect only if there were a rapid impact between the teeth, rather than the controlled closure of the mouth with a bolus of food between the teeth<sup>7</sup>.

The concept of keeping a provisional restoration slightly out of occlusion or narrowing the occlusal table during the progressive loading phase is also difficult to control. The phrase coined by Dr Leonard Abrams, "Food is a weapon" (personal communication, 1997), appears to be consistent with the Richter studies. It has been shown quite dramatically by Richter, in 2 excellent papers studying forces generated on implant restorations, that the forces of occlusion with food between the teeth are substantially higher than forces generated in an empty mouth clench. If the highest forces occur with food in the mouth, it is not likely that a slight lack of occlusal contact would be of any protective value during the period of progressive loading. While progressive loading may, in fact, be beneficial, the concept is not supported by the scientific literature. There is probably no negative aspect of progressive loading that would contraindicate its use, as long as the period of treatment is not increased

unnecessarily and as long as the total cost of treatment is not unduly increased by the practice<sup>7</sup>.

At this point it is safe to say that completely undisturbed healing of the implant/bone interface is not necessary for successful osseointegration to occur, and in some instances, implants placed into immediate full functional load can be expected to survive and function well. The requisite for predictable osseointegration of immediately loaded implant is yet to be determined.

One parallel consideration is whether provisional loading of the tissue borne prosthesis over an implant during the osseointegration period will affect the osseointegration of the implant – no scientific evidence that early failure can be attributed to early loading or overloading resulting from a tissue supported interim prosthesis<sup>7</sup>.

#### **E. IMMEDIATE LOADING**

The implant and the abutment are placed in one surgical procedure and the provisional restoration is placed at the same time.

During the last 15 years, several authors have reported that root form implants may osseointegrate, even though they reside above the bone and through the soft tissue during the early bone remodeling. The surgical approach has been called a one- stage or non submerged implant procedure and eliminate the second stage implant uncover surgery<sup>7</sup>.

#### **F. PASSIVITY OF PROSTHESIS FIT**

Many clinicians and authors have addressed the idea of passive fit of implant prostheses as essential to long-term success of treatment. Once again, while it makes intuitive sense that a mis-fitting prosthesis screwed into place between 2 or more ankylosed dental implants might negatively impact the long-term stability of those implants, evidence to support this assumption is lacking<sup>7</sup>.

In 1984 Roberts and coworkers demonstrated that titanium implants placed into the femora of rabbits which could withstand the load and even stimulate bone formation following constant orthodontic loading. Earlier attempts to use implants as an anchorage for orthodontic therapy met with variable results, although since the introduction of osseointegration the use of implants as orthodontic anchorage has been extremely successful. The important point illustrated by these early studies was that ankylosed or osseointegrated implants did not seem to get damaged by constantly applied loads of high magnitude.<sup>7</sup>

Book examined the quality of fit of implant-supported fixed prostheses retrospectively and found that, although none of the prosthesis examined were passive, there was no evidence of bone loss around any of the supporting implants, even after 5 years of function. They concluded that there must be a range of misfit that is tolerated by implants and still allows for long-term implant stability.<sup>7</sup>

If misfit is detrimental, the clinician must have the tools to measure it and to avoid it, at least at levels where damage is likely to occur. Level of misfit turns out to actually not be a

significant risk factor for long-term implant success, then the technology necessary to provide acceptable implant superstructures need not be extremely precise or expensive. While experimental evidence demonstrating a detrimental effect of misfit on osseointegration is missing and the issue of misfit as a biologic risk for implant success remains a major question, one can still assume that prosthesis misfit is likely to increase the incidence of mechanical component loosening and/or fracture. The literature describing prosthodontic complications is at best confusing, but some evidence exists that inaccurate prosthesis fit can be the cause of a high rate of component complications. From the aspect of mechanical stability, the need for accurately and passively fitting superstructures can be justified. The issue of passively fitting superstructures leads directly into the next topic of discussion<sup>7</sup>.

### **G. SCREW-RETAINED VERSUS CEMENTED IMPLANT RESTORATIONS.**

Now, there are 2 different approaches to dental implants. In many cases for many patients prostheses use screw retention and remain normal designs. Some tend to create more conventional implant dental restorations, including restore cementation. The selection between cementation and shield preservation seems first of all to be one of the clinician's personal preferences<sup>7</sup>.

There is no evidence that one retention strategy is superior to the other. The benefits of screw retention are mainly limited to issues of recovery, which is definitely an advantage for the redesign which holds a screw. On the other hand, the advocates of cement retained implant restoration mention the distinctive advantages of a cemented technique better esthetics, better occlusion, ease of production and reduced part cost as well as structure. Another potential benefit to a cemented treatment is that when put in the mouth it has the potential to be completely passive. Without a screw to draw incorrect components and a clamping pressure, strains inserted in the restoration / implant assembly will continue to be removed through the tightening power of the torques<sup>7</sup>.

If it is possible to passively restore cement on several abutments, it will not by itself be stressed to add a cement into the gap between prosthesis and abutments. Together with the others mentioned, this potential advantage makes cemented implant restorations more and more common. Cemented implant restorations proponents also note that restoration reclaimability can be preserved by using temporary cement. There is sadly no evidence that the various provisional luting agents are predictably recoverable when 2 or more metal elements are cemented together. Cement, which works alongside provisional cement for teeth-fired restorations, can in fact serve as a permanent graining agent for metal-fired concrete. Similarly, cements for permanent grinding can be inadequate when metal-to-metal is cemented. Work in this area is medically relevant<sup>7</sup>.

### **H. USE OF IMPLANTS AS OVERDENTURE ABUTMENTS**

Implants used in combination with prosthesis overdenture are a common means of improving denture consistency, stability and cost-effectiveness. Many strategies have been identified in the literature for attaching an overdenture to an implant, but 2 basic design principles are currently being debated.

The question to be answered is whether or not implants need to be separated in order to better cope with the load of overdenture support or whether individual implants alone can cope with the load. In the debate, maintenance problems often play a role. Others claim that joint splinting, replacements, and the risk of screw relaxation and part fracture is increasing. Some claim that the presence of a bar under the tooth will weaken the tooth and cause long-term fracturing problems. All claims can be slowly endorsed. Also, the option of how an implant overdenture is stabilized and maintained relies on the personal preferences of the clinician without significant scientific support for therapy<sup>7</sup>.

More clinical studies are required to determine the best use of implants in overdenture therapy. Overdenture retention magnets have been widely used. New magnet engineering advances have sometimes generated renewed interest in their use, but their findings have often not met expectations. Though new models and magnet forms are relatively common in the literature, there were no readily available follow-up studies of the problems associated with their use. Publications in the dental literature were also concerned with the chronic exposure of living tissues to strong magnetic fields<sup>7</sup>.

#### **I. NUMBER OF IMPLANTS NEEDED TO SUPPORT A RESTORATION**

How many implant procedures are needed to support the expected rehabilitation is one of the most difficult choices to take for the treatment of patients with dental implants. This issue involves the concern about the predictability of individual implants used to remove single postal teeth. No forward-looking data to date on this question are available<sup>7</sup>.

For the number of implants needed to restore the edentulous arch using a fixed implant-supported prosthesis, the literature can frequently be cited. Such guidelines, sadly, vary from one extreme, where four implants are considered appropriate to support a completely fixed arch prosthesis to the other extreme, which advises that a single implant will replace each missing tooth. The truth is that restorations focused on both ends of the requisite implant numbers can be shown to function in a specific medical situation. For many patients, where the financial support of implant rehabilitation is an important factor in their acceptance, the benefit of less implants is a cost-saving solution. On the other hand, where there are more than enough implants available to support the expected prosthesis, failure of 1 or more of the implants may not be crucial to successful end-restoration, and may prevent further implant surgery as well as the time necessary to achieve osseointegration<sup>7</sup>.

#### **J. CONNECTING IMPLANTS TO NATURAL TEETH**

Many of the problems associated with implant attachment to the teeth during the same restoration was reported. The phenomenon of natural tooth intrusion was mainly expressed as a question. Although many hypotheses concerning the etiology of the intrusion phenomenon have been developed, there is no experimental evidence to provide a solution. A prosthesis which contains a tooth as one terminal and an implant as the other is a mechanically complicated hybrid, which results from the unequal reinforcement of the two ends of the prosthesis<sup>7</sup>.

At least theoretically, the existence of a periodontal ligament as a connections and protection of the root of the natural tooth and the ankylotic character of a bone-integrated interface are of concern because, while the implant immediately absorbs load without interruption, a tooth may intervene to

the degree that its suspensional ligament fibers are charged. By developing the IMZ implant, Kirsch and colleagues tried to solve this problem<sup>7</sup>.

Rangert et al. suggested that the Branemark implant model permits an appropriate bent to fit the periodontal ligaments of natural teeth within the implant pillar assembly. The question about the difference between support for a tooth and an implant may likely have less effect than one would expect on the mechanical function of an implant restore. Bone is a versatile, robust material itself. Looking at the bone via a periodontal ligament, it is likely that the bone deformation caused by the implant loading results in similar deformation. The disparity between the tooth support and implant supports could be predicted, or at least in part, to be taken into consideration. There has been a common use of a single implant and a single tooth for a 3-to 4-unit fixed partial tooth made as a simple restoration process and cemented with a permanent stringent agent, with few long-term problems recorded. In fact, if you prevent the tooth from entering either with permanent or mechanical locking devices such as a horizontal screw attachment, the difficulty with the fixation of teeth on implants tends to decrease. The issue could be decreased<sup>7</sup>.

Although many advances in the design, engineering and implementation of implant prosthesis were the result of competitive trials and errors. The one basic principle of recent success is to acknowledge the need to learn, to adapt and to improve biological processes to further succeed<sup>7</sup>.

## ADVANCES AS RELATED TO CHANGES IN DIAGNOSTIC AND SURGICAL TECHNIQUE

### Advances In Diagnostic Technique

- A. Ridge Mapping
- B. Resonance Frequency Analysis
- C. Computed Tomography
- D. Cone Beam Radiography
- E. Cone Beam versus Conventional CT
- F. Magnetic Resonance Imaging
- G. Tuned Aperture Computed Tomography

## **RIDGE MAPPING**

When a single tooth in the anterior region of maxilla or mandible is to be replaced with an osseointegrated implant, the thickness and the quantity of the labiolingual bone can be gauged by the ridge mapping technique as described by Wilson. Ridge mapping is a procedure that allows the implant surgeon to determine the thickness or width of the alveolar bone before a mucoperiosteal flap is reflected during surgery. The ridge-mapping technique involves a series of measurements with a specially designed caliper (available from WBC, PO Box A70, Sydney South 2000, Australia). The sharp points of the caliper penetrate the anesthetized mucosa until the surface of the bone is reached. A millimeter scale near the handle end of the caliper will give an accurate reading of ridge thickness<sup>8</sup>.

Ridge mapping necessitates two measurements taken at each implant site: one at the level of the ridge crest and the other at a point approximately 7 mm vertically. A comparison of the two measurements will indicate any change in alveolar bone thickness below the crest. In longer edentulous spans or in the completely edentulous jaw, measurements are taken at 7-mm intervals along the crest of the ridge. Each crest measurement is followed by the second vertical measurement. In this way, the area of the alveolar ridge which is to receive the implants is "mapped" so that the dimension of the bone will be known at an early stage. These measurements will also highlight any significant reduction in width dimension that could preclude an implant in that area<sup>8</sup>.

## **COMPUTED TOMOGRAPHY**

In 1972 a computerized transverse axial scanning was developed by Godfrey Hounsfield. This technique allowed him to generate a narrowly collimating and moving X-ray beam to create an axial cross-sectional image of the head<sup>9</sup>.

The residual radiation of that beam is detected by a scintillation crystal and the analog signal is then fed into a computer, and digitized and analyzed using a computational algorithm. It is believed that this technique is 100 times more efficient than traditional radiation technologies. This software is also referred to as Computerized Axial Tomography, Computerized Tomography of Reconstruction, Computerized Tomographic Scan, Axial Tomography and CT. A computed tomography, CT is the commonly preferred term. The CT scanner consists of an X-ray tube spinning around the patient. Either the detectors travel with the x-ray tube or are in the shape of a fixed circular screen. A method of CT is known as incremental scanners as a sequence of adjacent or overlapping axial images are used for the final image collection. In a spiral or helical pattern, modern CT acquires images. The table on which the patient lies also shifts within the board, in addition to the movement of the x-ray tube around the patient's chest. This is how objects are

obtained spirally. Spiral CTs offer better reconstruction of multiplanar images, reduced time for exams (12 seconds compared to 5 minutes) and a reduced dose of radiation (up to 75%)<sup>9</sup>.



*CT scanning apparatus*

The CT image is a digital image that is captured and presented as a matrix of individual blocks called voxels (volume elements). The size of the voxel is calculated by the width of the x ray beam and is equivalent to tomographic surface. Each pixel is given with CT number reflecting size. The number ranges from 1000 to + 1000 HU (Hounsfield units). 1000 means rain, 0 is liquid and + 1000 thick bones. 3D CT utilizes the method of interpolation to construct sets of evenly spaced cuboidal voxels (cuberilles) that occupy the same volume as the initial voxel. When built 3D CT images may be further manipulated by rotation about any axis to view the structure imaged from many angles. Often, exterior surfaces of the image can be removed digitally to expose hidden deeper anatomy. This system is being used for CT guided implant placement<sup>9</sup>.

#### **Advantages of CT over traditional tomography and radiography are;**

- Completely eliminates the superimposition of images from objects outside the the area of interest.
- Because of the high contrast resolution of CT, variations between tissues that vary in physical density by 1 percent can be distinguished. Conventional radiography requires 10 percent difference in physical density to differentiate between tissues.
- Depending on the diagnostic criteria, data obtained from a single CT image can be replicated in coronal, sagittal and axial planes. This is referred to as multiplanar reformatted imaging.

CT is also of interest in determining the quantity and subjective consistency of bone prior to harvesting for a bone graft or ridge augmentation procedure. Since implants are not just placed in the jaws, CT is critical in assessing certain locations of an implant, including malar bones, before surgery. While requesting CT images for the pre-implant evaluation, it is important to connect closely with medical radiology practices. In practice the CT Radiogram should be made clear exactly what information is needed and this is especially true when the data is imported using pre-implant planning technology for further manipulation<sup>9</sup>.

CT limitations include a relatively high dose of irradiation as against the other imaging types, no appropriate technology, a relatively high test cost and not always medicare reimbursable, a lower

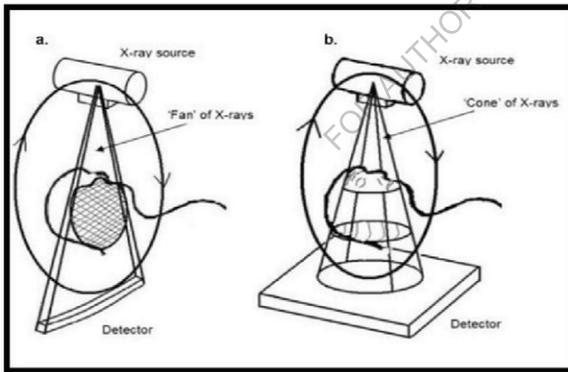
dental channel is not always well displayed and hardening devices and metal scatters which obscure areas of interest<sup>9</sup>.

Structures with low density, including osteoids, typically surpass CT resolution units. It should be recommended to scan the patient in such a way as to maximize the information collected and to guide the patient to eliminate objects from metal restorations and avoid ports from tilt wherever possible. The fact that post is present in the tooth next to or near to the region of interest will lead to too much 'light hardening' artifact or scattering to make the test worthwhile. CT is usually present around the implant on CT images not useful in evaluating the integration of implantes as a radiolucent unit, but the implant can be measured on three dimensions using CT<sup>9</sup>.

### **CONE BEAM RADIOGRAPHY**

Computer tomography can be divided into 2 categories based on x-ray beam configuration acquisition: fan beam and beam of the cone. An x-ray source and solid state detector are connected to a rotating panel in fan beam scanners. Data is collected with a patient transmitted narrow fan-shaped x-ray laser. The patient is imaged in part, usually in the axial plane, and visualization by stacking the parts to create several 2D representations achieved<sup>9</sup>.

In addition, a multi-detector array is the linear array of detector elements used in conventional helical CT beam scanners. The Multi-Detector CT (MDCT) scanners can acquire up to sixty-four slices at once, considerably reducing the scanning time compared with single-slice systems and permitting 3D images to be produced at significantly lower radiation doses than single-detector fan-beam CT arrays<sup>9</sup>.



Cone-Beam Volumetric Tomography was developed in the 1990s and first machines were commercially available during 2000 at the Nihon University School of Dentistry<sup>9</sup>.

The CBCT scanners use the 2D extended digital range which includes an area detector for the volumetric tomography. This is paired with a three-dimensional ray tube. A single 360 degrees cone-beam technique involves coordinated motion of the X ray origin and of a reciprocal area detector around the patient's head, which is balanced with a head holder. Single objects known as the "basis" images are obtained at certain degree intervals. These are identical to lateral cerebrospinal images, each of which is slightly offset. The projection data is called this sequence of base projection pictures. The image data is used for a 3D volumetric data set to produce primary

images in three orthogonal planes (axial, sagittal and coronal) that implement advanced algorithms, including back-filtered projection<sup>10</sup>.

Although the CBCT concept has been in effect for nearly 2 decades, it has only recently come into commercial use with the production of inexpensive x-ray tubes, high quality detector systems and powerful personal computers. The NewTom QR DVT 9000 was unveiled in April 2001 and includes the 3D Accuitomo–XYZ Slice View Tomo-graph (J. Morita Mfg Corp.) and iCAT (Xoran Technologies, Ann Arbor, Mich.), the iCAT system (Charlousers, Mich., and the ICAT system). The new systems are the ones that were developed by CB MercuRay (Hitachi Medical Corp., Kashiwashi, Chibaken, Japan)<sup>10</sup>.

Such units can be identified by the x-ray detection system. The image intensifier tube (IIT)–load-coupled device is used by most of the CBCT systems for maxillofacial applications. A program has recently been released using a flat panel imager (FPI). The FPI consists of a cesium iodide scintillator for an amorphous silicone thin film transistor. The image created with an IIT usually produces more noise than the images in a FPI and must also be pre-processed to reduce the detector configuration geometric distortions<sup>10</sup>.

### **CBCT advantages**

- 10-70 seconds quick scan time. Further time is needed for scanning high-resolution images. It leads to incorrect information in patient movement.

Increasing the radiation dose even in high resolution images.

### **Photo resolution**

- A voxel isometric in CBCT compared to conventional CT anisometric voxel. It enables small, up to 0.4 mms to 0.125 mts (tomographic layer) images of high resolution.

### **Dose Reduction**

- The effective radiative dose is 4-15 times that of modern radiography (2,9-11 $\mu$ Sv) compared with 1,320-3,324 $\mu$ sv of traditional CT.

In-offices do not have to be set expensively up to standard CTs.

- Reduced image artifacts
- Low metal artifacts result in the elimination of image algorithms from these devices<sup>10</sup>.

## **CONE BEAM VERSUS CONVENTIONAL CT**

Given the similar capabilities of CBCT and CT multi-slice, the distinctions between the two modalities are prudent. A 16-slice CT scanner is faster than the fastest CBCT scan, with modern 64-slice CT systems reducing scanning time. It reduces the risk of patient motion effectively. The CBCT's theoretical resolution is higher than CT but the gap may not be as significant as once assumed because of the effect of the patient movement caused by increased scanning time<sup>9</sup>.

Performance of the picture was discussed extensively and there is currently no direct reaction. Cadaver studies show cone beam engineering capabilities, but patient images were less impressive. The low exposure parameter of CBCT leads to a poor contrast between soft tissue and CT and the inability to change exposure parameters on the majority of machines contributes to image quality in larger patients. However, in patients with metal restorations, posts or surgical

boards, CBCT suffers from the very same hardening phenomenon that CT does; restricting its utility in exams. Dental implants creating a similar artifact on CBCT pictures were recently reported<sup>9</sup>.

While it is known that CT multi-slice screening is higher than CBCT, reports indicate that CT protocols with low doses lead to considerably less exposure than previously thought, without significantly affecting image quality. Reduced contrast and therefore image quality are a result of the lesser dose of the CBCT scan. Image noise is also significant, especially when patients are large or when scans are higher resolution. It should be noted that while the CBCT test radiation dose may be lower than low-dose CT, the radiation dose is still significantly higher than other types of dental x-rays<sup>9</sup>.

The 3D CT data allow the surgeon to prepare the implant procedure including the choice and placement of implants in advance. The different softwares are now available. Those data are then used to create an operating guide used during the actual implant procedure. Commercially available technology for CT guided operations is the Nobel Guide and Simplant<sup>9</sup>.

Local CT Local CT is a CBCT edition. This uses a small high-resolution sensor in the field to provide a specific 3D area with high resolution. The fields or sizes of intraoral radiographs are equivalent<sup>9</sup>.

LCT produces low dose, low cost and accurate images.

Tomography Optical coherence Tomography (OCT), Everett M J et al (2000) developed optical coherence tomography. To produce cross sectional pictures, Optical coherence tomography uses infrared light sources. Biological tissues can penetrate infrared rays without any biological effects. For the composition of objects, variations in light reflection are used<sup>9</sup>.

## **MAGNETIC RESONANCE IMAGING**

MRI utilizes non-ionizing electromagnetic spectrum radiation from the radio frequency band. The patient is located within a broad magnet to build an MR picture which causes a comparatively powerful magnet field from the outside. It leads to the interaction of the nuclei with the magnetic field of many molecules, including hydrogen. After an RF signal has been applied, energy is released, detected and used for computing the MR image. The atoms do not align themselves with the external magnetic field and create a usable signal in tissues such as bone, where hydrogen atoms are tightly bound. Proton density, which is higher in soft tissues, is called the concentration of the atoms of loosely organized hydrogens in the tissue<sup>9</sup>.



MRI scanner

**MRI benefits** include,

- MRI's high tissue differential contrast sensitivity
- Absence of ionizing radiation.
- The imagery of the body is electronically monitored so that the patient can be directly imaged multiplanned without redirected.
- MRI is mainly used for the localization of the lower dental canal for pre-implant imaging.
- If the channel is surrounded by sclerotic bone, then it will be difficult to visualize the channel, like the spongy bone around the channel, visualization with CT will then be difficult.
- Potential hazard of ferromagnetic materials such as cardiac pacemakers, aneurysm clips in the brain.
- Claustrophobia
- There will be a considerable artifact on the images if certain metals, like amalgam and nonprecious alloys, exist.
- No MRI artifacts can be found in pure titanium implants, but artifacts will exist if there are impurities in titanium<sup>9</sup>.

### **COMPUTED TOMOGRAPHY TUNED APERTURE:**

It is a radiographic technique in which information is collected by passing an x-ray beam through an object at several different angles. TACT can map the incrementally collected data into three-dimensional matrix. The advantages of this technique include less radiation dose and movement of the patient is less significant.<sup>9</sup>

## ***Scan Ora***

Uses complex broad beam spiral tomography and is able to scan in multiple planes. In addition to less radiation dose and less significance of patient movement, it has the additional advantage that the picture can be captured on radiographic film unlike CT Scan. It has the disadvantage that object outside the focus appear blurred and also the slices are much thicker hence not very good detail reproduction.<sup>9</sup>

## **European Academy of Osseointegration (E.A.O) Guidelines for the use of Diagnostic Imaging in Implant Dentistry**

### **A. Clinical Considerations**

1. What radiological information does a surgeon require when planning for implant surgery and at what stage should it be obtained?

In investigating an implant site, a surgeon requires information on bone volume and quality, topography and the relationship to important anatomical structures, such as nerves, vessels, roots, nasal floor, and sinus cavities. This information is obtained with a clinical examination and appropriate conventional radiographs. The decision to proceed to crosssectional imaging must be based on clearly identified needs and the clinical requirements of the clinicians involved. Implant failure may be related to poor bone quality at the implant site. Information about bone quality can be obtained preoperatively based on radiographic images and partly during the surgical performance<sup>11</sup>.

2. What type of clinical situations might potentially benefit from crosssectional imaging?

- a) When reference to such images can help minimize the risk of damage to important anatomical structures.
- b) To provide more information in borderline clinical situations where there is limited bone height and/or bone width available for successful implant treatment.
- c) To improve implant positioning and axial direction that will optimize biomechanical, functional and aesthetic treatment results. The diagnostic information can be enhanced by the use of appropriate radiopaque markers or restorative templates.

However, this information cannot be transferred exactly to the surgical site as long as no intraoperative navigation is used.

3. Who should decide whether a patient requires cross-sectional imaging?

Clinicians should decide on the basis of the clinical examination and treatment requirements, and on information obtained from conventional radiographs whether or not cross-sectional imaging will be of benefit. If the patient is to be referred then a radiologist with specialised knowledge in the field should decide on the appropriate cross-sectional imaging techniques based on the information provided by the clinician. Circumstances may dictate that it is the clinician who must decide. Clinicians must clearly indicate the reasons for

requesting the investigations and provide the radiologist with sufficient information to allow the production of accurate and relevant images of good quality. It is the duty of the clinician to understand the fundamental principles of cross sectional imaging and to be capable of interpreting the images. The technique chosen should provide the required diagnostic information with the least radiation exposure to the patient<sup>11</sup>.

## **B. Radiological Considerations**

1. What imaging modalities are available for investigation of potential implant sites?

Standard radiographic imaging techniques are intraoral, panoramic and profile (lateral) radiographs. In certain special indications, cross-sectional imaging [i.e. spiral tomography and multiplanar reformatted computed tomography (CT)] may be necessary.

2. What is the recommended technique performing these imaging modalities, and what is the resulting radiation dose?

Table beneath delineates the recommended technique for each imaging modality together with the resulting maximum radiation dose acceptable. It is essential that the ALARA (as low as reasonably achievable) principle is adhered at all times. This may result in significantly lower doses in certain circumstances. Digital radiography might reduce the dose even further.

3. What is the biological risk from the dose incurred in each of the techniques?

The use of radiation involves a certain amount of risk. To assess the significance of this risk it is important to set it in context with other commonly encountered risk factors (NRPB 1998). A few examples are:

A: Annual risk of death in the UK Smoking 10 cigarettes 1:200 per day, Heart disease 1:300, Accident in the home; 1:15,000, Accident on the road ; 1:17,000,

B: Radiation exposure in context the annual dose averaged over the whole European population is about 3 mSv per person. However, 85% of this is due to natural background radiation, and only 14% from medical and dental radiation. The International Commission on Radiological Protection (ICRP) has estimated the risk per mSv as 1 in 20000. For younger age groups the risk is estimated to be twice as high. Based on the above estimated values, the risk for the various imaging modalities is as follows<sup>11</sup>:

Intraoral radiography	Cephalometric lateral skull with wedge form
Frontal -1:10,000,000	Collimation- 1:2,000,000
Premolar -1:5,000,000	Computed tomography- 1: 40,000/jaw
Molar -1:3,000,000	Spiral tomography
Full mouth survey -1: 476000	Maxilla _1:2,000,000/cut,
Panoramic imaging -1:667000	Mandible _1:4,000,000/cut

#### 4. What is the recommended imaging modality for different clinical situations

This applies to those cases where more information is required after appropriate clinical examination and standard radiographic techniques have been performed. The choice of techniques is based on the lowest dose giving the required diagnostic information. For example, the assessment of a single tooth gap requires approximately 25 times less radiation using one spiral cross-sectionals tomogram as compared to a CT examination. If the suggested cross-sectional imaging modality is not available, the alternate cross-sectional modality may be used, but this may result in a higher dose and/or lower diagnostic quality<sup>11</sup>.

#### *C. Diagnostic benefits*

What are the potential diagnostic benefits of cross-sectional imaging?

- (a) Preoperative assessment to identify bone volume, jaw topography, bone structures, location of important anatomical landmarks, etc.
- (b) Treatment planning to identify optimal locations of implant sites in relation to available anatomical conditions for best aesthetics, function and loading conditions. The techniques can also be helpful as part of the preoperative planning for various augmentation protocols.
- (c) Postoperative monitoring cross-sectional imaging is not a part of the routine protocol of postoperative examinations, unless there is a need for assessments in situations where some kind of complications have occurred, such as nerve damage, postoperative infections in relation to nasal and/or sinus cavities close to implants<sup>11</sup>.

#### *D. Recommendations for the use of cross-sectional imaging in implant dentistry*

##### **Single Tooth Implant Sites**

If the clinical examination indicates there is sufficient bone width and recommended standard radiographic examination reveals adequate bone height and space, no additional imaging is required. Additional cross-sectional imaging may be required when an implant site lies in close relationship to nerve canals as occurs in the posterior mandible and the maxillary

central incisors. It also may be of benefit in investigating defect sites to allow for more precise treatment planning<sup>11</sup>.

### **Edentulous Maxilla**

In many cases, clinical examination in conjunction with recommended standard radiographs will provide sufficient information on the available bone volume. Additional cross-sectional imaging may be required to determine the adequacy of the available bone volume and the need for bone augmentation/grafting procedures. Cross-sectional images can also help in the planning and predictability of prosthetic results that involve a fixed prosthesis and in the transfer of this information to guide the surgeon in implant positioning. Special techniques such as zygomatic implants may also dictate the need for additional imaging<sup>11</sup>.

### **Partially Edentulous Maxilla**

Clinical examination in conjunction with recommended standard radiographs will form the basis for treatment planning and indicate if further cross-sectional imaging is required. Assessment of bone volume and topography, the position of adjacent anatomical structures and the need for restorative planning particularly in the aesthetic zone may indicate a need for additional imaging<sup>11</sup>.

### **Edentulous Mandible**

In almost all cases, clinical examination in conjunction with recommended standard radiographs will provide sufficient information for treatment planning. In certain circumstances, involving extreme atrophy or unusual anatomy, additional imaging may be beneficial<sup>11</sup>.

### **Partially Edentulous Mandible**

Clinical examination in conjunction with recommended standard radiographs will form the basis for treatment planning and indicate if further cross-sectional imaging is required. When implants are to be placed in proximity to the inferior alveolar nerve, cross-sectional images can provide useful additional information on the available bone volume and shape in relation to the position of the nerve canal<sup>11</sup>.

### **III. ADVANCES RELATED TO IMPLANT COMPONENTS.**

- 1. IMPLANT BIOMATERIALS**
- 2. IMPLANT DESIGN AND SURFACE TREATMENT.**
  - A. Implant Body Geometry**
    - Wide- And Narrow-Diameter Implants and Platforms**
    - Small-Diameter implants**
    - Transitional Implants**
  - B. Implant Surface and Coatings**
  - C. Thread Design**
- 3. THE ABUTMENT CONNECTION**
- 4. A CRITICAL LOOK AT THE IMPLANT/ABUTMENT INTERFACE**
- 5. ABUTMENT SCREW DESIGN**
- 6. VARIOUS OSSEOINTEGRATED IMPLANT SYSTEM**

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## 1. IMPLANT BIOMATERIALS

An osseointegration benchmark has been developed in implants made of commercially pure titanium that few other materials compare. Similar materials such as niobium can produce high rates of osseointegration and some titanium alloys and hydroxyapatite coated implants report good clinical results. Recently resorbable coverings are created that increase the original bone healing rate against the implant surface and then absorb the bone to metal contact in a short time period<sup>12</sup>.

CLASSIFICATION OF DENTAL IMPLANT MATERIALS

	METALS	CERAMICS	POLYMERS
Biotolerant	Gold		Polyethylene
	Co-cr.		Polyamide
	Stainless steel		Polymethyl acrylate
	Zirconium		Polytetrafluoroethylene
	Niobium		Polyurethane
Bio inert	Commercially pure titanium	Aluminum oxide zirconium oxide	
	Titanium alloy (Ti-6Al-4V)		
Bioactive		Hydroxyapatite	
		Tricalcium Phosphate	
		Tetra calcium phosphate	
		Calcium pyrophosphate	
		Fluorapatite	
		Brushite	
		Carbon-silicon	
	Bioglass		

Aluminum and calcium phosphate ceramics are important in endosteal implantology, as are the use of bioactive ceramics, such as aluminum oxide, good supporting bone with lamal orientation, which can usually grow in close proximity on the ceramic surface to provide contact osteogenesis. A new ceramic implant material has been launched with partially stabilized zirconia, which are equal to highest oxide values.

Yasumasa Akagawa says the mechanical properties of this ceramic are more important than the stable zirconia. In addition, due to its energy-absorbing properties during martensitic transformation of tetragonal particles, zirconia possesses high fracture resistance. Zirconia can therefore act as metal, biocompatible and mechanically robust. In fact, this material is highly radioactive and simple

to cut for preparation of abutments. Partially stabilized zirconia is therefore seen as an attractive dental implant endosseous material<sup>13</sup>.

Results of the Yasumasa Akagawa study suggested that osseointegration in 2 separate loading conditions of non-submerged new zirconia implants mounted in the one-stage procedure is possible. Although the latest Zirconia implant was mounted, it was well encapsulated with newly formed bone tissue and primed implants. The quality of tissue with partially stable Zirconia and the strength of polycrystalline alumina were two times higher<sup>13</sup>.

## **METALS**

Endosteal implantology forefront. The main reason is because dentistry implants must be slim to match the alveolar bone available. Better experimental results with niobium have been obtained most recently<sup>12</sup>.

## **COMPOUND MATERIALS**

All materials containing a single element, but have major or minor advantages, but also disadvantages. Endosseous metal implants incorporate mechanical factors, though biological shape would theoretically at least seem more conducive to bioactive ceramics. Compound substances were therefore established which incorporated the beneficial properties, but restricted their drawbacks of two different materials. For example, the development of a ceramic hydroxyapatite biologically stable layer of titanium.

Titanate calcium consists of the reaction of titanium oxide hydroxyapatite on the surface of a metal and helps to mount titanium implants in a ceramic coating. Many of the problems caused by different thermal expansion coefficients and the various elastic properties of the various materials employed tend to afflict the coating process for titanium implants. The adverse histological effects may be correlated with even minor changes of the ceramic or transformation during thermal treatment of the coating procedures. The problem of long-term prognosis and medical usefulness in hydroxyapatite coverings has been identified. Nonetheless, recent studies on HA-coated implants indicate that concern is more theoretical than medical about their long-term prognosis<sup>14</sup>.

**Biotolerant:** Characterized through the interaction of bone with toxic ions as a result of connective tissue surface (distance of osteogenesis) between the implant and the bone.

**Implant Bioinert:** No reaction because the foreign ions are not released with the implant pad. No intervening connective tissue surface is directly linked. (Osteogenesis contact).

**Bioreactive** materials demonstrate that the implant bed and bone have physiochemical bonds. Bone adaptation (binding osteogenesis) is chemical and micromorphological. The biomimetics are fabric-based integrated materials designed to imitate particular biological processes and help improve the host microenvironment's healing / regenerative response.

Also called osteoconducting Bioinert and Bio-active materials can act as grooves that enable the growth of bone on their surfaces.

The objective of the biomaterial research is and continues to be to develop materials for implants that induce the interfacial tissue, both hard and soft tissue, to be predictable, regulated, directed and fast<sup>14</sup>.

Wilhelm Gregor, a clergyman who discovered the metal in the dark, magnetic sand of Cornwall in 1791, found the product of Titanium and Titanium Alloys—6 ALUMINIUM—4 VANADIUM. In 1925, Van Arkel refined and manufactured a metal that had reasonable properties, using titanium tetra iodides.

Most doctors defined two types for bio-materials of titanium implants; 1) pure (cp), 2) titanium alloys for business purposes.

It was split into six distinct materials between these two classes, American research and material culture (ASTM). Four grades of titanium CP and two alloys of titanium comprise them.

#### **Uses:**

In the pigment market, however, bulk is used to manufacture Cp titanium and titanium alloys only 5-10 percent of the titanium ore.

1. Titanium tennis rackets, golf clubs and glass frames are also used

2. Mainly used in industrial applications such as jet engines, aircraft and aerospace, requiring a high weight strength and good resistance to corrosion.

Many uses include water storage, containment of nuclear waste, heat exchanges, marine desalination and drilling equipment, as well as food processing centres, which require chemical resistance and cleaning agents to prevent corrosion.

For their high biocompatibility and durability, titanium and its alloys are important in medical implants. These include joint replacement tools, biosubmerged appliances including pacemakers for repairing the site of a break and encapsulation<sup>15</sup>.

#### **Benefits:**

1. Ti's high cost is the biggest downside to its broader usage although over the past 10 years, the cost has been rising.

2. Ti is hard to cast and risky. The former metal oxidizes so easily, that an explosive reaction will happen at high temperatures. It is used in the desired shape in either machined or plastic form.

Fitness: ASTM Committee F-4 accept four grades of commercially pure titanium and titanium alloys in products for surgical implants. It is commercially pure titanium of grade I, commercially pure titanium of grade II, also known as titanium unalloyed<sup>15</sup>.

#### **The Ti-6Al-4V and Ti-6Al-4V Extra Low Interstitial (ELI) alloys.**

The thin, non-magnetic component is pure titanium. In the event of carbon and chlorine, heat titanium oxide (rutile, ilmenite), then reduce to a titanium sponge the resulting titanium chloride using molten sodium. This sponge is then mixed into ingots made up of the common metal in a

vaccine or in an inert environment. Titanium is burnt into light, and in the presence of nitrogen it is the only metal that burns<sup>15</sup>.

The crystallographic transition of pure titanium occurs on heating at 882<sup>0</sup>C. This method of processing takes place in many materials and produces substantially different properties than in the original condition. A variety of other elements, such as Gold, Al, Ar, Cu, Fe, Ur, Va and Zn, are dissolved by titanium<sup>15</sup>.

The 3 types of alpha, beta and alpha beta titanium alloys of interest to dentistry are found. Both forms are derived from the fact that pure titanium is heated at certain concentrations with elements Al and Va. This method provided truly solid solutions. Such additional elements will serve as stabilizers of phase conditions.

As an alpha phase stabilizer, aluminum has been named. Alpha also helps to boost alloy strength and lower alloy weight. As a beta-phase stabilizer, Vanadium has been named.

Once Al or Va is applied to titanium, a number of temperatures change at which alpha-beta change takes place. Alpha and beta may be found in these ranges. At the desired shape, room temperature alloys are relaxed at the temperatures. These alloys, especially alpha-beta, can be treated with heat in order to increase this power. Alloys of the alpha-beta type are the most widely used in dental implants. Among these, 6% Al and 4% Va. (Ti-6 al-4V) are the most common<sup>15</sup>.

**Mechanical characteristics:** The titanium elasticity unit from grade I cp to titanium grade IV cp varies between 102 and 104 G Pa (only 2%).

In contrast to titanium alloys, the characteristic pattern of rising strength is:

- 1.The elastic unit is somewhat greater (113 MPa compared to 104 MPa in titanium of CP class IV).
- 2.For Ti alloys the yield strength increases by more than 60% to 860 Mpa for CP Ti.

Similar with alloys Co-Cr-Mo. The titanium alloys are twice as strong and the elastic modulus is half as strong.

In contrast with most other alloys titanium exhibits a relatively low elasticity and tensile strength unit.

Cp titanium elasticity module is 5 times higher than the compact bone, and the significance of layout in proper distribution of mechanical stress transmission is highlighted in this property. The elasticity of the alloys is much greater than the elasticity of titanium, about 5.6 times the compact bone.

Coining, stamping or forging accompanied by controlled ringing therapies are commonly used during the metallurgical processing of implants in order to prevent bending due to local strain on insertion.

Although more rigid than bone, their elasticity modulus is similar to the bone than any other large implant metal; pure titanium is the only exception. This property leads to more equal pressure distribution at the vital interface of the bone implant, as the bone and implant can contract more likewise<sup>15</sup>.

### **Oxide Coatings**

When exposed to the air, most metals form oxide layers. The form of the oxide depends on the metal and its oxidation conditions. Everything that comes into contact with the implant surface is

able to change it, so that a metal in the body's physiological conditions are rather stable, depends on the character of the oxide layer. Pure titanium can form a variety of oxides in principle. The most stable and therefore most widely used in physiological settings are  $TiO$ ,  $TiO_2$ , and  $Ti_2O_3$ . Such oxides form spontaneously when titanium is exposed to air. A  $10A^0$  oxide layer on the pure titanium surface can be formed within one millisecond of air exposure in one minute; this may be  $100A^0$  times the same layer<sup>16</sup>.

Even if the US. Food and Drug Administration allows titanium implant manufacturers to move their products before sale with a nitric acid bath. Many of the titanium alloys in which titanium is present at 85-95% hold pure titanium inert.

Ti is easily reactive, both as a pure metal and as alloys form a stable surface oxide of  $TiO_2$ , which makes them resistant to corrosion. When damage occurs during implant insertion, this oxide can instantly repair itself<sup>16</sup>.

The dissolution rate of  $TiO_2$  is extremely low in a passive state. With time, the surface of the metal implant is slowly altering however titanium deposition can be seen in the tissues. The standard human tissue titanium rate is 50 ppm. In the healthy tissue surrounding Ti implants, values of 100-300ppm are often found at these levels; tissue discoloration with Ti pigments are seen. The dissolution frequency is among all passive implant metals one of the lowest and tends to be well tolerated in the organism.

There have been several adverse effects, increased concentrations of titanium are observed, particularly in the lung and in liver, kidney and spleen, both in perimplant and parenchymatic tissues<sup>16</sup>.

### **Corrosion:**

Surface oxide formation can be theoretically as well as medically observed. Theoretically, the mode of oxide production can be represented by the Nerst equation and Pourbaix equation diagrams. Stress can produce a combination of mechanical and environmental impacts on a metal and alter its surface oxides properties<sup>17</sup>.

The cracking of stress corrosion and corrosion fatigue in implant systems are critical because they can lead to a complete mechanical implant failure. Under physiologic conditions, stress corrosion cracking of pure Ti is unknown; potentially, Ti alloys are subject to this phenomenon in physiological conditions. Due to the formation of titanium-Al compounds, alloys are especially vulnerable to this problem with the presence of aluminum at a level above 6%.

Due to vanadium formation blocked, the presence of vanadium increases the susceptibility to corrosion cracking. Titanium alloys are very corrosion-resistant and render titanium alloy an ideal metal if it is desired to achieve high fatigue strength.

Fluid irregularities, such as friction or scratches, can affect the oxide film and lead to disturbance in isolated areas. The process of cervical corrosion and pitting corrosion is involved in this form of breakdown<sup>17</sup>.

Other characteristics: Ti is one of the metals, which can be combined without losing passivity, with other metals. In combination with metals with greater corrosion potential, the process of galvanic corrosion may become corroded. They remain passive in combination with metals and provide a balanced mix. It would be smart, instead, to avoid extremely passive materials, such as stainless steel. In the choice of surgical instruments for the positioning of titanium implants this should also be considered<sup>17</sup>.

**Implant selection:**

Clinical evidence indicates that there was excellent biocompatibility and tissue responses in all six marketably available biomaterials for the dental implant. None of the Ti-based materials have proved to be more biocompatible. In a choice of implants for a particular patient, considerations such as implant design, volume and material strength should be determined. If you have a history of para-functional behaviors, you should choose a titanium-type implant made from Ti alloy instead of Cp grade I. Therefore, tiny implants within thin walls demonstrate the need for high-resistance materials<sup>17</sup>.

**Tissue response**

Metals and alloys, namely commercially pure (CP) titanium and Ti-6Al-4V, are the most commonly used biomaterials for dental implants while Co-Cr-Mo is typically used in subperiosteal implants.

Low-density metals with chemical properties for implantation applications are Cp Ti and Ti alloys. Ti has a low shear strength and is immune to articulating the ground or bone screw. The surface oxide layer Ti has high resistance to corrosion which creates a chemically unresponsive surface for the surrounding tissue.

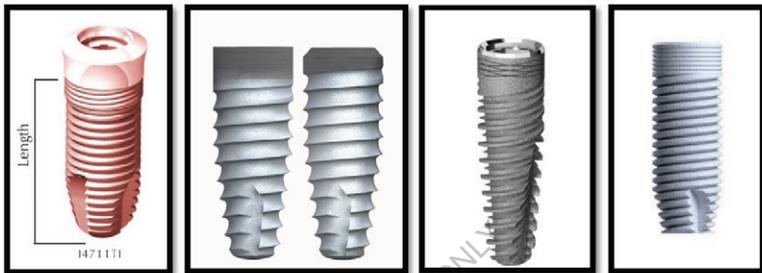
The selection of an implant material is based on both elastic modulus and strength. The implant must be immune to occlusal forces without permanent deformation and has a small modulus to maximize the transfer of force<sup>17</sup>.

**2. DESIGN AND TREATMENT SURFACE.****A. Body Geometry**

Typical cylindrical shape of the endosteal implant body geometry. There were at first 3 basic forms: the threaded screw; a press fit cylindrical and a hollow basket cylindrical. The classic distinction was that threads and a solid or hollow cylindrical occurred or were not present. The macro locking of the screw implants is shown while microlocking is shown by press fit cylinder. Different body geometries have resulted in the creation of the implant in the root type over the past 20 years. The impetus for improvement was motivated by desire for surgical simplification, higher predictability in poor bone performance, immediate positioning rather than lag, better pressure distribution, increased initial stability and differentiation in marketing.

Classical geometrical variations are no longer applicable as different features are incorporated into a wide range of geometrical shapes. Threaded screws may be flat, tapered,

tapered, conical, ovoid and extended. Thread patterns were also updated and now range from implant neck (Astra Tech, Lexington, MA) microthreads (Biohorizons, Birmingham, AL; Steri-Oss, Nobel Biocare) to large middle-body macrothreads (Implant Innovations, Palm Beach Gardens, FL; Nobel Biocare); a wide range of altered pitch threads to cause bones self-tapping, as well as thin, small, long threads. Cylinder press fit may be defined as smooth, tapered, conical, trapezoidal and trapezoidal stages. On the basis of moves, ledges, more distinctions can be made. Threads, windings, groovings and a hollow inner recess. The body of the implant may also be distinguished by the presence or absence of a cervical collar that differs in width and angle and the presence of a straight or flared arm<sup>2</sup>.



Straight body

Tapered body

Conical

Cylindrical



Hollow basket



Press fit geometry variations-(a)Standard Cervical Cylinder (b)Trapezoidal cylinder with steps (c) Trapezoidal cylinder with threads (d)Straight wall configuration (e) Finned taper design

### 1.Length

Implants in different lengths from 6-20 mm are available. The lengths of 8-15 mm are the most common. In certain cases, however, short and wide implants, such as in the vicinity of the mandibular canal, may be required. The use of short and wide implants does not, however, provide the required initial stability. Nerve repositioning techniques are therefore constantly being used<sup>2</sup>.

### 2.Diameter of implant

The implant diameter in terms of load distribution to the surrounding bone is more important than long. Diameters for implants from 3.75 to 6 mm can be used. The origin of an implant with a broad-diameter can be traced to the ITI and Ventplant hollow basket models<sup>2</sup>.

### 3.Wide-and narrow-diameter implants and platforms

For threaded screws, the osteotomy site is designed to be a rescue implant. Since then, several therapeutic benefits have been demonstrated. For posterior areas with greater stability and resistance to chewing loads, it is particularly suitable. A straight or tapered screw, a trapezoidal piston, a phase cylinder or a hybrid cylinder tapered screw are the usual models.

Threaded implants often range from 3 to 4 mm with the most commonly used diameter. The standard threaded implant with a thickness of 3.75 mm has a wall of-mm. It is vulnerable to fatigue fractures due to crestal bone loss. In comparison, implants 5-mm and 6-mm have been stated to be 3 and 6-fold more powerful and are subject to risk of fracture, with rating levels of 3,75-mm for

commercially pure titanium (CPTi) implant (7 percent), 13 percent, and 16 percent over the respective 5, 10, and 15 years, respectively. Regardless of its physical properties, a wider body increases the available area for integration considerably and lowers pressure on the interface of the bone-implant (unpublished data). It also reduces load transmission off-axis, which is the strongest at the implant neck and crest; due to its increased circumference. It reduces the risk for crestal overload, normally related to bone loss. A wide platform also improves rough stability by lowering the occlusal table to load platform cantilever and the resulting pressure<sup>2</sup>.

No matter the size of the external hex engagement, large diameter implants perform cyclical charging tests extremely well and display improved screw-loosening resistance (unpublished data). The larger charging system also allows for an emergence profile which is more closely correlated with its natural tooth. Anecdotal reports of increased bone loss were documented on the early clinical experience of broad-diameter implants threatened. Although limited information appeared in literature, it was suggested to overcome these initial difficulties by improving thread pattern and collar layout and gentler and faster surgical techniques<sup>2</sup>.

The need for narrow-diameter implants for maxillary side incisors and mandibular incisors emerged with the introduction of a single-tooth replacement. There are 3.25 mm (hex) and 3.3 mm (octagon) of smallest diameter external implants available. The external male portion has been altered to provide adequate lateral stability and strength, thanks to a reduced charging frame. For thinner and narrower buttons, the 3.25 mm spline is the only exception. The inherent wall density constraints and fracturing capacity make internal partnerships more difficult to change to a small framework. The 3.5 mm Astra implant is actually the narrowest internal communication implant available. Cone screw connection's interface bending strength was 40 per cent higher than a 3.75-mm hex top which means that this diameter and interface can be used confidently. On any other small diameter links, no published data is available<sup>2</sup>.

#### **4.Small-diameter implants: signs, contraindications**

The use of small-diameter implants is demonstrated by unique medical circumstances: a small amount of bone (small alveolar crest) and a small cervical diameter for replacement of the tooth. The use of small implants in some cases prevents regeneration of bones. Several longitudinal studies have shown osseointegration efficacy in treating various types of edentulousness.

The majority of these studies have included 1-4 generic implants (3.75 mm or 4.00 mm). For the installation of a standard implant a certain minimum bone volume is necessary. The whole implant layer must be covered by a minimum of 1 mm bone. Increased risk of complications and failures if the generic implant is put in suboptimal anatomic circumstances. A limited implant diameter (3.0 to 3.4 mm) can be defined where the alveolar crest is narrow or where there is less than 7 mm mesiodistal space. Small-diameter implants in some circumstances can prevent reconstruction of the bone (bone graft, regeneration of the directed bones, expansion of crests) or expansion in the mesiodistal area, at the bone level or in potential prostheses (orthodontics)<sup>2</sup>.

##### **Small diameter Implant indications**

Depending on the kind of edentulousness, residual bone density, amount of usable prosthesis storage, emergence profile, type of occlusion, the choice of diameter depends.

- (1) reduced interdicular bone volume
- (2) narrow ridges and

(3) substituted tooth with decreased mesiodistal predictive space are the signs for small-diameter implantations.

Two types of small-diameter threaded implants (3i Implant Innovations) are present: the miniimplant for small ripples (4,1 mm regular collar), and the Micromini for small rim (3,4 mm narrow ripples).

All types of implants are made of commercially pure titanium of high strength grade 1 in order to guarantee maximum strength. However, the original small-diameter implant body design offers more bulk material between threads. The goal of this model is to increase the strength of the implant and reduce the risk of fracture<sup>2</sup>.

### **Narrow Ridges**

Increasing impact on the esthetic outcome is at the stage in which the crown emerges. If the alveolar crest is less than 6 mm thick, consideration should be given to the use of small-diameter implants. A buccal undercut or advanced mouth resorption may result in a lingual emergence too much. The choice of implants depends on the diameter of the cervical margin crown and on the profile of emergency, when space available for the prosthesis is limited. In lowers incisors and sometimes in maxilla lateral incisors, the mesiodistal prosthesis area is less than 4.5 mm. Often with regular implants with a diameter of 4.1 mm on a collar it is impossible to achieve a satisfactory esthetic result. In order to achieve a better esthetic outcome it is important that the cervical mesiodistal diameter of the implant be slightly smaller than the potential prosthetic crown. The root diameter is inevitably less at this point. An implant with a small collar diameter (less than 4 mm) needs to be considered and may give rise to a natural profile in order to replace a tooth of the mesiodistal diameter equal to or under 4 mm<sup>2</sup>.

### **Morphology of the denture and hypodontia**

There is often a small amount of bone or space in cases of hypodontia (e.g. missing incisor in the mandibular or lateral incisor). Convergence of the neighbouring teeth roots or crowns may be fixed with the care of the anterior orthodontic denture prior to the implant. The potential prosthesis crown morphology should be identical to that of the anterior portion. An esthetic loss may be considered an important difference. The incisor teeth and sometimes the premolars median cervical and coronal dimensions are an indicator for the choice of a specific implant diameter<sup>2</sup>.

### **Biomechanical considerations**

The smaller diameter implants have a lower anchor layer and a decreased resistance to fracture relative to generic implants. The occlusal forces must be sufficiently evaluated before the use of this type of implant is contemplated. Caution is determined by the lack of a long-term analysis for all types of small implants. For the replacement of canines and molars, small implants are

contraindicated. The risk of fractures with fixtures 3.3 mm in diameter is increased, according to Forsmalm. The failure tolerance is 25% less than the standard fittings<sup>2</sup>.

### **Transitional implants**

Some patients may be hesitant to wear the RPD for psychological reasons during an induction phase, while others may find the duration of implants 10-14 days after insertion without prosthesis difficult to accept. These were initially designed for temporary restore and for the load-free incorporation of traditional implants. The MDI system includes a miniature titanium implant that serves as the tooth root and a retainable brace in the dental foundation. The implant head is like a bat, and the retaining attachment functions like an O-ring socket. The Pring clips over the ball when the tooth is sitting and keeps the prosthesis to a standard degree of power. The prosthesis lies on the gum tissue while sitting gently. The implant attachments require micro flexibility while being resistant to natural lifting forces<sup>17</sup>.

Putting the implants in a dentist's office is quick and easy with local anesthesia or mild sedation to make you more relaxed. MDI implants are mounted in the jawbone with a precise, regulated, minimally invasive technique. The implant heads protrude from the gum tissue and give a solid, strong basis to. It is a procedure with minimally invasive surgery and does not suture for the usual months of healing. There will be a little discomfort, but the pain medication that you were given should be limited and regulated. Take the pain reliever only as prescribed if possible. The tooth should be healthy. Any soon as you like, you should eat, but for the time recommended by the dentist avoid overly hard and sticky foods. When the tooth is removed, rinse your mouth with antiseptic mouthwash and clean with a cotton swab and toothpaste around each implant fixture. Four days with a cotton swab. The normal protocol for implant placement in a close mandible following implant placement recommends patients not to wear the tooth decals up to two weeks to avoid immediate loads of the implant<sup>17</sup>.

### **Modular Transitional Implants and Prosthetic System**

Transitional modular implants require transitional implant to be mounted simultaneously with permanent implants.

#### **Uses:**

Makes load free osseointegration for transitional phases.

#### **Techniques for bone strengthening help.**

- Replacement of lateral incisors which are congenitally absent.
- Reparation of bridges that have been destroyed.
- Stabilization of dentures existing.

#### **Use of transitional implants to endorse a surgical guide:**

Enhancing the precision of positioning of implants.

The operative advice for edentulous patients frequently lacks the necessary consistency for the proper placement of the implant. The complexity of the tissue-supported ceramic implant

reconstruction, which involves the precise placing of implants, is highlighted in the edentulous mandible.

Harel Simon has shown, by endorsing radiographic and surgical models in modern implants, that proper planed transitional implants can provide a significant advantage. Nonetheless, it may be difficult to place conventional implants properly between transitional implants and to create a radiographic and operating model using these transitional implants<sup>17</sup>.

## **B. Implant Surface and Coatings**

The implant-to-bone surface has also undergone a number of different developments. The original offerings consisted of machined titanium implants (Branemark), TPS (ITI group),

HA coated (Sulzer Calcitek, Carlsbad, CA) implants. Progressively, the implant surface has been sintered and coated with spherical titanium powder; treated with leaching agents (nitric acid, hydrofluoric acid, hydrochloric acid, sulfuric acid); and air-abraded or particulate blasted (aluminum oxide, tricalcium phosphate, or titanium dioxide of different sizes (25 to 250  $\mu$ m) either singularly or in combination to obtain a controlled surface texture to enhance cellular activity and bone-to-implant contact (BIC). Little question remains that a controlled surface texture enhances cell activity and increases BIC and the strength of integration.<sup>2</sup>

Specific details of the processes are usually proprietary in nature. Manufacturers have marketed these surface conditions under a variety of designations such as Endopore (Innova Corp, Toronto, Ontario, Canada), TiO blast (Astra Tech), SLA (ITI), Osseotite (Implant Innovations), Osteo (Osteo Implant Corp, New Castle, PA), RBM (Lifecore, Chaska, MN), i1TX (Sulzer Calcitek), THD (Steri-Oss), and others. In contrast, the titanium plasma-sprayed surface process, originated by ITI and characterized by high-velocity molten drops of metal being welded to the implant body to a thickness of 0.3 to 0.4 mm, remains essentially unchanged. Its original intent was to obtain a greater surface area for bone attachment. The results of ITI research on surface characteristics have changed its focus from TPS-coated implants to the sandblasted, acid-etched surface (SLA), which produces significantly greater BIC (55%) in comparison to TPS (37.5%).<sup>2</sup>

### **1. Titanium plasma spray coating:**

It is the most common coating method for dental implants because almost all the commercial HA coatings are produced by this technique. This method involves the use of a carrier gas which ionizes (thus forming a plasma) and superheats the particles of the starting material (generally HA), undergoes partial melting as they are propelled toward the substrates to be

coated. Coatings around 50 microns are typically produced on a roughened titanium or alloy surface for a HA plasma sprayed endosseous implant. The most stable of the plasma sprayed calcium phosphate coatings is fluorapatite (FA), which is capable of retaining in large part both its fluorine constituent and high crystallinity during the high temperature plasma spray process. This process has a crystallinity of around 60% to 70%, but higher content can be obtained if the coated implant is heat treated at a suitable temperature after the deposition process. One study showed that a low crystallinity (46% HA) plasma-sprayed implant exhibited about three times the dissolution of Ca ions as a higher crystallinity (75% HA) material. This process leads to more than 6-10 times enlargement of the surface area of the implant body<sup>18</sup>.

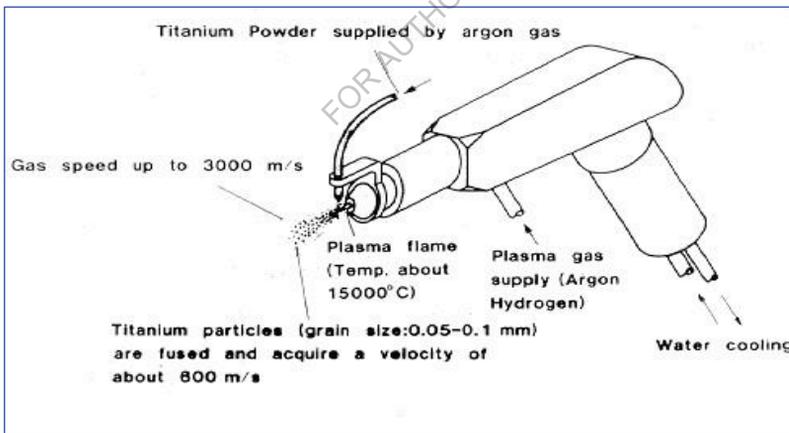
**Advantages:**

It is relatively inexpensive.

The mechanical properties of the metallic substrate are not compromised during the coating process.

**Limitations:**

1. Forms mechanical bonding only with the metallic implant surface.
2. The main source of contamination appears to be copper from the nozzles of the sprayer.



**(ii) Laser induced roughening of the surface**

The eximer laser was used to establish surface roughness (microstructures).

Advantage–Laser can be precisely guided to achieve regularly orientated micro-retention with predetermined angulation.

**(iii) Surface etching and sandblasting:**

Causes implant surface roughness.

The downside of this is that the technological methods avoid contamination. The downside is that metal oxides are removed, allowing the initially rough surface to smooth and flatten.

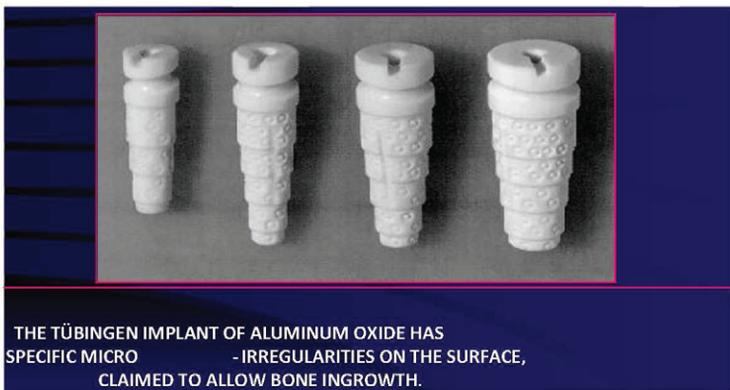
**(iv) Hydroxyapatite coating**

Such coating results in a rapid healing of the osseous tissue and an overall improvement in the bone-implant interface region. On the other hand, precisely this function appears to have an adverse effect on the surface of the implants over the medium to long term due to its instability which results in a breach or total loss of HA. The surface structure is also bioreactive and contributes to a faster treatment of the osseous compared to a metal implant. Bone loss is especially rapid in cases where part of the HA is in direct contact with the oral cavity environment after periimplant osseous resorption. Implant bodies with plasma spray software are also coated with hydroxyapatite. Earlier and greater bone bonding were demonstrated by highly bioactive and osseoconductive, HA-coated implants).

Although the crystallinity and amorphous material are proprietary variations, the surface layer has generally remained similar, with one notable exception. Hydroxyapatite MP-I (Sulzer Calcitek) coatings use a pressurized hydrothermic post-plasma spray system that increases the crystalline HA content of the material from 77 to 96 percent, with 4% amorphous content of the product. The MP-I surface demonstrated considerable reduced solubility over a wide range of pHs, with a decline in HA-coated implant popularity in its early history attributable to anecdotal reports of catastrophic failure and modes. Proofs to the contrary revitalized clinic use. There remains to be seen further development of new techniques for surface coating. The goal of this development is to achieve controlled bioresorption of HA after the anticipated faster osseous healing. Both processes will eventually bring the implant body and the underlying bone into direct contact<sup>19</sup>.

**(v) A combination of various surfaces.**

The use of 2 or more different surfaces on a single implant body is an interesting recent development in surface engineering. The purpose is to enhance the soft tissue response, stability, and attachment in a cortical bone with a coronary implant surface machined or etched and to better mechanically secure the medullar bone with a tough, TPS or HA surface in the middle to apical portion of an implant. Each model involves 4 different surface textures (engraved, stiff-blasted, HA or TPS and an etched apical end) on the same implant corpus<sup>19</sup>.



#### vi) Biomimetic Ca-P coatings

Biomimetic Ca-P coating on surgical, orthopedic, dental, implants to exploit the superior mechanical qualities of substrates including titanium and alloys, alumina, and polyethylene with an ultra-high molecular weight and an exceptional biocompatibility of Ca-P materials.

The biomimetic coating technique is intended to build a thin Ca-P surface of metals or other implant materials from a supersaturated physiological solution for calcification at the ambient temperature by imitating the natural mineralisation of bones or teeth. The biomimetic method provides numerous advantages in comparison with the plasma scraping and is an effective alternative to plasma scraping for medical implants<sup>19</sup>.

A number of different techniques can change the surface of the titanium implant to allow the formation of biomimetic Ca-P coatings. A newly introduced alternative strategy is to substitute titanium dioxide with fluoride phosphate, resulting in a localized deposition of calcium apatite. This fluoroxide surface has low (one atomic percent) fluoride content which contributes to enhanced calcium precipitation by substituting titanium fluoroapatite for titanium phosphate residues which acts as the primary kernel for calcium precipitation. This layer also has special effects on the promotion and differentiation of human proliferation of stem cells with high morphogenic bone protein2 (BMP-2), RunX-2 and bone sialoprotein expression<sup>19</sup>.

The best known method of transport is the packaging of therapeutical and bioactive agents in a Ca-P coating. Ca-P materials are considered to be among the main drug carriers because of their exceptional biocompatibility and wide medical acceptance.

The molecules dissolved in calcificating solution may be adsorbed or incorporated into the forming Ca-P coating throughout the covering process. This allows for incorporation of the respective agent(s) into the coating after processing. The following are a brief overview of studies on the Ca-P coating application, including albumin, BMPs, bisphosphonates, antibiotics and amelogenines, as carriers of various proteins and therapeutic substances<sup>19</sup>.

**Benefits** of the biomimetic method in application of calcium phosphate (Ca-P) covering on medical implants with plasma-sprayed hydroxyapatite

1. Of implants with a complex shape or porous structure, a conformal coating can be shaped
2. Coating for sensitive materials such as plastic implants and tissue engineering scaffolds can be added.
3. In order to achieve the desired Ca-P cycle, a biomimetic system can more be managed than plasma scratcher, which can be accomplished by simply changing the calcificating solutions ' composition
4. The bio-mimetic apatite layer formed by a simulated physiological solution is similar to bone minerals and can have a higher capacity to bind than the PSHA layer
5. A low-temperature biomimetic coating system allows therapeutic agents, such as osteoinductants and antibiotics to be integrated and released sustainably
6. Biomimetic apatite coating adsorbs far more serum protein and amelogenin as nanoporous structure than plasma-sprayed coating<sup>19</sup>

### **Thread design**

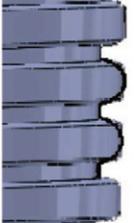
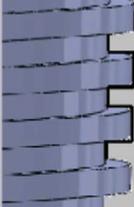
The original Branemark screw, which was introduced in 1965, was put into a threaded osteotomy using a pattern of V-shaped thread. In 1983, the model was modified as an implant for self-tapping in a soft bone at the untreated osteotomy site. The number and angle of cutting threads, a 3 edge conical tip and a wider chip chamber were also further developed. However, the basic V thread and body for a simpler and more efficient positioning has been changed by other manufacturers. Even other manufacturers use a different thread pitch and shallower depth reversed buttress thread for improved load distribution<sup>20</sup>.

Although operational success rates over 95 percent have been achieved generally in most bone densities, bone density appears to be correlated with subsequent performance following loadings. Studies also show a strong impact on the long term maintenance of the Implant-to-Bone interface from biomechanically dependent conditions. High stress levels that are not distributed through the implant body can easily jeopardize the device<sup>20</sup>.

. The design features covering differences in occlusal charges and bone density have been investigated recently. Square threads, with a 3 degree thread angle, were suggested that the shear force should be decreased by a factor of 10 and the compressive load increased, as bone responded to that form of charge distribution more favorably. While conceptual mathematical models predict a more practical load distribution layer, the biomechanically improved layout of the implant will be subject to controlled clinical trials. The implementation of a rounded thread model that causes "osteocompression" for immediate loading was another recent solution. The effect is an improvement in the region of surface loading and a uniform distribution of stress. Potential clinical

trials are expected before any final results can be obtained. The development of dental implants should now include biomechanical theories and principles to further improve clinical performance<sup>20</sup>.

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Type of thread	
<b>Buttress</b>	
<b>Reverse Buttress</b>	
<b>V-shape</b>	
<b>Sinusoidal</b>	
<b>Square</b>	

### **Different thread design**

Astra Tech Fixture ST autocutting screws were originally launched in 1992 to restore a missing tooth and are a high quality autocutting implant with threads designed to secure primary fixation while enabling the charging forces to be distributed favourably. Six lengths from 9 mm to 19 mm and two diameters from 4.5 mm and 5.00 mm are required for Fixture ST. The mount is conical to facilitate installation and reduce surgical pressure on the bone and has a special and optimized texture of the surface, obtained through a strictly controlled production process called 'TiOblast' by Astra Tech<sup>20</sup>.

### **3. THE ABUTMENT CONNECTION**

Definitive abutment connections can be characterized in many different ways.

Available are:

- a One- and 2-piece flat-top.**
- b One- and 2-piece conical shouldered**
- c UCLA-type plastic castable**
- d UCLA machined/plastic cast to cylinders**
- e UCLA gold sleeve castable**
- f One-piece fixed post**
- g Two-piece fixed shoulder**
- h Preangled fixed**
- i Telescopic millable post**
- j Ceramic**
- k Single-tooth direct connection**
- l One- and 2-piece overdenture abutments.**

The initial connections consisted of sleeves of several lengths that were attached to the implant with connecting screws or flat or conical extensions of an I-piece. The original focus was on restoring the entirely edentulous mouth involving multiple implants and a transition region via soft tissue, which could readily break all root analogs with metal bars secured with smaller prosthesis screws (fixed or removable). The resulting renovations looked like a bridge, which was highly functional yet esthetically constrained. The increased use of the implants resulted in a wide range of abutment links and versatility in order to address the ever increasing range of medical challenges. The early transition from an all-edentulous arch to FPD resulted in the creation of 2-piece conical abutments that brought the coronal area ever closer to the implant interface and enabled angulation changes<sup>2</sup>.



Abutment geometry - Flat top

conical

UCLA

### THE UNIVERSITY OF CALIFORNIA AND LOS ANGELES (UCLA)

The advent of the UCLA connection eliminated the intermediate transmucosal connection completely and improved esthetics dramatically. The concept was modified to include an all-machined metal cast to cylinder, a machined interface with a plastic burnout extension, and all plastic castable sleeves. Each one is available with and without an antirotation engagement. The subgingival placement of restoration not only helped with the interocclusal distance limitations but also provided improved esthetics. This also allowed the emergence profile to be more gradual and natural in appearance but it could also be in porcelain instead of usual titanium cylinder<sup>21</sup>

To fabricate UCLA – plastic pattern was designed. This pattern (UCLA abutment) fits directly on top of either the implant fixture intraorally or on the laboratory analogues<sup>21</sup>.

#### Abutment design

Casting is made of at least 50% gold (to decrease adverse galvanic response when connected to titanium). UCLA abutment is made of gold-palladium alloy. The plastic pattern is designed to provide for 1mm collar at the base, located just above the osseous crest on top of the implant fixture. This metal collar at the base of the restoration provides structural integrity for the metal framework and the porcelain without compromising esthetics. The slight vertical extension at the edge of the plastic pattern allows the final casting to be milled for improved marginal integrity between restorations and implant fixture<sup>21</sup>.

The cut back design – allows for porcelain coverage. Two configurations to the base of the plastic pattern are available. One type contains a hexagonal base that matches the top of the branemark implant fixture and the other has round base. The resulting castings that incorporate the hex are non-rotational and are used for single tooth restoration or telescopic

copings. Castings with round bases are used for multiple implant restoration where connection to multiple implants will prevent any possible rotation<sup>21</sup>.

A main consideration with UCLA abutment technique is that the conventional titanium transmucosal abutment cylinder is no longer used. Instead of a titanium epithelial junction, a porcelain or gold alloy epithelial junction exists as the restoration emerges through the soft tissue<sup>21</sup>.

### **Disadvantages**

Verifying the fit of the casting to a transmucosal abutment cylinder supragingivally is much easier than verifying the fit of casting directly to implant fixtures at the level of osseous crest. The conventional branemark implant component consists of gold alloy screw that serves to retain the restoration. This screw is designed to be a weak component of the system. If unfavorable forces are placed on the implant, the gold screw breaks before harm comes to the abutment or implant fixture.

The UCLA abutment restoration however incorporates only 1 screw that connects the restoration directly to the implant fixture. The screw is made of titanium alloy and has higher mechanical properties than pure titanium. Hence unfavorable forces can damage the implant fixture before the screw breaks<sup>21</sup>.

### **Clinical uses:**

- a) Limited interocclusal space – by eliminating transmucosal abutment cylinder (TMC), and the gold alloy cylinder, especially useful for partially edentulous patients and for fabrication of some overdenture tissue bars where it was critical to have a low profile bar.
- b) Better esthetics – as restoration is subgingival with better emergence profile.
- c) Improving angled implants – buccally inclined implants would normally result in a screw access hole on the facial surface of the restoration. Manufactured angled abutments may solve this problem by compensating for the malalignment. However, it is best to fabricate custom telescopic copings. These copings made with the UCLA single tooth pattern so as the antirotational can compensate for various angulation problems. The final restoration can be connected with lingual screw attachment.
- d) Slight angulation problem may be solved with UCLA abutment without the extensive step of fabricating custom telescopic copings<sup>21</sup>.
- e) When implant fixtures are placed too close together – conventional abutment cannot be seated as they contact each other. The UCLA abutment allows the contours of the restoration to be altered to compensate for closeness of the implants. The subgingival portions of the restoration can be made narrower than the manufactured abutment cylinders to allow seating of the restoration.

In some patients, a chronic gingival hyperplasia surrounding the titanium abutment cylinder has been observed, which is unexplained. The solution to this problem may be achieved with the use of UCLA abutment. It allows the emergence of highly glazed porcelain or polished gold alloy through the soft tissues, therefore less plaque.<sup>21</sup>

Although a major advancement, the inevitable problem of a screw access channel persisted. This was especially problematic with angulation changes. The same direct-connection concept was extended further to include a machined hexagonal body with a low-profile shoulder (e.g., CeraOne, Nobel Biocare; and STA, Implant Innovations) that would

receive single-unit cemented restorations. This refinement eliminated the esthetically compromising abutment screw access channel and the vulnerable porcelain-to-metal occlusal interface. Two sophisticated variations of the UCLA concept used to produce custom cast abutments are AurAdapt (Nobel Biocare) and Aurabase (Friadent, Irvine, CA). These permit replication of natural-tooth cervical profiles and can be used in esthetic areas having limited soft tissue height with virtually no facial metal collar. Similarly, machined 1- and 2-piece straight and preangled cementable abutments became readily available. The driving forces were simplicity and esthetics. Initially rather crude with respect to cervical collar size and flare, they have been refined into very user and tissue friendly components that have integrated implant prosthodontics into the arena of conventional fixed prosthodontics. The full extension of this concept is the 2 -piece cementable straight or angled abutment that permits axial correction and shoulder modification to conform to a given clinical situation. Refined examples of this design type are the Angled Esthetic Abutment (Steri-Oss) and MH-6 (Friadent)<sup>21</sup>.

### **Ceramic abutments**

Additional demand for optimal single-tooth implant esthetics has led to perhaps the most exciting development in implant abutment design, the ceramic abutment. The use of a ceramic abutment may be considered when an implant-supported single-tooth restoration is fabricated in an esthetic zone where the occlusal forces are slight to moderate.<sup>22</sup>

It is preferable to take the impression and prepare a ceramic post after the gingiva heals so that the shoulder of the abutment is designed at the correct subgingival height (crown cemented onto ceramic post approach). The ceramic post is especially advantageous when the mucogingival complex is thin and translucent. The risk of decreased luminosity and greyish gingiva shadowing is thus eliminated<sup>22</sup>.

Three different designs are currently available. CerAdapt (Nobel Biocare) consists of an internal hexed high-strength aluminum oxide cylinder that is shaped and prepared with diamond tooling and copious water, quite similar to natural-tooth preparation. Ceramic behavior, however, is significantly more brittle and technique-sensitive. Specific handling requirements must be followed in every detail. The ceramic abutment is directly retained on the implant with an abutment screw at 32 Ncm, and an all-ceramic crown can then be cemented in place. Clinically, whenever ceramic and metal come into contact, the metal will most likely abrade and wear. The same is true for the contact of aluminum oxide with the titanium implant body and gold-alloy screws. The most problematic area is the possible rounding of the corners of the hexagonal during the fabrication process when seating and reseating of the abutment takes place<sup>22</sup>.

The Cera One abutment (Nobel Biocare), mentioned previously, has prefabricated aluminous oxide caps that are used as a core for the production of an all-ceramic crown. The resulting restoration is luted with permanent cement onto the titanium abutment. This eliminates any ceramometal abrasion at the screw seat and implant interfaces but requires absolute confidence in long-term screw joint stability. Another approach in ceramic abutment technology is Cera Base (Friadem), which uses a metal screw seat and platform with a

preparable high-strength ceramic cylinder. A ceramic cylinder or pre-shaped abutment form is tooled with rotary instruments under a copious water supply to conform to the desired clinical form. A conventional all-ceramic crown can then be luted to the ceramic abutment with permanent cement, or the abutment itself can be used as a core for an all-ceramic crown that is screw-retained. In both instances, the ceramic abutment is bonded with resin cement onto the metal-retaining platform.<sup>22</sup>



**Ceramic abutment**

#### **A custom titanium abutment for the anterior single tooth implant.**

Criteria for STR abutment include antirotational capability, titanium construction, ability for mechanical alteration, a machined fit to implant body and retrievability. Christopher Marchack, described an abutment technique given an understanding of the criteria.<sup>23</sup>

##### **Technique**

This technique uses a custom single tooth Procera abutment. The **advantages** of such an abutment include:

Titanium biocompatibility

Non-rotating abutment implant junction

Machined fit to implant

Screw tightening to 32NCms by use of counter torque device of Nobel pharma.

Alterability so that crown-abutment margin can be placed at an ideal level to the gingival crest.

Creation of transitional contours of the tissue and the emergence profile in the gingival sulcus instead of as part of the crown or the prosthesis<sup>23</sup>.

A surgical index described by Hochwald was used to obtain a record of the implant placement at stage 1 surgery. A diagnostic cast that register the implant portion is used to complete a full contour wax up of an ideal restoration with proper emergence profile. The diagnostic wax-up is then converted to acrylic resin template that incorporates a provisional cylinder attached to the head of the implant. The acrylic resin template is duplicated from the diagnostic wax-up by use of vacuum formed matrix. The final root and crown contours are carved with a bur. The template is then cut horizontally to the desired abutment height. The external form of the counter torque is formed with cera-one impression coping, filled with

acrylic resin and the formed template is lifted out. The template of the hex is attached to the root form half of the abutments with cyanoacrylate cement. The final step is to drill an access hole in the center of the abutment. The cast and acrylic resin template are sent to the custom solution lab facility<sup>23</sup>.

The Procera copy milling machine has 2 co-rotating elements. One hold the template and the other titanium block. The template and block are mounted on rotating elements which allow simultaneous longitudinal displacement and rotating along their axes. The milling device automatically cuts and duplicates the outer surface of the acrylic resin template. Provisional restoration is made with previous diagnostic wax up and standard cera-one provisional components.<sup>23</sup>

### **Fabrication of a digitally scanned, custom shaped abutment.**

Numerous implant systems exist that have the versatility to create a custom implant abutment with an anatomic shape. There are “add – to” systems such as non-segmented abutment or the AurAdapt with gold cast to the machined abutment<sup>24</sup>.

CerAdapt abutment has porcelain added to the machined aluminous oxide abutments. In the “preparable” or adaptable abutment category, cylindrical blocks of machined titanium are available in varied diameters and heights. Implant abutments are available in varied diameters and heights. Implant abutments can be prepared with diamond burs or milled to desired shape. Christopher Marchcak describes the use of a digital scanner with CAD/CAM technology to create (copy mill) an anatomically shaped abutment. The advantages of using Procera copy milling have already been enumerated<sup>24</sup>.

The only disadvantage is that the use of titanium abutment necessitates thin gingival tissue, therefore esthetics is questionable. Whereas in the previous technique, the custom abutment had to be prepared by the dentist before sending to the custom lab facility, in this technique the cast that contains the implant analogue is sent to the laboratory. The computer then designs an abutment that would be most suitable for the given situation. This is then copy milled from a titanium block.<sup>24</sup>

## **Ethetic Option for the Implant-Supported Single-Tooth**

### **Restoration — Treatment Sequence with a Ceramic Abutment**

A recent application of Computer Assisted Design/Computer Assisted Machining (CAD/CAM) technology consists of machining an abutment adapted to each clinical situation. This method was first applied to titanium abutments. The initial technique used the Procera 3D CAD (3 Dimensions Computer Assisted Design) (Nobel Biocare AB, Göteborg, Sweden), a computer program that reproduced the position of the implant and allowed for the design of an abutment of ideal shape and tilt. This information was then transmitted to a device that machined the final abutment in a titanium cylinder. Another technique consists of first waxing an abutment on the master model. The surface of the wax-up is then digitalized and the final abutment is machined identically in titanium.<sup>22</sup>

With advances in dental materials and biomechanics, it is now possible to apply CAD/CAM technology to ceramic. Pierre Boudrias, Élise Shoghikian, Éric Morin, Paul Hutnik describes the use of this type of abutment which is composed of a densely sintered

high-purity aluminum oxide. Because of its color, similar to that of natural teeth (~A3 Vitapan: Vita Zahnfabrik, Bad Säckingen, Germany) and its light transmission properties, the reduced luminosity of the gingiva or greyish gingival discoloration sometimes observed with metal abutments is avoided<sup>24</sup>.

Today, the technique to design a ceramic abutment uses only the Procera 3D CAD computer program. The shape of the abutment is transmitted to a machining device that shapes the aluminum oxide ceramic at the green (immature) stage to prevent hairline fractures. The completed high-density ceramic abutment is obtained after the final sintering.

The crown restoration may be done 2 ways. When the longitudinal axis of the implant passes through the center of the lingual surface of the final crown, a screw retained crown is produced by curing the porcelain directly onto the abutment. When the longitudinal axis of the implant traverses the incisal edge of the final crown, the abutment is shaped to receive a cemented crown. Knöde and Sørensen showed that the aluminum oxide abutment had 40% less fracture resistance when compared to a prefabricated titanium (CeraOne: Nobel Biocare AB, Göteborg, Sweden). This component has been designed primarily for a single-unit restoration and a short-span bridge in an esthetic zone where occlusal loads are moderate.<sup>24</sup>

The use of this ceramic abutment is limited to incisor and premolar restorations. Its mechanical resistance is inadequate for molar, canine or incisor replacement when there is an overbite superior to 50%. However, when the occlusal forces are light to moderate (minor vertical overlap, little or no lateral or protrusive guidance), a single-tooth restoration built with a ceramic abutment is acceptable, especially in the anterior maxillary zone where the occlusal loads are less significant and the esthetics more important.<sup>22</sup>

It is possible to machine a ceramic abutment to correct a slight labial tilt of the implant. However, a distinctly labial longitudinal axis of the implant (through the labial middle 1/3) leads to a severe thinning or elimination of the buccal wall of the access cavity. Furthermore, the labial reduction of the abutment to correct its angulation causes a marked weakening of its axial walls and of its labio-gingival collar. The angle created between the longitudinal axis of the implant and the labial surface of the abutment should be well under 30° to avoid excessive thinning of the labial surface of the ceramic abutment that may result in a cohesive fracture.<sup>22</sup>

These ceramic abutments benefit from CAD/CAM technology. With the “crown-cemented-onto-abutment” approach, the shoulder is prepared following the contour of the gingival scallop to a subgingival depth of no more than 2 mm. The regular and uniform placement of the abutment/crown interface facilitates the removal of excess cement. Conversely, prefabricated machined abutments have a circumferential collar and a shoulder at a predetermined height, and the subgingival depth.

Papavasiliou and others compared the stress produced with the 2 restorative methods (crown cemented onto a ceramic abutment and screwretained crown) using 2-dimensional finite-element analysis. The crown cemented onto a ceramic abutment generated a better distribution of occlusal loads and reduced the stress on the thinner portions of the abutment<sup>22</sup>.

Prestipino and Ingber recommend a type of cement based on the desired degree of reversibility. Temp-Bond type temporary cements (Kerr Manufacturing Company, Romulus, United States) offer reversibility. However, these cements offer poor retention and are too

opaque. Adhesive composite resin cements have superior physical properties and do not interfere with light transmission<sup>22</sup>.

The aluminum oxide ceramic abutment is contraindicated when its height is less than 7 mm and the thickness of the axial walls is less than 0.7 mm. The angle formed between the labial surface of the abutment and the longitudinal axis of the implant must be less than 30°. With the “ceramic crown-cemented-onto-abutment” approach, a visible supragingival collar of the aluminum oxide ceramic abutment blends better with a crown that presents a gingival 1/3 with saturated colors.<sup>22</sup>

### **Techniques to Restore Unfavorable Inclined Implants**

An unfavorable inclined implant is a common problem that may compromise esthetics, phonetics and function of the implant supported fixed prosthesis. Several methods have been reported to compensate for malaligned implants; however most techniques are complicated and expensive<sup>25</sup>.

Lewis et al described a technique to resolve severe angulation problems where the UCLA type abutment was used to fabricate telescopic copings with the final restoration cemented over the telescopic retainer. The biggest problem with this procedure was its irretrievability.

Balshi reported a double casting technique to resolve esthetic complication with unfavourably aligned implants. An overcasting was secured to a rigidly fixed substructure with a tube and screw system producing a screw retained restoration, which was retrievable. However, it was bulky and only suitable for multiunit fixed detachable prosthesis. Standard angulated abutments are available from most implant manufactures. These abutments can be used to fabricate esthetic screw retained prosthesis. Mc-cartney et al have described a technique to modify the angled abutment to maximize esthetics. Recently a technique that uses custom fabricated abutment was introduced to correct the angulation of implant. This system incorporated a manually milled screw access hole in to the custom abutment for the set screw that retains the final prosthesis.<sup>25</sup>

### **Disadvantage**

Cannot be used for single tooth replacement as the system does not contain an anti rotational component.

It is impossible to transfer the exact position of the initial thread to the implant analogue, hence the custom abutment may require over or undertightening to ensure precise seating.

### **Advantages**

Inexpensive, uncomplicated technique for creating access holes in virtually any location with most desirable angulation.

### **Maintenance of a complete retrievability.**<sup>25</sup>

A combined technique has been developed by Marcus Lima that incorporates the advantages of the UCLA abutment (plastic bur out pattern) and the just described IMPAC custom abutment but eliminated the disadvantages of both systems.

### **Technique:**

Final impression is made to make a master cast. Place castable UCLA type hexed plastic abutment onto the implant analogue to evaluate angulation. Use surveyor to determine the

most favorable path of insertion. Trim the excess length from the UCLA abutment and develop a custom wax pattern with a chamfer margin for each abutment to reorient the inclination of the abutment along the predetermined path<sup>25</sup>.

Drill a hole at least 3mm deep in each wax pattern accessory kit for the desired setscrew location. Place ceramic rods into the access holes. This is then invested and cast in type IV gold alloy. Upon divestment, place the custom abutment on the master cast and verify path of insertion. Use the IMPAC custom abutment kit to prepare the screw threads in the custom abutment. Place the retaining screws in each abutment with a 0.5mm space between screw head and abutment surface. Lubricate the abutments and develop a plastic burn out pattern. For the coping create a housing or countersink in the plastic pattern for the head of the setscrew that retains the final prosthesis.<sup>25</sup>

#### **4 CRITICAL LOOK AT THE SCREW MECHANICS INTERFACE / ABUTMENT**

It is necessary to understand why screws are loose, to understand how the torques can be stable. This device is called a screw joint when two pieces are locked together by a screw. The torque rises only if external forces are greater than the pressure to separate the pieces.

Powers that aim to decommit bits are referred to as combined powers of separation. It can be called the clamping force the force holding the pieces together<sup>26</sup>.

(1) Maximize the clamping force and (2) minimize joint break forces.

There are two key factors involved in tightness of implant tissue. Screws are tensioned to produce the clamping force larger than the external force that tends to separate the joint in order to achieve secure assemblies. In the design of a rigid screw joint, the first clamping force produced by tightening the screw is the most important functionally. Fastening pressure more than tensile strength of screws influences joint stability. Tightening torque is typically the proportion of the clamp load<sup>26</sup>.

Torque is a simple and observable way to create the desired tension. Too small a torque will separate and lead to failure or loosening of the screw tiredness. Too big a torque will cause the torque to fail or screw threads to be removed. The torque applied generates a force called preload in the screw. The initial pressure load on the screw is preload. This tensile pressure on the screw creates a compressive force of clamping between the parts. The preload of the screw is therefore proportional to the force of the clamping. The following factors decide preload:

1. Applied torque.
2. Screw alloy.
3. Screw head design.
4. Abutment alloy.
5. Abutment surface.
6. Lubricant.<sup>6</sup>

Torque is used for the primary preload determinant. The greater the torque, the greater the preload. The torque that can be used is limited by two factors. Both the physical limit of the torque and the way the torque is used are limited by the torque. Torques may usually be applied more than those with small handles by scrubbers with larger handles. Usually no hand screwdrivers can exceed 20 Newton cm (N-cm) torque. If larger torques are required, a wrench can be used. With a screw, it is practically possible to apply more than 30 N-cm torque. Total preload is formed theoretically shortly before a torsional screw fracture takes place<sup>26</sup>.

Therefore, a safety margin is developed in order to increase preload and reduce the risk of screw fractures during use. Tightening a screw until a torque fails will decide the optimum torque quality, 75% of which is the maximum torque on the screw. In this way an effective clamping force with a minimum risk of screw fracture can be created. A pre-load is formed if a screw is tightened for a crown to an implant. With the tensile force generated within the screw, the implant is compressed to the crown. The fact is that restorations with implants are constantly vulnerable to joints. The following factors play a role like<sup>26</sup>:

- . Excursive contacts.
- . Off-axis centric contacts.
- . Angled abutments.
- . Wide occlusal table.
- . Interproximal contacts.
- . Cantilever contacts.
- . Nonpassive framework.

Maximizing joint resistance for close implant screws, major procedures are summarized as follows:

1. Implants paralleled to occlusion forces.
2. Occlusion in a long implant axis that is calibrated to control forces.
  - a. Eliminate connections for posterior function and stability.
  - b. "Centralize" centric "contacts.
  - c. Share anterior guidance with natural teeth.
3. Antirotational feature engaged for single teeth.
4. Components tightened with 20 to 30 N-cm of torque (unless specified by manufacturer).
5. Passively fitting frameworks for multiple unit restorations.

In 1992, English published an overview of the then available external hexagonal implants, numbering 25 different implants, all having the standard Branemark hex configuration. The external hex has since been modified and is now available in heights of 0, 7, 0.9, 1.0, and 1.2 mm and with flat-to-flat widths of 2.0, 2.4, 2.7, 3.0, 3.3, and 3.4 mm, depending on the implant platform, the available number of hexagonal implants has more than doubled<sup>26</sup>.

## **5 IMPLANT/ABUTMENT INTERFACE**

The implant/abutment interface connection, by convention, is generally described as an internal or external connection. The distinctive factor that separates the 2 types is the presence or absence of a geometric feature that extends above the coronal surface of the implant. The connection can be further characterized as a slip-fit joint, where a slight space exists between the mating parts and the connection is passive, or as a friction-fit joint, where no space exists between the mating components and the parts are literally forced together<sup>2</sup>.

The mating surfaces are further characterized as being a butt joint, which consists of 2 right-angle flat surfaces contacting, or a bevel joint, where the surfaces are angled either internally or externally. The joined surfaces may also incorporate a rotational resistance and indexing feature and/or lateral stabilizing geometry. This geometry is further described as octagonal, hexagonal, cone screw, cone hex, cylinder hex, spline, earn, cam tube, and pin/slot<sup>2</sup>.

Currently, there are some 20 different implant/ abutment interface geometric variations available. The geometry is important because it is one of the primary determinants of joint strength, joint stability, and locational and rotational stability. It is critical and synonymous with prosthetic stability. With few exceptions, most of the long-term clinical data on performance reported in the literature involve the external hexagonal. This is primarily the result of its extensive use, the broad number of prescribed clinical applications, the level of complications reported, and the resultant efforts to find solutions<sup>2</sup>.

In its original context of utilization, the hexagonal was used to restore the completely edentulous arch. All the implants were joined together with a rigid metal superstructure, and the external hexagonal and simple butt and bevel joints performed quite well. Long-term stability simply required an accurately fitting framework and adherence to basic mechanical principles. In more complexes, in-line, partially edentulous, and single-tooth applications, the interface and its connecting screw are exposed to more rigorous load applications. The retaining screw is no longer shielded from stress and is subject to lateral bending loads, tipping, and elongation, which result in joint opening and screw loosening. Short, narrow external geometry is particularly vulnerable because of the limited engagement of its external member and the presence of a short fulcrum point (small platform) when tipping forces are applied<sup>2</sup>.

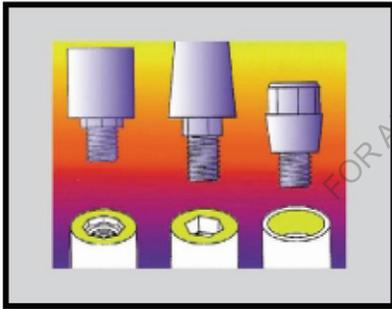
This deficiency was originally noted by Branemark, who recommended that the external hex connection be a minimum of 1.2 mm in height to provide both lateral and rotational stability, particularly in single tooth applications. The original 0.7-mm design and its countless clones, however, remained unchanged until recently, when wider and taller hexagonals were introduced. Hexagonal screw joint complications, consisting primarily of screw loosening; the consequences of maintaining an unstable geometry in practice can be significant. A 22-month follow-up on external hex implant prosthesis in a private prosthodontic practice reported the incidence of loose screws in fixed and removable prostheses at 27% and 32%, respectively<sup>2</sup>

During the past 10 years, all major manufacturers have recommended specific torque application to abutment screws and sell system-specific torque wrenches. Although controlled torque application and altered screw designs have significantly improved performance, they have not eliminated the joint problem entirely. Haas et al reported on 76 single hex implant/abutment interfaces with high torque and improved screw configuration and observed 16% loose screws during a mean observation time of 22.8 months. In a 5-year follow-up report, the same authors reported a 9% occurrence of abutment screw loosening during the last 3 years. Subsequent modification of hex

height and width, in concert with an increased loading platform, has further improved performance in laboratory tests (unpublished data, 1997). However, several factors still remain unresolved<sup>2</sup>.

Clinically, it is often difficult, even for the experienced operator, to seat components on the hex easily and with confidence, especially in the posterior part of the mouth. From a clinical perspective, perhaps the most vexing problem is the rotational misfit that occurs when an abutment is fitted to the working cast analog and then transferred to the implant in the mouth to receive a cemented FPD framework. Minute rotational changes at a single abutment location can result in misfit of the superstructure.

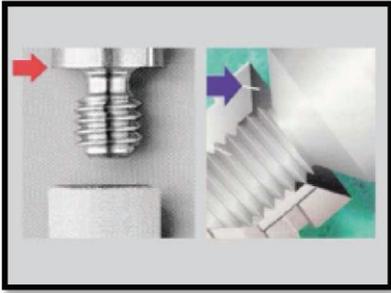
This problem is compounded further in complex, multiple-implant-supported FPD at each transfer. In response, some manufacturers have made great efforts to improve the tolerances of the standard hex and the corresponding abutment recess. The wider and taller hex configurations have reduced this problem, since they are easier to machine and generally have tighter tolerances (unpublished data, 1997). As such, they have demonstrated reduced rotational misfit but have not completely eliminated it. However, 2 different design changes have essentially eliminated all rotation between the implant hex and the abutment. One consists of adding a 1.5% taper to the hex flat and a corresponding close-tolerance hexagonal abutment recess that is friction-fitted onto the hex (Swede-Vent TL, Paragon Implant Co, Encino, CA). The other involves the addition of microstops in the corners of the abutment hexagonal that engage the corners of the implant hex (2R Abutment, Implant Innovations Inc)<sup>2</sup>.



Internal non rotational features: (a)octagonal (b) hexagonal (c)cone screw



Spline attachment



2 piece internal connections (a) Butt joint (b) Bevel joint(angular)



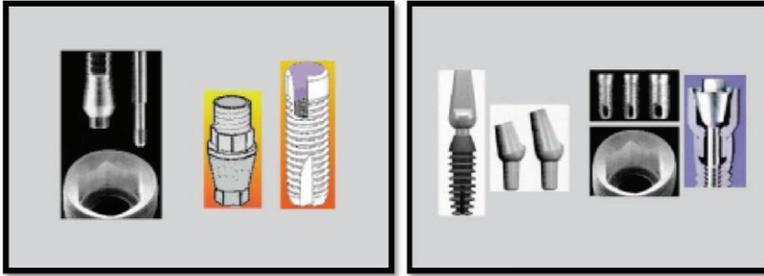
Figure 1

Figure 1-Example of slip-fit, 2-piece, threaded anti rotational cylinder



Figure 2

Figure 2-Examples of slip-fit, 2-piece, non-anti rotational, resilient hex with hermetic seal interface and non resilient internal connection.



2-piece interface tapered hexagon that incorporates a frictional wedging effect and a retention screw

A number of alternative connections have been built to address the inherent design limitations of the existing hexagonal connection. The most notable of these are the cone pin, the cone hex, the internal axis, the hexagonal, the Morse taper, the spline, the inside spline and the strong attachment.

The octagonal model provided a minimum of rotational and lateral stability during operation, thanks to its 0.6 mm thin walls and small diameters that had a geometry profile similar to a circle. A polymethylene insert theoretically replicating the periodontal membrane and buffered implant charging was provided by the robust IMZ link. Chronic maintenance issues impacted success with a metal insert and prompted a redesign. The North American sales effectively ended ownership exchange and conflicts over distribution rights. Ultimately there are 2 other external links besides the hex. One is an outside octagon, and the other is a parallel key or a break<sup>2</sup>.

The external axis is a single I-piece implant with a narrow diameter of 3.3 mm and 3.5-mm for mandibular anterior use. (ITI Narrow Neck). The high octagonal extension with a highly tolerant size offers a 45 degree rotation, moderate lateral resistance and rotational force. There are 6 external parallel keys (splines) alternating with 6 grooves in the Spline implant connection (Sulzer Calcitek).

Geometry of splines is available in 2 models and 3 platforms. The platforms of 4 mm and 5 mm have the same geometry and are solid and mechanically stable, with minimal rotational motion and loosening of the screw. Nevertheless, there is a quite different structure of the spline in the 3.25 mm implant. Thinning, narrower splines, and narrow loading platforms, make the design brittle and insecure. On the reliability of this system no medical reports have been released. Internal interface designs offer reduced platforms of vertical height for restore components; deep lateral load distribution in the implant; shielded abutment screws; long wall mounting to create a strong, cohesive joint opening body that can withstand the joint; wall mounting with the implant which buffers vibrations. It was built upon a mechanically sound, steady and self-locking interface from an inner tapering link<sup>2</sup>.

The suppression of submergence during osseointegration, resulting in a 1-stage functional procedure, was another development that was first promoted by this model. Although the contact is known as a Morse taper, the angle of connection between the components is 8 ° C. There is a genuine Morse taper at 2 ° and 4 ° and it has special thread-free locking characteristics. Without its retaining screw part, the eight-degree relation would be doubtful. Nevertheless, the combination of

two stabilizers has led to a solid, reliable and foreseeable connection. Conical links need precise machining and tolerances, which are consistent and excellent for this manufacturer. There are basically two separate abutments: the initial "octa" shortened abutment with machined cast-to-coping which uses existing implant bevels for screw strengthening, while a straight post for cemented FPD applications can be adjusted. There is no antirotational feature in the joint structure, and the application of the proper tightening torque and the friction resistance of its tapered walls is most important. The long wall mount supports the screw and increases the screw resistance. There are however instances of screw loosening in certain medical studies. A survey of 174 implants in a multi-center study reported that 8,7% of prosthetic and 3,7% of the cone shafts were loose at 6 months.

Astra Tech is available with a similar cone screw connection with a 11 degree taper. It does not connect the existing belt to the implant and offers different length extensions with a 20 ° and 45 ° conical face. The abutment configuration is different. The original 11 degree cone design was based entirely on the resistance of the screw and friction. This geometry has been adapted for single-implant applications into a 2-piece abutments with anti-rotation hex at the tip of the cone (ST, Astra Tech). A screw is fixed to the abutment in the implant. The long conveyed wall mount provides excellent lateral load resistance, some resistance to friction and a stable interface shield. Mechanical test values are excellent and medical results are very reliable. The conical joint is nearly 60 percent stronger in terms of stiffness characteristics between the conical and outer hexagonal joint. There is conflicting evidence of the cone screw which requires a loose torque higher than the torque originally applied. Sutter et al. registered a loosening torque greater than the original tightening torque needed for ITI connections (124%)<sup>2</sup>.

Other tests have shown that the loosened torque is 80 percent to 85 percent of the original tightening torque for both 8-degree and 11-degree connections (Unpublished data, 1997). This basic concept has grown into a number of specific interfaces. The initial offer is a slippery reference, close to the inner octagonal, with the male hex extending from the abutment. The vertical height of the repair platform was reduced successfully and the sitting components were facilitated. Following changes from one supplier, the result was a longer hex with a 1 degree friction-fitting taper (ScrewVent TL, Paragon Implant Co).

In the narrow (3.5-mm) configuration, in conjunction with insufficient treatment preparation and overload, the inner leads obtained by the male hex, a small implant wall, and the press-fit seat interference may result in a fracture in the wall. A horizontal shelf sits directly below the plumb in the 4.5 and 5.7 mm bodies underneath the plumbing. This has enhanced strength and fatigue resistance together with increased wall thickness. The slip fit hex interface is a special interior design that stretches up to 5 mm (Frialit-I and Friadent) in the implant body. On the abutment link, the hexagonal interposes the top to the bottom cylinders. The hex offers 60-degree indexing and rotational resistance. The cylinders have great lateral stability, joint opening resistance, anchor safety and very high strength values. If the joint fails, the implant remains intact and only the abutment fails. The gui is also very touchy and almost sits down on the edges. The interface has a circumferences to allow the bacterial penetration of the joints (Hermeseal, Friadent), to be minimized effectively by a silicone joint. Mechanical tests show good strength, minimal rotation, superior stability of the screw and loosening resistance and excellent tolerances for machining. There's a wide range of abutments and they're incredibly easy to sit. The manufacturer is scheduled to release a narrow platform (3.3-mm or 3.5-mm) this year, available on 3.8-mm, 4.5-mm, 5.5-mm, and 6.50-mm platforms<sup>2</sup>.

Two modern, concept-like but very different internal models have entered the market. Replace Select is a profound cam tube system incorporated into an existing body layout that is growing. The long tube insert gives excellent lateral stability and the cams are comfortable to sit and index. The second entry is a cylinder cam which was available in Europe for short periods, called Camlog (Altatec Biotechnologies, Irvine, CA). It is also fitted with a deep cylinders which are 60% stronger than existing hex models on the internal walls of the implant. Three projections of lateral cam include indexation and anti-rotation. The implant body of Camlog is a hybrid tube, with 6 wide threads on top of 1/3 of its surface. No information from the manufacturer or literature is available on either model at present. A true Morse tapered implant interface communication without a threaded part is possible (Bicon, Boston, etc.). The abutment is tapered 1-2 degree to fit into a smooth mirror-image shaft in the implant. The pillar is positioned on the long implant axis with a sharp blast. To ensure the friction match and provide optimum resistance to dislodgment it requires a dry, clean stall post and an implant shaft. The exact abutment position cannot be transferred with consistence and repeatability without any indexing function. Intraoral adjustment of the straight and angled abutments is complicated in complex multi-implant FPD applications<sup>2</sup>.

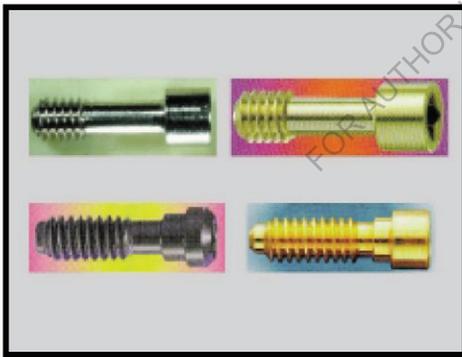
For the intact abutment, the manufacturer's preferred removal approach is to twist and turn with forceps. Therefore, it can be difficult to remove a fracturing abutment post and retrofit a new abument. Although the attachment has shown durability, it lacks versatility from a restorative perspective. The general emphasis is obviously on profound internal joints, where the screw is loaded or unloaded and provides intimate contact with the implant walls to endure micromotion, resulting in a strong stable interface. In order to avoid joint failure, it is necessary to comply with unique medical and mechanical criteria. The resistance they provide to joint separation forces is a potential advantage of the anti-rotational characteristic used with dental implants. Applied strength may clarify the partial solution given by these instruments if vertical walls are linked between the hexagon and the crown. This event also explains why shorter hexes will break some screws under heavy loads. If fit is right and the occlusion is appropriately calibrated, further medical gain should be a longer and closer presence of features. One of the best strategies of screw loosening is to maintain the tightness of the twins. The clinician for novices sometimes underestimates the aspect of the implant. Yes, using a counter-torque method is the best way to apply higher intraoral torque values. The total strength of the bone interface should be zero, if the countertorque is added to the abutment when the screw is tightened. Torque levels are currently expected to deliver substantial preloads in the 20-30 N-cm range without risk for the bone interface<sup>2</sup>.

#### **ABUTMENT SCREW DESIGN:**

Material, shank size, numbers of threads, diameters, weights, thread sizes and torque applications have also modified the abutment-retaining screw (data not released, 1998). Completely new interface coupling geometries of second and third generation were also implemented in the implant environment to address intrinsic hexagonal shortcomings. A number of new implant body forms, diameters, thread patterns and surface topography were added alongside the evolution of the coupling geometry. The abutment screw has developed in order to maximize preload and mitigate the loss of the input torque in frictions to address additional problems with joint instability. It currently has a pan (flat) head table, long stem length and 6 long lengths of thread. The increased length of the stem tends to achieve maximum extension and the shorter lengths of the thread reduce friction. A greater preload is obtained if less torque is lost to friction and heat<sup>2</sup>.

The construction material is the most important factor in the bolting characteristics of the pipe, and many changes have been made by manufacturers. The frictional resistance from "galling," which results in adhesive wear that occurs in the slipping contact of 2 such materials, restricts preloading characteristics of titanium tissues, between the titanium of the implant threads and the titanium of the tissues filling. Hence the transition to a gold alloy screw which is lower in friction, is tightened more effectively to higher preloads and doesn't hang on to titanium, a gold alloy screw may achieve preloads of more than 890 N at approx. .75% of its yield strength, which is more than twice as high in titanium (S. Hurson, personal com screw).. Proper handling of gold screws is a problem because the tightening of the threads will deform. The use of the gold screws should therefore be limited to the final application. It is therefore recommended<sup>2</sup>.

Dry lubricant coatings on top screws are added to further reduce frictional resistance. TorqTite (Nobel Biocare) and Gold-Tite (Innovations Implant) are the most notable. TorqTite is a patented Teflon coating used on titanium alloy screws that has been reduced by 60% (S. Hurson, Personal Contact, 1999). The data indicate a significantly lower cost than its gold alloy equivalent for feasible preload of titanium alloy screws. The method of Gold-Tite is to cover the standard 0.76 pm gold-alloy screw. The supplier estimates that the preload for the coated screw has increased by 24% by a tightening torque of 32 Ncm. Another problem is the rubbing by repetitive tightening sequences of the laminated / plated screws. Despite independent research and clinical trials, the effectiveness of this technology on screw joint stability still has to be thoroughly reported.<sup>2</sup>



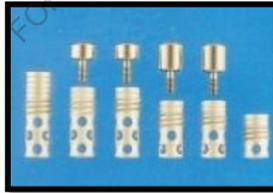
New screw designs: titanium (alloy) and gold-palladium alloy pan head screws with fewer threads and long shank for optimal elongation. Coated screws to reduce frictional resistance titanium-coated Teflon screw (TorqTite, Steri-Oss) and gold-plated gold-palladium alloy screw (Gold-Tite, Implant Innovations).

## 6. DIFFERENT OSSEOINTEGRATED IMPLANT SYSTEMS

Endosseous implant growth in material and design improvements continued through the early implant research. The successful and sound work of the Swedish team will lead to an effective and previsible predicted clinical treatment for the osseointegrated endosseous implant. Other implants have been marketed as osseointegrated implant systems since the initial marketing of the Branemark Program. For the design of the other program now on the market, the knowledge gained by the Swedish team from its years of experience was used. While research into comparing all the system simultaneously is minimal, there should be some analysis of the process.

### THE CORE-VENT IMPLANT SYSTEM

The main implant system consists of 5 root type implant cylinders and 2 prototypes for plates or blades. The advantages of a hollow-ventilated tube is the apical section and of a straight autotaping thread in the upper part are combined with a second stage implant. It was designed in 1984, 1985, 1986 by Grenald Niznik. Such devices offer a variety of schemes, including Core-Vent, Screw-Vent and Micro-Vent. Constructed of titanium alloy (Ti-6Al-4V), with a tensile strength that is 60 percent higher than pure titanium commercially. The implant grade with or without the bone can be mounted on the implant in 8.0 mm, 10.5 mm, 13.0 mm, 16.0 mm length and 3.5 mm, 4.5 mm and 5.5 mm width with a smooth chest. Internal 4.3 mm, 5.3 mm and 6.3 mm thread diameter are available<sup>27</sup>.



Lyndon studied the impact on osseointegration of commercially pure titanium implant surface topography and noted that cPTi enhances contact bone and mechanical properties at interface to implants.

Screw Vent is available in 4 sizes 16 mm, 13 mm, 10 mm and 7 mm, which is 0.5 mm narrower as a core vent implant with diameter 3.75 mm than the shortest. Similar to Noble Pharmaceuticals and Swede-vents, it is made of pure titanium similar in industrial nature, content and size.

Threaded up to top, self-tapping is given, although a hand tap.

The dimensions of the neck equal the diameter of thread so that counter sinking is not required<sup>37</sup>.

Implant for a cemented angled or straight abutment attached to the abutment with a straight screw.

Acid is painted on the surface.

Microvent-made of hydroxyapatite coated titanium alloy with a length and width of 3,25 mm, 7 mm, 10 mm, 13 mm and 16 mm, with a central hole in hex thread for the connecting of a threaded pad or a hex hole for a cemento link. It comprises parallel pins, 3 apical threads, with vertical anti rotational opening. Collar 0.25 mm is broader than the core vent and the fluted body only withstands the same load. The vent system is the core vent<sup>28</sup>.

**SWEED**–Wind Implant–Nobel drug direct copy but the surface is acid etched. These are sold in lengths of 3.75, diameter of 4mm and 7,10,13,15, and 18 mm.

**Biovent**–the corevent's latest addition. Form and similar in nature to the Interpore or Calcitek Integral Hydroxyapatite Coated IMZ Implant. This implant system is fitted with vertical anti-rotational slots and an apical loop and apex depression to ensure complete implant location and rigid integration in the presence of horizontal forces. For Biovent, all core vent abutments can be used<sup>28</sup>.

**Sub-vent**–The implant is a frame or blade type, with widths of 1.2 mm & 2.4 mm & 26 mm lengths. 34 mm and every 14 mm height. Two abutments, tapered titanium abutment for modern FPD and a castable plastic surface for a fixed flexible prosthesis are used to be bendable posts<sup>28</sup>.

The strong vent or Microvent implant is indicated in the following conditions over the hollow cylinder core vent implant

1. Due to smaller dimensions, it is possible to put the mesio distal length in the resorbed ridge or in situations where the max lateral incisor is restricted or removed.
2. The lower lumbar tube, maxillary sinus or nares may be filled with fibrous tissue as a bone when perforated by core vent implant. Used as a solid pin, the penetration can be dressed and the implant body can grow bones<sup>28</sup>.

### **Prosthetic Applications**

This system offers 12 threaded and 10 cemented prosthetic abutments options to achieve the esthetic and functional goals of restorative dentistry. It may be designed with hex holes for threading of implants, with hex portion extending full length of the hole to accept cemented abutments or with internal threading below 2mm of a hex hole to accept both cemented and threaded abutment<sup>28</sup>.

### **Fixed prosthesis**

4 abutments for fixed prosthetic application having tapered and straight emergence profiles with narrow neck, allowing extension of the margin of restoration subgingivally, if necessary. two of the abutments are designed for cementation.

Plastic coping insert made from, castable acrylic can be modified either directly in the mouth or indirectly by a transfer system of analog on working cast. The custom cast post can be fabricated in semiprecious alloy or type IV gold alloy.

Titanium coping insert provides 4° of taper on 3 sides and 9° of taper on the fourth side. It is used when implant is placed in almost perfect angulation compared to adjacent abutment.

Titanium threaded insert, connects to a threaded implant and hence cannot be bent. Used for retention of fixed – detachable prosthesis with a fixation screw.

Rudd in a study stated high degree of frame accuracy can be more difficult to achieve when a single fixed prosthesis uses different root form implant systems. He states the use of semiprecision attachment or modified abutment system and one piece frame design as possible solutions<sup>28</sup>.

### **Fixed – detachable prosthesis**

4 Different attachments in this system are available; these attachments can be used with internally threaded implants for support of fixed bridges retained by fixation screws. If angulation is not within 7° on all inserts framework can be fabricated wrist on top of the inserts with screw being placed independently, eliminating the concern of parallelism. The titanium screw insert denture and titanium straight inserts have a straight walled head on a bendable, cemented or thread post. The insert can be bent slightly to prevent encroachment of soft tissue and can be splinted with a over denture bar<sup>28</sup>.

### **Complete – edentulous prosthetic option**

A fixed prosthesis similar to a 12 unit conventional FPD can be fabricated. A fixed hybrid prosthesis, which is a combination of acrylic teeth and metal framework may be cantilevered off anterior implants or connected to anterior and posterior root or blade forms. An implant-supported overdenture retained by attachments can also be done<sup>28</sup>.

### **The Steri – Oss implant system**

This system by Denar corporation incorporates 2 stage screw shaped implant made of 99.5% commercially pure titanium. Versatility of 5 types of prosthetic attachment allows for flexibility in treatment planning.

These implants are available in 3 diameters which are color coded. 3.8mm mini series. Color coded – white has 2mm long straight polished neck and is available in lengths of 8mm, 10mm & 12mm indicated when bone height is limited. 3.5mm series (red) and 4.0mm (blue) have

4.5mm long tapered neck, with uppermost 2mm polished available in 3 lengths, 12mm, 16mm & 20mm used when uneven ridge shape will cause a portion of neck to be exposed<sup>29</sup>.

Implant has 3 different areas

1 Highly polished neck to enable long term maintenance of soft tissue around the implant. Tight fit prevents the invasion of soft tissue during healing phase, also as internal threads to accept a wide range of prosthetic attachments.

2 Screw shaped body – immediately rigid fixation in to the bone is provided by this part. Thread design distributes vertical occlusal loads uniformly throughout the bone while maximizing the volume of bone between the threads. Acid etching produces extremely clean uniformly textured surface for better integration.

3 Self threading implant tip allows for implant to be screwed in to soft bone like maxillae without tapping.

### **Prosthetic Attachments**

4mm tissue abutment is used as an extension of implant through the soft tissue which accept both threaded and cemented restorations. Adjustments of 2mm in abutment length can be achieved by combining the different – length abutment with the tissue abutment. For example 3mm –o ring attachment is used for tissue thickness of up to 2mm. 1mm – o ring attachment may be combined with tissue abutment to accommodate tissue up to 4mm<sup>29</sup>.

Transfer pins are used to transfer implant location from mouth to the cast. Coronal screws are available in 5.5mm & 12mm lengths for construction of tissue bars for overdentures, full arch fixed removable bridge work. Each screw is with a matching plastic sleeve used as a burnout pattern and incorporated in to the wax up of the prosthetic superstructure, the sleeves mate to the tissue abutment or implants with flat surface, therefore nonparallel implants may be restored without correcting path of insertion<sup>29</sup>.

### **Telescopic abutments**

Available in 5.5mm & 7.5mm length. Each come with a transfer coping, plastic laboratory coping and coping screw abutments are available in 18 degree taper. These are used as distal abutment and for short span fixed removable bridges<sup>29</sup>.

### **Fixed abutments**

7mm & 9mm screw in tapered abutment with 5 degree taper. 7mm straight cementin, 15 & 20 degree cementin abutment plastic castable abutment for ‘O’ ring & magnetic attachments. Surgical kit – internally irrigated titanium nitride coated surgical burs. Anterior pilot drills – 12mm, 14mm, 16mm & 20mm. Posterior pilot drills 8mm, 10mm & 12mm with 2mm diameters sizing drills.

3.8mm series. Anterior drills 12mm 14mm & 16mm. Posterior drills 8mm, 10mm & 12mm. 3.5mm & 4.0mm series – Anterior drills 12mm, 14mm & 20mm. Posterior drills 12 & 16mm. Counter bores, thread formers, for 3.8 series of implant length 12mm, 14mm & 16mm & posterior thread formers of 8mm, 10mm & 12mm for 3.5 & 4.0mm series. Anterior thread formers for implant length 12mm, 16mm & 20mm & posterior thread formers for implant length 12mm & 16mm length<sup>29</sup>.

## **THE ITI IMPLANT SYSTEM**

In 1974, the ITI implant system was formed as an international implantologist team which consisted of dentists, bioengineers, histologists and dental scientists. On insertion and promotion of the bone implant system, they use the principle of primary initial stability<sup>30</sup>.

By sprayed ITI-Titanium plasma screw two separate implant systems were created.

Titanium plasma sprayed screw.

-Titanium plasma sprayed hollow – Cylinder implants.

### **Titanium screw sprayed plasma**

It was developed together with Philip Lederman and Strauman. Titanium screwed plasma Initially used for treating edentulous mandible, which is now used to treat one tooth replacements, bridge abutments made of commercially pure Titanium and Titanium pulverized plasma that increases the contact of the region with 6 folds. 5 lengths available in 9 mm, 11 mm, 14 mm, 17 mm and 20 mm and 3.5 mm and 4.2 mm. 12-degree conical head with four slots to avoid prosthesis rotation and support implant seating. The head is also threaded internally with 5 mm deep bowels which allow the super structure to be removed by anchoring 4 or 8 mm long 2 mm wide occlusal screws. Below the head is a slightly concave, highly polished chest, which ensures good oral hygiene. The remainder of the piece is coated with plasma. In order to allow the self-stopping of threaded implants, Apical HP is fluted to 120°. The value of the chemical performance of implant surfaces has been stated by Per-olof Glantz. The material properties of alloplastic materials affect implant retention and stability and thus allow osseointegration to be achieved<sup>30</sup>.

### **Prosthetic Technique**

Transfer coping of prosthetic technique is positioned over the heads of an implant. Impression and transfer copings are created and removed. In the copings, the master die is inserted and sealed with sticky wax. The Master Model is poured— the implant heads are reproduced exactly with gold telescopic coatings. A set of rods are welded to every gold coping, whether pre-made or casted, securing the whole structure rigidly. This connector bar is then inserted into the implants and sealed using an occlusal screw within 48-72 hours<sup>30</sup>.

### ITI hollow cylinders

Hollow, geometric, titanium plasma sprayed surface are developed of which 3 shapes have evolved F K & H.

Implant	Site	Indication	Contraindication
F	Max or Mandible	Single tooth replaces & fixed bridge prosthesis	Inadequate bone width
H	Maxillae or Mandible	Narrow alveolar ridge, fixed removable prosthesis	- - - - -
K	Maxillae or Mandible	Single tooth replacement Abutment for fixed or removable prosthesis	- - - - -

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### Implant dimensions

	Diameter	Length
F	3.5mm, 4.8mm	7.0mm,9.0mm,11.0mm,15.0mm,17.0mm.
H	3.0mm wide 5.0mm long	3.0 head 4.0, 5.5 neck 5.5 body.
K	4.0mm wide 10.0mm long	3.0 head 4.0, 5.5 neck 5.5 body.

Lennart Mollersten studied the mechanical weakness of 7 implant systems. He stated deep joints in implants favoured resistance to bending moments in contact to shallow joints. In construction of implant systems joints depth should be taken in to cosideration<sup>30</sup>.

## **The Mini – Dental Implants**

Mini dental implants are ultra – small diameter (1.8mm width) biocompatible titanium alloy implant screw. It was designed by victor I. Sendax.

Donna L. Dixon studied the micro movement and torque needed to loosen abutment screws of minimatic, spectra system, calcitec implant system. The amount of torque needed to loosen abutment screw before and after testing was recorded and compared. The results indicated no difference between straight and angled abutments<sup>31</sup>.

Presently IMTEC Corporation has started IMTEC Sendax MDI (mini dental implant)

Implants are available in 4 lengths 10mm, 13mm, 15mm & 18mm and MDI MAX in 10mm, 13mm & 15mm length. MDI MAX differs from standard one in that it has different thread design that enables the implant to bite in to softer bone & hence used in-patients with low bone density.

These implants are so narrow that they are inserted directly through the overlying gum tissue and in to the bone underneath. Hence, the need to surgically cut & flap open the gum tissue, routinely required for standard implant systems is avoided in most MDI system. Due to this post insertion patient irritation & soreness is significantly reduced & there is increased margin of safety on encroaching vulnerable nerve, sinus or bony structure.

After single minimally invasive surgery, they can put into immediate biting or loading function due to self tapping design. These implants are indicated in resorbed mandible. Where in 2 – 4 mini implants are screwed into front of lower jaw between mental foramina. The mini implants, which are approximately the size of toothpicks, are placed about 4mm apart. Because of unique, minimally invasive procedure, minute size of implants, characteristic placement area, immediate loading property, allows the patient to enjoy a light meal within an hour time form having the mini implants placed<sup>32</sup>.

Steven E. Eckert studied 1170 implants placed in 4 anatomic locations anterior maxilla, posterior maxilla, anterior mandible and posterior mandible. They stated implant survival was independent of anatomic location of implants. Performance factor for all implants improved by design changes in implant restorative component.

Mini dental implants clearly represent an enormous break through for the dental implant specialty as the most patient friendly, cost effective, proven implant system available today<sup>32</sup>.

## **The Laminoss – Immediate – Load Implants, The Laminoss implant system**

The Laminoss sinusoidal thread design, together with its surgical technique provides an increase in bone lamination and volume for support as an immediate functioning implant. The increase of implant load bearing area (LBA) horizontal plane and controlled surgical osseous lamination technique excites bone cells by the action of osteocompression around the sinusoid implant threads. This implant system works on principle of force equilibrium and the relationship between implant design and bone<sup>33</sup>.

Biomechanically bone is reported to be 65% weaker when tested under shear versus compressive loading. The need for multiple implant designs capable of supporting the range of forces generated in these different occlusal forces to bone density regions of the jaw supplied the determining guidelines for implant design. Improving the implant design by increasing the implants load bearing area (LBA) as the primary functional mechanism to osteocompression. Support in the bone has been proposed as the primary factor in immediate load implant success under compression strain – related potentials are produced by piezoelectricity. These electric potential excites bone cells and influences the regenerative osseous capacity and induces these cells to deposit extracellular matrix if ideal magnitudes of force and direction is applied. Strain – related potentials are more specifically related to streaming potentials. Streaming potentials of osseous compression with in physiology limits generate extracellular fluid to flow over positively charged cell surfaces of osteoblasts. This creates a streaming electrochemical potential that stimulates osteogenesis<sup>33</sup>.

Controlling force transfer to the osseous tissue through implant design is imperative, since bone and metal have dissimilar moduli of elasticity different mechanical properties and their interfacial relationship is devoid of physiologic attachment mechanism. Therefore, the magnitude of force to bone architecture can be in equilibrium through an implant design having increased horizontal planes of support (LBA) that are equal in magnitude, opposite in direction and colinear in nature<sup>33</sup>.

Laminoss immediate load implants load bearing areas and total surface areas.

For dense bone

Implant length	9.0mm	11.0mm	13.0mm	15.0mm
3.3mm implant diameter				
Load bearing area	57.2	69.5	81.7	94.0
Total surface area	105.2	129.7 1	54.2	178.8

For spongy bone

4.0mm implant diameter

Load bearing area	68.0	82.2	96.4	110.6
Total surface area	122.0	150.5	178.9	207.4

The areas of an implants surface capable of providing maximum bone support and stimulation are the horizontal compressive plates and not the vertical implant interface under shear force. If horizontal planes of implants geometry are not significant enough to sustain the forces generated in a specific bone region, a fibro – osseous condition may occur. The minor diameter of all sinusoidal functional profile thread design is approximately 2.5mm, including implant neck, which will not compromise vascularity. The outer diameter of the aggressive thread designed for spongy bone is 4mm. The diameter of less aggressive thread is 3.3mm with a thread pitch of 1.3mm for denser bone. A 3.3mm implant with an aggressive thread pitch of 2mm is provided for narrow ridge with spongy architecture<sup>33</sup>.

All threads are designed for maximum LBA to sustain muscular forces by the elevator muscle and maintain equilibrium on a long term basis. It is recommended that the laminoss implants be selected for a specific region of the jaw based on occlusal force to bone density classification by 3 factors like region of bone density. Force magnitude and implant LBA to attain equilibrium<sup>33</sup>.

William M. Locante studied sinusoidal design has several advantages over traditional implants which simplified surgical procedure, significant decrease in treatment time, minimal implant emerging crestally etc. Final position of soft tissue can be determined with greater tissue reattachment<sup>33</sup>.

Laminoss implant selection guide based on load bearing and occlusal force to bone density classification.

Implant length (mm)	Force to bone region	Implant placement	Implant Load bearing area(mm <sup>2</sup> )
9	FB <sub>1</sub>	anterior	57-68
11	FB <sub>2</sub>	U&L bicuspid	69-82
13	FB <sub>3</sub>	lower molars	82-96

FB<sub>1</sub> indicates ideal bone formation for implants.

FB<sub>2</sub>, FB<sub>3</sub>& FB<sub>4</sub> indicate a decrease in bone quality.

### **Surgical procedure**

Following flap elevation pilot drill used for making purchase point over the implant site. Then 2mm depth drill is used to establish trajectory and depth. The finishing drill (2.5mm) is then taken to the appropriate depth, 1mm deeper crestally than the implant thread. Sharp edges and turning action of tap (50rpm) scores the bone, followed by osteocompression by the flat surface of the tap. Primary tap is used in osetopenic bone, which ensures minimal bone removal and compact the bone laterally<sup>33</sup>.

Tapping can be eliminated in maxillary bone; implant is equipped with a passive pilot cutting thread and hence can be placed in untapped site. For dense bone secondary tap is provided to widen the osseous thread areas laterally, followed by immediate placement of implant. Since bone is viscoelastic, bone may move towards the center of its osteocompression after compaction and make insertion of implant difficult. The insertion of implant to its final depth, 1mm below the ridge will accomplish the final threading of the osteotomy, creating maximum three dimensional bone engagements. Use of ratchet to manually deliver the last two implant thread will permit solid bone to implant contact with in the osteotomy<sup>33</sup>.

### **Nobel Pharma Implant System**

The Branemark system has been well received throughout the world. The branemark system has become a major influence in the field of implantology by the introduction of Nobel pharma implant system. The history of this system can be divided in to three stages: the early stage (1965-1968), the developmental stage (1968-1971), and production stage (1971-present). The system in use includes surgical components and drilling equipment's that were established in early 1971<sup>34</sup>.

The components for first stage surgery include the following.

1. Stainless steel instruments.
  - a. Organizer
  - b. Dissector: Instrument used to mark the proposed implant site. Also to detect location, position and angulation of nerve canals.

- c. Screw drivers: Available in three sizes. The short one is used to tighten and loosen the cover screw. Hexagonal screw driver is used to place hexagonal cover screw. The long one is used along with open wrench for placing fixture mounts on to fixtures.
- d. Open ended wrench: It is used to help place and remove fixture mounts on fixtures in conjunction with long screw driver.
- e. Connection to handpiece.
- f. Screw driver to contra angle.
- g. Cylinder wrench: The wrench fits on top of the fixture mount and used to tighten the fixture after placement.
- h. Guide drills: There are 4 types of drills available
  1. Guide drill; Round shaped which is used to mark the fixture site by making initial entry in to the cortical bone.
  2. Twist drill; the drill has a 2.0 mm diameter, available in three lengths 7.0-10.0mm, 7.0-15.0mm & 13.0-20.0mm. Each drill has lines on the surface to indicate depth of prepared site.
  3. Pilot drill; this drill is used after 2.0mm twist drill. It is used to enlarge the fixture site from 2.0mm to 3.0mm.
  4. Twist drill; these drill is used after pilot drill. The 3.0mm diameter drill is available in three lengths 7.0-10mm, 7.0-15mm, 13.0-20mm. They are used to enlarge the fixture site.
  5. Counter drill; this drill is used for self tapping fixture, only. It available in two configurations standard type and conical type for standard self tapping and conical self tapping respectively.
  6. Counter sink; Used after the twist drill to enlarge the coronal portion of the fixture site. By counter sinking, the fixture and cover screw are positioned level with the crestal bone level.

Wang in a study by finite element analysis stated that one piece implant unit showed greater stress distribution at bone implant interface than multi unit implant system<sup>34</sup>.

#### Titanium Instruments

1. Organiser
2. Fixtures; Two fixture diameters are available, 3.75mm & 4.0mm. The 3.75mm diameter fixture has six different lengths 7.0, 10.0, 13.0, 15.0, 18.0 & 20.0mm. The 4.0mm diameter fixture has five different lengths available 7.0, 10.0, 13.0, 15.0 & 18.0mm. The 7.0mm fixture does not have transverse holes in the apical end. For primary fixation in low density bone, two types of self tapping fixtures are available in 3.75mm width and 10.0, 13.0, 15.0, & 18.0mm lengths.
3. Fixture mount; It is used in placement of individual fixtures.
4. Screw tap; Used to create threads in to the walls of fixture site. 4 different lengths of screw tap are available, 7.0-10.0mm, 7.0-13.0mm, 7.0-18.0mm, 7.0-20.0mm..
5. Cleaning needle.
6. Direction indicator; Double ended instrument to check the parallelism during drilling procedure.
7. Direction indicator for fixture; The direction indicator of fixture is placed over the fixture after fixture placement to check parallelism.
8. Titanium bowl.
9. Depth gauge; The graduated end is used to measure the depth of fixture site with lines indicating 7.0,10.0,13.0,15.0,18.0 &20.0mm.The opposite end is used to measure the distance between adjacent fixture site.
10. Forceps.
11. Cover screw; Two types of cover screw are available, flat type for maxilla and round type for mandible.

Steven E. Eckert evaluated the clinical performance of implant systems certified by the ADA and found no difference in the survival of different implant systems. 5 year survival rates easily exceeded the minimum recommended by the ADA<sup>34</sup>.

Instruments for second stage surgery include.

#### Stainless steel instruments.

1. Punch blade; Used to remove the soft tissue surrounding the fixtures. It is designed as a spring loaded instrument with blunt needle and cylindrical blade. The needle is placed

over the cover screw center hole and the cylindrical blade is pressed and rotated in to the soft tissue.

2. Cover screw mill; It is used to remove the excess bone growth over the cover screw. It is a spring loaded instrument with a blunt needle and sharp milling blade. The needle is placed in to the cover screw hole; activate milling by pushing on the spring and rotating the blades around the cover screw.
3. Short screw driver; Used to tighten the cover screw.
4. Long screw driver; Used to loosen the cover screw during the second stage surgery.
5. Hexagonal screw driver; Used to tighten or loosen healing caps on to abutments.
6. Hexagonal screw driver, long (inner hexagon); Used to tighten or loosen healing caps on to the abutments.
7. Hexagonal screw driver ( outer hexagon); Used to place or remove the hexagonal cover screw on to the fixture.
8. Gauge; Used to measure the depth from the head of the fixture to the gingival margin.
9. Abutment clamp; Used to hold the abutment and rotate it on to the hexagonal nut located on the head of the fixture.

Robert Hass conducted a study on branemark single tooth implants. The common complication occurred was screw loosening. Acceptable implant function was noted clinically and radiographically. This encouraged the use of implants for single tooth replacements<sup>35</sup>.

#### Titanium Instruments.

1. Forceps; There are of two types. Titanium tipped stainless steel instrument and other made entirely of titanium.
2. Titanium bowl.
3. Abutment; It is made of titanium and available in 3.0, 4.0, 5.5, 7.0, 8.5, & 10.0mm length. Each abutment cylinder size has a corresponding abutment screw for use with that particular size.
4. Healing cap; It is a plastic cap that fits in to the threads of the abutment screw. Merle compared the geometric forms of five interchangeable implant prosthetic retaining screw. The results revealed significant changes between the systems. It was concluded that by interchanging the components can introduce unknown variables in treating the patients<sup>35</sup>.

## **Surgical procedure**

The incision line is marked using the dissector and is marked 10mm away from crestal ridge region. Make the surgical incision with no. 15 blade and cut through the mucosal tissue. The periosteum is cut carefully 5.0mm below the crestal ridge. Expose the alveolar crest using dissector. Remove adequate crestal bone to create an adequate width and check the fixture length prior to insertion. Use pilot and twist drills to create the fixture site. Use counter sink once fixture site is enlarged to 3.0 or 3.15mm<sup>35</sup>.

All the above procedures are done at a speed of 2000 rpm. Next tapping of fixture site is done using screw tap attached to the hand piece. Do not apply pressure during threading and continue irrigating the site. When threading is completed to the desired depth, remove the screw tap by activating the reverse button on the control unit. Fixture mount attached to the fixture in hand piece is brought near the surgical site. The fixture is installed without irrigation until the horizontal hole of fixture has threaded in to the site. Use cylinder wrench if resistance is encountered<sup>35</sup>.

After complete insertion of fixture remove the fixture mount. Position the cover screw on to the fixture and use low speed hand piece to engage the threads. Final cover screw tightening is performed manually. Flaps are sutured with 3/0 nylon suture material using interrupted vertical mattress suture to achieve primary closure<sup>35</sup>.

In second stage surgical procedure, first surgical incision is made 5mm in length to locate the center of cover screw. Punch blade needle is inserted in to the cover screw center hole, pushed apically, and rotated to cut tissue circumferentially. Use screw driver to remove the cover screw. Depth gauge is used to measure the depth of tissue between the fixture head and gingival margin. In maxilla, the abutment selected may be 1mm above or at the level of gingival margin. In mandible abutment should be one to two millimeter higher than the gingival margin. After this healing cap is placed over the abutment and the site is packed with surgical pack and sutured<sup>35</sup>.

## **Prosthetic procedures**

After 3-4 months of healing, impression copings are used to obtain impression of implant location. The impression can be obtained by open method or closed method. Following which implant analog is placed over the impression copings and cast is poured. Over this implant analogs abutment analogs are placed over which wax pattern is made which is casted. This restoration is either cemented or threaded over the implant<sup>35</sup>.

Ban Fui Tan studied the critical bending moment of implant abutment screw joint interfaces of various implant systems and stated no difference between various implant systems, implant diameter, and torque levels. The torque level mentioned by the manufacturer should be followed<sup>35</sup>.

## **The Ankvlos Implant system**

This implant system is a product of Dentsply, Friadent, which is an endosseous root form implant made of commercially pure grade 2 titanium. The implants are available in various lengths and diameters. For ease of identification the system is color coded by diameter 3.5 mm , Red, 4.5mm yellow, 5.5mm blue and 7.0mm green<sup>36</sup>.

This implant is indicated for surgical placement in the upper or lower jaw to provide a root form means for single or multiple unit prosthetic appliance attachment. These can be placed with a conventional 2 stage surgical process with an option for transmucosal healing or can be placed in a single stage surgical process for immediate loading<sup>36</sup>.

### **Intended use of system**

1. Implant supported prosthetic concept:  
Single tooth restoration, retaining bridges and full dentures.
2. Implant supported prosthetic restoration:  
Two – stage procedure.
3. Time of implantation:  
Immediate implant placement, Delayed implant placement, Late implant placement.
4. Drills, reamers and taps:  
Preparing implant site, implant placement.
5. Handle for Ratchet, Ratchet, Ratchet inserts:  
Preparing implant site using reamers and taps also to – implant placement.
6. Paralleling Guages:  
Alignment aid when drilling pilot and parallel holes.
7. Tweezers (titanium):  
Grasping objects.
8. Assembly device, insertion instruments for narrow gaps placing implants in single tooth gaps of less than 5 mm.
9. Instrument handles extralong:  
Implant site preparation using the reamer and tap.
10. Insertion handle for implants extralong:

### **Implant placement.**

Diner studied the effects of external geometry and occlusal load magnitude on bone failure modes for 5 commercially available denture implants. They stated up to 300 N of occlusal load, compact bone was not over loaded for any implant system. A 100 N load, over loading characteristic of implant was dependent on geometric shape<sup>36</sup>.

### **Surgical procedure**

After incision and flap elevation, round bur is used to make purchase point over the bone after which pilot drill in a speed range of 800 rpm is used to make the osteotomy. Once implant site has been drilled, shank hole corresponding to the tapered core of the implant is enlarged. Insert an implant matching reamer in to the ratchet insert and then in to the ratchet. Ream the implant site clockwise without exerting pressure. Gentle pressure may have to be exerted when preparing last quarter of the implant site. After reaming, upper edge of the reamer must be slightly below the bone crest, if this is not the case, increase the implant site depth. In very less dense bone reamer can be rotated counter –clock wise with gentle pressure to condense the bone. Now insert an implant matching tap in to the ratchet insert and then into the ratchet. Tap the thread clockwise. After tapping remove the tap by rotating it counter clock wise. In very less dense bone, site need not have to be tapped. Implant thread is designed to be self tapping in such cases<sup>36</sup>.

Correct insertion instrument is seated over adapter and rotate the selected implant in to place to avoid heat necrosis. Should the implant jam before the polished collar is reached, remove the implant and retap the thread. For final positioning of the implant, remove the handle and place the reversible ratchet on the insertion instrument. Guide the ratchet insert stud with an open end wrench. Once final position has been reached use integrated screw driver to loosen the retaining screw in the adapter and remove the insertion instrument, adapter and ratchet<sup>36</sup>.

Extra long instrument handle can be used instead of the ratchet in hard to reach maxillary areas. Implants are leftcovered with soft tissue flap for 3-4 months in submerged healing. A sulcus former is placed over implant and edges of the wound are adapter to sulcus former using mattress suture for transgingival healing<sup>36</sup>.

## **BioHorizons Implant System**

### **Indications**

Single tooth replacement (mandibular central lateral incisor, maxillary lateral incisor)

### **Design:**

Square thread design – imparts 10 times less destructive stresses, maximize compressive low transfer, Excellent primary stability

3 different thread forms – for different bone density.

Square thread

Conventional V thread

Coronal 2/3rd parallel walls – initial stability, surgical simplicity.

Apical taper

-Self tapping apex–simulates convergent roots

Diameter: 3.5, 4, 5, 6mm.

Length: 9, 12, 15mm

Threads: D2, D3, D4

6mm diameter implant – used in posterior extraction sites

3mm implant – missing laterals mandibular incisors

-Surface treatment – RBM (Resorbable blast media, pure titanium oxide)

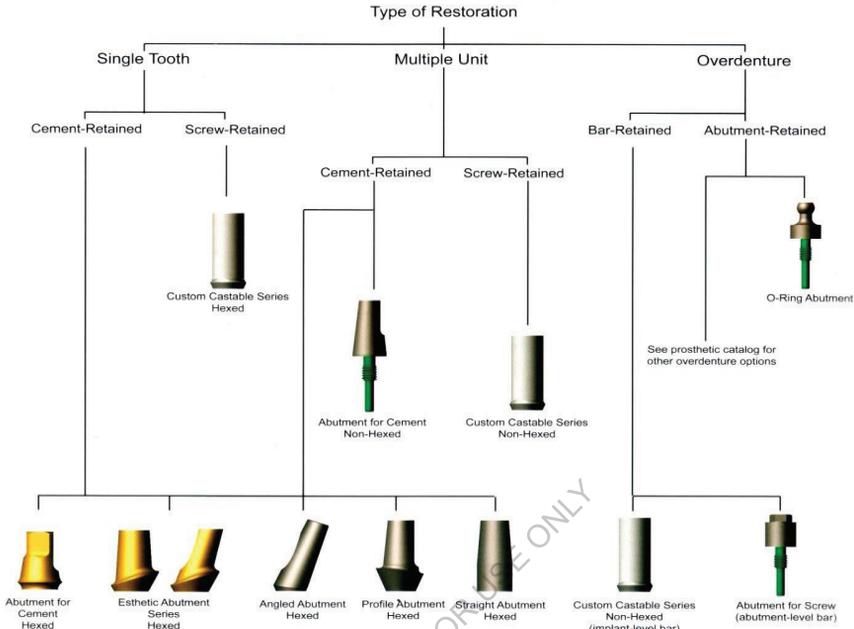
Hydroxyapatite – used in soft bone.

D4 type bone -D4 implant<sup>37</sup>

### **Advantages**

- 1 Less marginal bone loss because of 0.5mm length polished collar = better esthetics.
- 2 Spiralock technology reduces the chances of screw loosening.

## Abutment Selection Flow Chart



## The IMZ – Interpore Osseointegrated Implant System

Intra mobile cylinder and 2 stage osseointegrated implant system with an intramobile element was developed by Dr. Axel Kirsch over 17years ago. If rigid fixed prosthesis were placed between a natural tooth unit and an ankylosed implant with no shock absorbing element one of the following occur<sup>38</sup>.

1. Flexure of the metal substructure which would fracture veneers.
2. Bone resorption under implant, natural tooth or both.
3. Cement that bonds the rigid cast appliance to the natural has a high modulus of elasticity and cement bond could fail.
4. Micro movement of the retainer on the natural tooth could create continous micro trauma causing complications to natural.

5. Failure of solder joints.

The implant shock absorbing mechanism IME reacts to the applied forces in a manner similar to natural dentition. A cylindrical implant configuration combined with a spherical apical area and a viscoelastic IMF provides for the transfer of occlusal forces evenly to the bone – implant interface. The IME is made from polyoxymethylene which was introduced in 1961 by E.I. pont de numours & co.

Extensive testing of IME was done, which was subjected to 9,00,000 to 1.2 million continuous cycles of a cyclic load of 10 lb at 70 times per minute, which equates to approximately 550 days of use. Test data revealed dimensional changes not exceeding 0.0127mm & polyoxymethylene appeared to be a very durable and resilient material that does not undergo significant dimensional changes when subjected to cyclic forces<sup>38</sup>.

### **Uses of implant**

1. Single tooth replacements.
2. Unilateral free end saddle.
3. Bilateral free end saddle.
4. Wide edentulous span.
5. Fully edentulous span.

In fully edentulous span either,

2 implant connector bar – overdenture with an internal clip fixation.

3-4 implant custom designed connector bar – overdenture with internal clip fixation.

5-8 implant with a screw on type of denture which is totally implant supported.

5-10 implants with fixed cast removable bridge work.

### **IMZ IMPLANTS**

Available in 2 diameters- 3.3mm & 4.0mm. 3.3 diameter in 8mm, 10mm, 13mm & 15mm lengths. 4mm diameter in 8mm, 11mm, 13mm, & 15mm lengths. CPTi that is coated with titanium plasma spray is used. Coronal 2mm is not coated but highly polished. The plasma spray coating is a very fine grain titanium powder applied to the CPTi cylinder in an argon environment under high temperature pressure & velocity. This would increase the surface area by 6 fold.

A set of 6 internally & externally irrigated precision drills have been designed for atraumatic preparation of osseous receptor site<sup>38</sup>.

### **Prosthetic phase**

Transmucosal implant extension is placed over the implant body to which may be attached different components like implant post, II stage healing screw and intramobile extension(IME). 3 implant post sizes are available with a transmucosal implant extension of corresponding size, one for 3.3mm implant and two for 4mm implant, among this one is 2mm high and the other is 4mm high<sup>38</sup>.

TIE is removed from the implant and connected to impression post and this assembly is placed over superior portion of seating instrument, carried to the implant site and screwed in to position in the implant body. Now impression is made of entire assembly, after which TIE is separated from the post and repositioned over the second phase healing screw and this assembly is placed over the implant body. Implant analog of appropriate diameter is screwed over the impression post, which was placed over the implant during impression making. This assembly, implant analog, impression post is now repositioned in final impression and cast poured. Impression post is removed from master cast and metal laboratory analog of IME is placed over implant analog and tightened firmly on which prosthesis will be fabricated<sup>38</sup>.

### **Coronal fixation screw and frame waxing**

IME should be replaced annually hence all prosthesis was designed to be retrievable. Titanium occlusal screws (11mm or 17mm) are used for prosthesis fixation. Particular screw is placed over laboratory IME and articulator closed to verify adequate vertical dimension, if not screw is reduced by cutting the threaded end to obtain screw head position approximately 1mm out of occlusion<sup>38</sup>.

Intimate adaptation of the final casting to the occlusal fixation screw is essential for proper retention of the prosthesis to the implant. Prefabricated, precision, machined plastic sleeves that adapt over the fixation screw are used over which wax patterns are carved. Precision attachments are used when implants are attached to natural teeth and frame work try in should always be done on the metal laboratory IME. Because, if done on compressible polymethylene IME, it would cast away the defects in the castings<sup>38</sup>.

During insertion of fixed – removable prosthesis, first fixed part of fixed – removable prosthesis is cemented over natural abutment teeth. The removable portion of the restoration is then positioned over the implant, seating precision attachment components together and the implant – born pontic on top of the IME. Titanium fastening screw is seated through the prosthesis and tightened firmly with the hand screwdriver. Indira G. Sahiwal studied various non threaded endosseous implant under radiographic film and documented features that would help dentist to identify various implants they devised tables and flow charts to describe various identifying features<sup>38</sup>.

## **Innova Implant System**

### Endopore implants<sup>39</sup>

- 1 Unique, truncated cone shaped design, multilayered porous surface – 3 dimensional bone ingrowth.
- 2 With threaded implants the fixation which occurs allow for rotation movement of the implant with endopore resistance to vertical, horizontal, and rotational movement.
- 3 Implant abutment junction
  - Internal hex
  - External hex
- 4 Abutment platform 4.8mm
- 5 Diameter 3.5, 4.1, 5mm
- 6 Length: 5, 7, 9, 12mm
- 7 Collar height: 1.8-2.8mm -Smooth coronal region
- 8 Abutment types are UCLA, UMA, Dalla Bona, Over denture system.
- 9 Surface treatment – Acid wash surface, hydroxyapatite surface, TPS surface, Machine surface

### **Advantages**

- A secure, three-dimensional interlocking interface with bone
- Predictable and minimal crestal bone remodelling
- Greater surgical options with shorter implant lengths
- An uncomplicated surgical sequence
- Minimal instrumentation and inventory<sup>39</sup>

## **UNITI Implant System**

- Single or two stage surgical protocol.
- Consists of straight abutment (4.3mm).
- Tapered abutments
- Ball abutments

### **Design**

- Diameter: 3.3, 3.7, 4.3, 5.3, 6mm – Based on every cervical diameters of natural teeth.
- Length: 10, 13, 15mm

### **Anatomic root shape**

-Upper 1/3rd – Cortical component of implant body is parallel sided with shallow threads one continuous pitch of 0.9mm – ideal atraumatic placement in dense cortical bone – optimal load transfer.

-Lower 2/3rd – cancellous component – anatomic taper and sharper, deeper threads (0.35mm) are nearly horizontal – high degree of stability in cancellous bone.

-Self cutting slots in the apical portion – accommodates displaced bone volume during implant insertion - prevents bone chips being packed at the base of the osteotomy site.

-Implant tip is rounded

-Microgrip surface – osteoconductive high porosity surface 1-5 micron.

-1mm highly polished collar – better soft tissue integration.

Implant abutment connection – twin hexagon internal connection.

The twin hexagon is sandwiched between two solid cylindrical guides above and below the hexagon – high degree of stability and stress distribution

Micro gap free and bacteria proof joint

The deep internal connection with an abutment extending 3.3mm into the implant body – offers strength and stability.

### **Indications**

Single tooth replacement

Multiple teeth replacement

### **Advantages**

Biological root form suited for immediate extraction cases.

Wide diameter neck + tapered form = ideal for peri-implant defect size in sockets

(obviates additional augmentation materials) Wide platform – esthetic emergence profile.

Tapered root – minimizes risk of damaging adjusting teeth and structures.

### **Astra Tech Implant System**

- Two stage implant – manufactured from pure titanium

- Submerged implant

- Got unique conical seal design

- Surface treatment

- Grit blasting – Ti oxide particles

- Conical head

- Taper is 11°

## **Implant components**

- Fixture (length 8-19mm; Diameter 3.5 to 4mm)
  - Self tapping
  - Parallel sided
- Cover screw
  
- Abutments
  - Healing abutment
  - Straight and angled abutment (20-30°)
  - Uni abutment (20° & 45°)
- Drills
  - Twisted drill
  - Tiger drill – Ti N coated with laser etched bands.

## **Advantages**

Implant abutment junction is conical junction – prevents microbial contamination

## **Fixed detachable implant supported prosthesis retained with precision attachment.**

The implant supported maxillary anterior, fixed detachable prosthesis is often fabricated with a gingival flange to enhance esthetics and phonetics. However only the dentist can remove the prosthesis and the esthetic labial flange invariably impedes patient access for cleaning. A 2 piece, fixed detachable prosthesis that incorporates a substructure retained with conventional set screws and a superstructure retained with precision attachments has been developed by Steven Margano.<sup>40</sup>

The substructure is contoured to facilitate for access for oral hygiene because it will be covered by superstructure and neither esthetics nor phonetics is a concern. The superstructure is easily removed by the patient for routine cleaning and can be designed for favorable esthetics and phonetics.<sup>40</sup>

## **An alternate treatment method for fixed detachable hybrid prosthesis – a clinical report.**

The inability to consistently achieve a passive fit with multiple unit implant ceramo-metal prosthesis led to the development of fixed detachable hybrid prosthesis<sup>40</sup>.

Short coming of screw retained prosthesis include:

- Passive fit of the metal substructure may require sectioning and soldering after initial fabrication.
- Access holes must be present to allow for screw tightening – compromise on esthetics and occlusion.

- Complex clinical and laboratory techniques.
- Loosening of screw
- Fracture of various components.

A criterion for optimal fit of implant abutments in implant fixtures is 10 micro meters or less, which is difficult to achieve consistently with fixeddetachable hybrid prosthesis made with conventional methods and materials.

This technique by George Cobb et al uses cement retention for the hybrid prosthesis. This may not initially produce a perfectly passive fit but use of disclosing media and adjusting the internal aspect of the casting can result in non-binding, fully seated prosthesis. Although the possibility exists that sectioning, indexing and soldering may be required to obtain a passive fit, but modification of the internal aspect may be sufficient in majority of the case. Elimination of the screw access hole, will improve occlusion and esthetics and yet permit retrievability of the prosthesis for hygiene and repair. Also the problem of fatigue component fracture and screw loosening are eliminated<sup>40</sup>.

Disadvantages of cement retained prosthesis:

- Selection and milling of modification (preparable) abutments requires an experienced clinician and technician.
- Implant angulations beyond 15 degrees may require angled abutment or a castable abutment to achieve an acceptable path of insertion.
- Numbering or other methods of matching the correct abutment and orientation of correct implant fixture is imperative.
- Patient with limited interarch space – may compromise retention and resistance form for the framework/ abutment interface, or it may result in framework with deficient thickness or insufficient space for setting denture teeth.

### **Inaccurate Fit Of Implant Superstructure: Efficacy of Preci-disc**

System for The Correction Of Errors

The preci-disc system is designed to compensate for casting inaccuracies and to decrease stresses generated on the superstructure and implant components<sup>41</sup>.

A primary objective in fabricating an osseointegrated implant superstructure is to achieve a passively fitting prosthesis. The failure to produce passive fit leads to stresses in the screw retained prosthesis when the superstructure is connected to the abutment. This can result in mechanical failure<sup>41</sup>.

To optimize fit:

- Accurate impressions
- Master cast fabrication
- Accurate casting
- Preci-disc system

### **The Preci-disc system**

Titanium Preci-discs, 0.7mm thick are fixed to the metal casting with an anaerobic bonding composite. The shape of these titanium rings is said to allow the correction of both vertical and lateral fit discrepancies. Gap arising from errors during the clinical and laboratory stages are filled with resin composite.

### **Selection Criteria**

When osseointegration was first introduced into North America in 1981, the dominant force was the Branemark implant. Few manufacturers were on the scene, and there was a paucity of selection and training. Approaching a new century, some 19 years later, more than 25 manufacturers compete for market share in the United States alone. Worldwide, the number of implant companies is at least 1- or 5 times greater. Table 1 lists 21 manufacturers who responded, either completely or in part, to a questionnaire related to their products. The industry has gone from 3 or 4 basic designs to more than 95 variations, clones, and proprietary designs. The clinician has more than 1,300 implants and 1,500 abutments to choose from that vary in material, shape, size, diameter, length, surface, and interface geometry.

Reported recommended tightening torques range from none given to 1 to 5 per manufacturer. Eleven companies manufacture implants from titanium alloy, 7 from CPT4, 6 from CPT), and 1 each from CPT2 and CPT1. Two specifically indicated that even though they use CPT3 and/or CPT4, it has the elemental purity of grade CPTI (Astra Tech and Implant Innovations). Seven elected not to report tolerance specifications, which may mean that they are proprietary secrets, exceptionally good, or embarrassingly poor. Thirteen reported tolerance specification at:  $t-12.7 \mu\text{m}$  or better.

In the mid- to late 1980s the industry standard was  $t-25.4 \mu\text{m}$ , which meant that critical areas on the implant could vary by as much as 51  $\mu\text{m}$ . Based on the survey results, that standard has been improved to half that much. The best tolerance reported was 6  $\mu\text{m}$  (Friadent), with several others close behind at 8, 10, and 16. The number of inspections given to an implant body, from the start of production to inclusion into inventory, ranged from 3 to 41, with the majority reporting between 8 and 20 inspections.

With so many choices, so much advertising, and so little reliable scientific data available, how does one choose? As starters, perhaps ethical conduct, corporate morality, professional conduct, and veracity in advertising and promotion could be considered. From a purely personal clinical perspective, there are 10 criteria

- (1) predictable osseointegration;
- (2) controlled clinical studies that validate performance over a 5-year period or longer in different bone quality, loading, and restorative situations;
- (3) optimal surface interaction with bone;
- (4) prosthetic flexibility and applications;
- (5) cost-effectiveness-quality versus cost;
- (6) excellent tolerances;
- (7) tissue friendly/interface seal;
- (8) interface stability/screw stability
- (9) user-friendly, i.e., easy surgery, easy restorative; and
- (10) optimal emergence profile and esthetics. Perhaps engineering elegance, simplicity, refinement, and design logic can also help in the selection process. Presently, no one single design or manufacturer answers to perfection all of the above criteria and considerations because of the variance of the very substrate under consideration. Fortunately for the profession, the clinician, and the patient, today several come very close to meeting those needs.<sup>2</sup>

**Five techniques for single tooth replacement on endosseous root form implants. Jay R. Friedman.**

Internally hexed and threaded root-form implants provide the clinician with many new treatment options for single tooth restorations. Coupled with an interlocking hex on the abutment, they provide stability for single tooth restorations while maintaining the options of screw or cement retention. Five techniques for fabricating single tooth restorations are presented. Clinical and laboratory evaluations of implant angulation, quantity and quality of the gingival tissues, and limitations in vertical height are discussed in relation to design and abutment selection, and laboratory procedures for each restoration. These techniques permit design of each restoration to meet the unique anatomic, functional and esthetic needs. Both screw-retained and cement-retained abutments and prostheses are discussed<sup>42</sup>.

### **Technique 1**

The two-piece titanium alloy component is prepared to receive a cemented crown, provided the following criteria are met: The long axis of the implant must be parallel to the long axis of the adjacent teeth; there must be sufficient vertical height to accommodate a cemented crown on the prepared abutment; and there must be at least a 2 mm thickness of mucosa to provide a subgingival margin for esthetics. A supragingival margin can be created for the restoration when esthetics is not a concern.<sup>42</sup>

The coronal portion of the sheath is shortened and prepared on the working cast using a carborundum disc. Margins are placed 0.5 mm subgingival. The retention screw is cut flush with the top of the prepared abutment and provisional restoration is made.<sup>42</sup>

### **Technique 2**

When the implant is parallel to the long axis of the adjacent teeth, but there is limited vertical height, the two piece, hex-locking abutment can be used to fabricate a combined post-and-crown prosthesis.<sup>42</sup>

On the working cast, the sheath is shortened and prepared with grooves for mechanical retention. A framework pattern is waxed over the sheath and cast to the titanium abutment in type IV noble alloy after a low temperature burnout. Processed resin is applied to the framework to complete the prosthesis. Access to the fixation screw can be maintained through the occlusal surface. After clinical placement, the occlusal opening is filtered with composite resin.<sup>42</sup>

### **Technique 3**

When the long axis of the implant is not parallel with the clinical long axis of the neighboring teeth, a pattern can be cast to the two-piece, hex-locking abutment to change its angle, provided criteria previously cited for this abutment are met. This technique is normally used when the needed angle of correction is other than 15 or 30 degrees from the long axis of the implant and esthetics is not compromised.<sup>42</sup>

The abutment sheath is shortened and prepared with grooves for mechanical retention, and a gingival margin is defined. A pattern corresponding to the desired abutment angle and slightly bulkier than the final desired shape is waxed over the sheath. The center screw is removed from the abutment, and a reservoir sprue is attached to the pattern enveloping the sheath. After a low-temperature burnout, the pattern is cast in type IV noble alloy.<sup>42</sup>

The casting is divested and blasted. The permucosal section of the abutment is highly polished. The center screw is cut perpendicular to its long axis, reducing it to the level of the sheath. After placement of the custom-made abutment, conventional indirect techniques are used to make the restoration, which is cemented permanently or provisionally.<sup>42</sup>

### **Technique 4**

When the long axis of the implant is not parallel with the clinical long axis of the neighboring teeth by approximately 15 to 30 degrees, the three-piece preangled abutment can be used.

There must be acceptable gingival thickness to establish margins at 0.5 mm subgingival for esthetics. The preangled abutment can initially be used on the working cast to fabricate a provisional prosthesis.<sup>42</sup>

### **Technique 5**

The plastic abutment pattern is used primarily in the anterior maxillae when esthetic requirements preclude the use of a screw-retained abutment. These cast abutments are needed when the quantity and quality of the mucosa is limited, and/or when the implant extends above the mucosa crest and overlapping of the implant with the prosthesis is necessary for esthetics.<sup>25</sup> The coronal section of the abutment pattern can be severed from its base with a rotating disk, and reattached at the desired angle with autopolymerizing acrylic resin. All undercuts are blocked out with additional resin and the coronal section prepared. The finished pattern is removed from the working cast, sprued at the coronal section, and cast in type IV noble alloy. The casting is divested and blasted with nonabrasive glass beads, then refined and finished by use of conventional laboratory procedures. The perimucosal section of the cast abutment is highly polished. The custom abutment is cemented into the implant with composite resin cement, and the final preparation is made clinically.<sup>42</sup>

### **The design and fabrication of fiber-reinforced implant prostheses.**

The use of fiber composite technology in the creation of metal free implant prostheses may solve many of the problems associated with a metal alloy substructure such as corrosion, toxicity, complexity of fabrication, high cost, and esthetic limitations. As far as the veneer is concerned, the overlaying composite or denture base resin veneer will chemically bond to this fiber-reinforced composite substructure. In contrast, denture base resin does not chemically bond to the metal substructure currently used for full-arch implant prostheses. Additionally, there is no need to mask an FRC metal substructure with opaque materials to attain a good esthetic result. For partial-arch prostheses, composite materials have distinct advantages over porcelain veneers; the former are less brittle, do not wear the opposing dentition, may be repairable, and chemically bond to the FRC substructure<sup>43</sup>.

Decreased rigidity may result in fewer fractures of an opposing complete denture and a difference in the strain placed on the dental implant/bone interface. Laboratory and clinical research evaluating glass fiberreinforced composite prostheses used to restore and replace teeth has shown that these materials exhibit excellent mechanical properties and can form a chemical bond to resin-based veneer materials such as those used in the fabrication of certain types of implant prostheses<sup>43</sup>.

To meet the demands of implant prostheses, substructure materials supporting the prosthesis should meet criteria already established by Cox and Zarb. These materials should do the following: (1) be biocompatible in the oral environment, (2) fit the implant system with a high degree of precision, (3) have sufficient mechanical properties, (4) reduce the material costs to a minimum, and (5) create the prerequisites for good esthetic results. FRC materials possess all 5 of these characteristics.<sup>43</sup>

### **Proposed Implant Prosthesis Designs**

Two different designs of fiber-reinforced composite implant prostheses have been developed and placed in human subjects. One design (screwretained, retrievable prosthesis) is used with

implant abutments that allow for screw retained prostheses; the other design is used with abutments that retain prostheses with a luting material.

The system includes an (occlusal) screw retained, retrievable prosthesis design and a luted, nonretrievable prosthesis design. The FRC screw-retained prosthesis includes ceramic cylinders that are screwed into a standard (screw-retained) abutment and are designed to support, position, and retain the FRC substructure. The ceramic cylinders are made with horizontal grooves on the facial and lingual surfaces and vertical boxes on the proximal surfaces that facilitate the placement and adaptation of the FRC material, which is placed on and around the cylinders when the substructure is fabricated. Cylinders have been made from pressed ceramic materials such as Finesse (Ceramco) and 3G (Pentron, Inc). The use of zirconia-reinforced alumina cylinders is now being explored.<sup>43</sup>

The ceramic cylinder is air-particle abraded with aluminum oxide and etched with hydrofluoric acid to facilitate adhesive bonding between the ceramic cylinder and the FRC. Silane coupling agent then is placed on the ceramic surface before the addition of unfilled resin and the unidirectional, continuous-fiber FRC. Ceramic cylinders have been made with different vertical heights and with a variety of angles between the proximal boxes to allow for variation of implant height, location, and arch curvature. These special cylinders and methods for fabricating a variety of implant prosthesis components with FRC materials can be seen with an earlier alloy cylinder prototype.<sup>43</sup>

### **Proposed Procedures**

The occlusal screw channels are protected with silicone, then the ceramic cylinders are air-particle abraded, etched, covered with a silane-coupling agent, and then unfilled resin. Strips of FRC are placed and polymerized in the cylinders' proximal boxes, buccal surfaces, and lingual surfaces, and wrapped around the entire substructure. An additional layer is added to the cantilevers, perpendicular to the previous layers of FRC. The substructure is covered with aluminum foil, and a matrix is created with vinyl polysiloxane putty. The substructure is removed from the cast, and aluminum transfer copings are screwed into the master cast. The verification index is made by pouring resin into the putty matrix. After the accuracy of the master cast has been confirmed, the verification index is used as the foundation for setting the teeth. The denture setup is flaked and boiled out, leaving the verification index on one side of the flask and the denture teeth on the other. The verification index is removed, the FRC substructure is replaced, and PMMA resin is packed. The prosthesis is polymerized, finished, and polished.<sup>43</sup>

For the luted prosthesis, a combination fiber and particulate composite coping is made to fit over and bond to the standard solid metal abutment. As with the ceramic cylinder described above, this FRC coping is designed to support, position, and retain the unidirectional, continuous fiber FRC substructure. This coping also is fabricated with horizontal grooves on the facial and lingual surfaces and vertical boxes on the proximal surfaces that allow for precise, easy placement and adaptation of the unidirectional FRC material placed on and around the copings when the substructure is fabricated. The oxygen-inhibited layer is maintained on the surface of the coping to facilitate adhesive bonding between the composite coping and the FRC. Composite copings also have been made with different vertical heights and with a variety of angles between the proximal boxes to allow for variation of implant height, location, and arch curvature<sup>43</sup>.

For both the screw-retained and luted partial prosthesis designs, a particulate composite veneer can be placed over the substructure. This hybrid particulate composite is added directly to the oxygen-inhibited layer of the finished FRC substructure. Additional layers of composite are placed and built to the full contour of the prosthesis. After the final light-initiated polymerization, shaping, finishing, and polishing, the prosthesis is placed in an oven to additionally to polymerize the composite materials and provide optimum esthetic properties. The composite material offer many advantages over ceramic materials; the latter are more brittle, may cause harm to the opposing natural dentition or acrylic denture teeth and may place greater impact loading on the supporting teeth or implant.<sup>43</sup>

### **The Spectra-System implants.**

(Dentsply/Implant Division, Encino, Calif.) Provide three different externally threaded root-form body types: basket with threads, screw, and ledged, with apical threads to engage cortical bone. In areas here cortical bone cannot be ideally engaged, the system also provides a hydroxyapatite-coated cylinder design. Each implant in this report was placed by use of convention non-trauma surgical procedures with internally irrigated drills. After a submerged healing period of 3 to 6 months, the implant was re-exposed and clinical osseointegration was verified<sup>42</sup>.

The implant body type is not a concern because all the implants share the same internal hex and threaded prosthetic abutment connection. This connection bevels inward from the outside circumference of the implant neck to a 2.5 mm wide internal hex. This hex extends downward for 2 mm parallel with the walls of the implant before changing to internal threads. The abutment diameter selected must match the 3.5 mm or 4.5 mm outside diameter of the implant neck<sup>42</sup>.

Three titanium alloys (6A14V) and one castable plastic pattern are the abutment options for single tooth restorations with the Spectra-System implants. All abutments have a bottom hex that interlocks with the internal hex of the implant to prevent rotation. In the titanium alloy components, the hex is tapered to provide a press fit that tightly wedges into the implant's hex to resist lateral forces on the prosthesis. The titanium alloy components include a straight, two-piece hexed sheath with an independent retention screw and three-piece angled abutments that consist of a base, a head angled at 15 or 30 degrees, and a retention screw. The one-piece plastic component is a laboratory burnout pattern used to fabricate a cast, cement-retained abutment. It consists of a coronal section that can be angled and prepared, a per mucosal extension that seats flush with the top of the implant, a bottom straight-walled interlocking hex, and an apical extension that fits between the implant's internal threads for cement retention. The finished cast abutment is cemented into the implant with composite cement<sup>42</sup>.

To select the optimum abutment design and method of connection, both clinical and laboratory evaluations are needed. Initially, the long axis of the implant must be evaluated relative to the long axis of the remaining dentition. This relationship will determine whether a straight abutment is acceptable or whether an angled abutment is required to achieve clinical parallelism.

The quality and quantity of the mucosa forming the sulcus around the implant must also be evaluated. When the tissue is thick and bulbous, a screw-retained abutment can often

be used. The thicker tissue permits the fixation screw to penetrate the base of the abutment and engage the internal threads of the implant before the long axis of the abutment changes angulation. This thickness also permits placement of subgingival margins in areas where esthetics is needed. When the tissue is thin, a cast cement retained abutment can change its angulation at the neck of the implant if necessary. This option may be important in the anterior maxillae where esthetics is often challenging.

Limitations in vertical height must also be evaluated. This dimension will determine the type of prosthesis that can be made. With limited vertical height, a cement retained crown may not be acceptable. Where the top of the implant extends above the crest of the residual ridge, a cast, cement-retained abutment can allow the restoration to overlap the superior aspect of the fixture for esthetics.<sup>42</sup>

## **SUMMARY**

A well documented fact is now the long-lasting predictability of dental implants. Almost all leading manufacturers can claim success rates in excess of 90%, and for more than 10 years, the more advanced systems are well above that. The astute clinician is able to work and treat number of implants well. The long-term stability of the abutment and the prosthesis has been the problem area. Due to a number of factors, tremendous progress was made in this region. Critical tolerances for machining have improved in the last 20 years and will probably continue to improve with further advances in technology and strong competition from the industry.

Abutment relations have been reassessed from an engineering perspective and improved and refined significantly. In the fields of screw technology, torque and application, a lot has been learned. Although there are considerable redundancies in the abutment design, the subtle differences among the components are evident, notable and often clinically important. Various innovations in the design, manufacturing and casting process had made rehabilitation procedures easy even in the most challenging scenarios. New geometries of the interface have been made available which improve the stability of the abutment and simplify the restoration process. There was a gradual but profound transition to internal links.

This writing has introduced 2 new internal connections as well as an internal interface clone. Industrially speaking, it is highly reasonable to conclude that all major manufacturers who do not currently have an internal connection with their design options are working for this. The extended model life has been improved by the dimensions of the external hex along with enhanced binding and resistance, updated loading systems, better torque and higher torque applications. However, it is unlikely that the external hex will survive long into the new millennium with an excellent variety of new interfaces.

Today, the internals are more robust, physically stronger, easier to repair, more esthetic and certainly more user-friendly. The new entries in this area learned a lot from the hexagonal experience and applied it to every aspect of implant therapy.

Lay manufacturers's joint efforts to improve product quality and health have also brought renewed confidence and security to patients and clinicians alike. Developing more stable and secure implant

/ abutment connections has transformed the company into more user-friendly cementing protheses, from the difficult and troublesome screw-packed FPD and single-tooth restore. This trend continues and the fate of the restoration of gold film can be predicted by screw retained FPD and one implant restorations. As a result of market pressure for simplicity and stability, this phenomenon will eventually continue.

More refinements in ceramic engineering will lead to further changes in combination abutments of all ceramic and ceramic / metal products. Due to an internal link that makes a possible greater thickness of porcelain in the vital interface, some implant-to-abutment interface models (Friadent, Replace Select, Camlog, Astra Tech etc.) are in a position for this innovation.

In this dynamic engineering environment, it is almost impossible to keep up with the vast array of hardware available. Color coding of components usable in some systems has been a small but very commendable step towards user friendliness. Color coding for products but also labeling should be widely used across the industry. It is strongly recommended. Several companies made enormous strides in simplification in the catalog in combination with simplicity.

Friadent, Nobel Biocare, Steri-Oss, Implant Innovations and Astra Tech all offer excellent examples. The implant has come in full circle and its related components. The original Branemark 3.75 mm diameter was a result of 4 mm titanium bar stock in Goteborg, and the easy way of putting the screw into bone was through its horizontal interface design<sup>2</sup>. Today, substantial technological sophistication and internal analysis are primarily dedicated to the development of new components.

With the advent of precision machining and accurate digital dynamic processes, no ideas are impossible to implement and execute. For maximum quality and marketing differentiation, each detail is prepared and delivered. This not only enhances the marketing strategies, with this it truly welcomes another horizon which will be even better to look upon, to be studied and to be admired. There have been great progress and feats achieved, and there will surely be great outcomes in the next century.

Nevertheless, some things never change in some respects. Before the release of new drugs to the industry there is always a lack of independent lab testing and controlled clinical trials. Newer models should not be used as speculation, professional opinion and advertising positions but instead using scientific methods. Perhaps in the next decade this will no longer be a problem as the field matures and evidence-based treatment needs clinical verification before use.

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Diseases that are physical but get worsened by psychological factors like stress and anxiety are psychosomatic disorders. A lot of psychosomatic disorders have an influence upon health of oral tissue. Many diseases manifesting in the oral cavity have a psychological component in their etiology or have some effect of psychologic factors which have to be diagnosed and managed accordingly to ensure good oral and over-all health. Time and patience is required to handle such patients and are not easily treatable by medications. Frequently occurring oral psychosomatic disorders like lichen planus, stomatitis etc, do not receive appropriate treatment because of misinformation, ignorance and misdiagnosis by the doctor. In day to day life because of the increasing stress there is more probability of doctors and dentists encountering patients with such disorders. Hence one should be familiar with such manifestations and if accounted with such patients should try to manage them with psychiatrist whenever needed. This handbook aims to emphasize the oral manifestations seen in psychosomatic disorders.

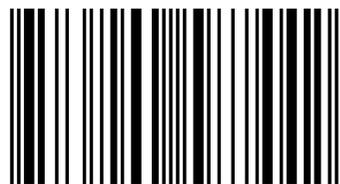


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# Oral manifestations of psychosomatic disorders

Oro-psychosomatic link

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## Oral manifestations of psychosomatic disorders

### CONTENTS

	<b>PAGE NO.</b>
1. INTRODUCTION	2
2. HISTORY	10
3. CLASSIFICATION	13
4. PSYCHOSOMATIC DISORDERS IN DENTISTRY	13
a. LICHEN PLANUS	
b. APHTHOUS STOMATITIS	
c. BURNING MOUTH SYNDROME	
d. XEROSTOMIA	
e. BENIGN MIGRATORY GLOSSITIS	
f. ATYPICAL FACIAL PAIN	
g. ATYPICAL ODONTALGIA	
h. IDIOPATHIC DYSGEUSIA	
i. ACUTE NECROTISING ULCERATIVE GINGIVITIS	
j. INFLAMMATORY PERIODONTAL DISEASE	
k. ORAL PSORIASIS	
l. TEMPOROMANDIBULAR DISORDERS (TMD)	
m. BRUXISM	
n. CANCEROPHOBIA	
o. EATING DISORDERS	
II. SUMMARY AND CONCLUSION	59
III. BIBLIOGRAPHY	61

## **INTRODUCTION :**

Psychology has been defined as "speciality of science, which studies the working of normal mind, the perceptions, sense organs, the personality formation, learning, anger, stress etc" Spering has called it "the science of individual behaviour and experience".

Psychiatry has been defined as that, "branch of medical sciences which deals with the diagnosis and treatment of the disease of the mind and also tries to elucidate the diseases such as those in the twilight zone of mind and body i.e. the psychosomatic disorders" sparkling has defined it as "the study and the treatment of mental disorders". There has been an increasing evidence of awareness in the medical profession of the interplay between psychological and organic factors in the causation and presentation of illness.

Psychosomatic disorder, also called Psychophysiological Disorder, condition in which psychological stresses adversely affect physiological (somatic) functioning to the point of distress. It is a condition of dysfunction or structural damage in bodily organs through inappropriate activation of the involuntary nervous system and the glands of internal secretion. [3]. The term psychosomatic is derived from the Greek words psyche and soma. "Psyche" in earlier times meant "soul or mind" which now also implies "behaviour." "Soma" refers to "physical organism of the body." It has been known for centuries that psychological/emotional factors are related to many physical illnesses. Traditionally, we regard mind (psyche) and body (soma) to be separate, but where and how do they interact? As an answer, the basic concept in psychosomatic medicine was described clearly by Sigmond Freud, who used the term "conversion hysteria," which is nothing but change in expressive behavior, i.e. from an unresolved emotion to somatic symptom [4]. The term "Psychosomatic" was first used in 1818 by the German psychiatrist, Heinroth. Felix Deutsch in 1922 was probably the first author to introduce the term "psychosomatic medicine" [5]. The mouth represents an organ of the expression of certain 'instinctual' cravings and is charged with a high psychological potential. Certain diseases which affect the oral mucosa may be the direct or indirect expression of emotions or conflicts. Psychosomatic disorders may affect almost any part of the body, though they are usually found in systems not under voluntary control.

Physical symptoms may be exacerbated by psychological distress or may be due to entirely due to an underlying psychological disorders.

**Health-** Health is a state of complete physical, mental and social well being and not merely the absence of disease or infirmity.<sup>1</sup>

### **Mental health**

WHO- A state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community

**Stress** Coined by Hans Selye

It is an undesirable or health threatening response of the body, which is brought on by deleterious external influences (stressors)

Stress is not what happens to someone but how someone reacts to what happens- Breivik et al, 1996

Chronic stress is defined as a “state of prolonged tension from internal or external stressors, which may cause various physical manifestations. eg, asthma, back pain, arrhythmias, fatigue, headaches, HTN, irritable bowel syndrome, ulcers and suppress the immune system”.

“The general adaptation syndrome”. Mind and body influence each other

Influences of psychological processes on the biological processes is documented in Indian history in Ayurveda. According to Patanjali - “yoga as a way to healthy mind, strong body and spirituality which enables an individual to attain self actualization”

Concept of psychosomatic medicine was given by Sigmond Freud

### **Psychological Factors Affecting Physical Conditions**

Psychosomatic (psychophysiological) medicine has been a specific area of study within the field of psychiatry for more than 75 years. It is explained by two basic assumptions:

1. There is a unity of mind and body (reflected in the term mind-body medicine)
2. Psychological factors must be taken into account when considering all disease states.

The concepts of psychosomatic medicine are subsumed in the diagnostic entity called **Psychological Factors Affecting Medical Conditions**. This category covers physical

disorders caused by emotional or psychological factors. It also applies to mental or emotional disorders caused or aggravated by physical illness

### **Stress Theory**

**Stress** -circumstance that disturbs or is likely to disturb, the normal physiological or psychological functioning of a person.

- **Walter Cannon** -conducted the first systematic study of the relation of stress to disease. He demonstrated that stimulation of the autonomic nervous system, particularly the sympathetic system, prepared the organism for the fight or flight response characterized by hypertension, tachycardia and increased cardiac output.
- **Harold Wolff**-observed that the physiology of the GI tract appeared to correlate with specific emotional states. Hyperfunction -associated with hostility. Hypofunction–associated with sadness.
- **Hans Selye** - He considered stress a nonspecific bodily response to any demand caused by either pleasant or unpleasant conditions.  
Model of stress: General adaptation syndrome.

Three phases:

- (1) the alarm reaction
- (2) the stage of resistance-adaptation is ideally achieved
- (3) the stage of exhaustion-acquired adaptation or resistance may be lost.

### **Neurotransmitter Responses to Stress**

#### **Amino acid and peptidergic neurotransmitters**

- are also intricately involved in the stress response.
- Studies have shown that corticotropin-releasing factor (CRF), glutamate (through N-methyl-D-aspartate [NMDA] receptors), and  $\hat{\text{I}}^3$ -aminobutyric acid (GABA) **all play important roles in generating the stress response or in modulating other stress-responsive systems, such as dopaminergic and noradrenergic brain circuitry.**

## Endocrine Response to Stress

- In response to stress, CRF is secreted from the hypothalamus into the hypophysial-pituitary-portal system.
- CRF acts at the anterior pituitary to trigger release of adrenocorticotrophic hormone (ACTH).
- Once ACTH is released, it acts at the adrenal cortex to stimulate the synthesis and release of glucocorticoids.
- Glucocorticoids themselves have myriad effects : promoting energy use, increasing cardiovascular activity (in the service of the flight or fight response), and inhibiting functions such as growth, reproduction, and immunity.
- This HPA axis is subject to tight negative feedback control by its own end products (ACTH and cortisol) at multiple levels, including the anterior pituitary, the hypothalamus, and such suprahypothalamic brain regions as the hippocampus.
- In addition to CRF, numerous secretagogues (substances that elicit ACTH release: catecholamines, vasopressin, and oxytocin.) exist that can bypass CRF release and act directly to initiate the glucocorticoid cascade.
- Different stressors (e.g., cold stress versus hypotension) trigger different patterns of secretagogue release

## Immune Response to Stress

- Part of the stress response consists of the inhibition of immune functioning by glucocorticoids.
- This inhibition may reflect a compensatory action of the HPA axis to mitigate other physiological effects of stress.
- Stress can also cause immune activation through a variety of pathways.

CRF itself can stimulate norepinephrine release via CRF receptors on the locus ceruleus -> activates the sympathetic nervous system (centrally and peripherally) and increases epinephrine release from the adrenal medulla.
- Direct links of norepinephrine neurons synapse on immune target cells.

- Profound immune activation also occurs, including the release of cytokines: IL-1 and IL-6 which cause further release of CRF, which in theory serves to increase glucocorticoid effects and thereby self-limit the immune activation.

### **Life Events**

- A life event or situation, favourable or unfavourable (Selye's distress), often occurring by chance, generates challenges to which the person must adequately respond.
- **Thomas Holmes and Richard Rahe**-social readjustment rating scale after asking hundreds of persons from varying backgrounds to rank the relative degree of adjustment required by changing life events.
- **Accumulation of 200 or more life-change units in a single year increases the risk of developing a psychosomatic disorder in that year.**
- Persons who face general stresses optimistically, rather than pessimistically, are less likely to experience psychosomatic disorders; if they do, they are more apt to recover easily.

### **Treatment of Psychosomatic Disorder**

GOAL: Mobilizing the patient to change behavior in ways that optimize the process of healing

- General change in lifestyle
- Specific behavioural change
- The quality of the relationship between the doctor and the patient.
- In rare cases in which negotiations break down and an impasse is reached it may be necessary to threaten to terminate the relationship.

### **Cognitive Behavioral Therapy**

Used to help individuals better manage their responses to stressful life events.

- help individuals become more aware of their own cognitive appraisals of stressful events

- to educate individuals about how their appraisals of stressful events can influence negative emotional and behavioral responses and to help them reconceptualize their abilities to alter these appraisals
- to teach individuals how to develop and maintain the use of a variety of effective cognitive and behavioral stress management skills.

### **Stress management and relaxation therapy**

- Self-observation : daily diary
- Cognitive restructuring : positive thinking
- Relaxation training :
  - Hypnosis
  - Biofeedback: humans being able to learn to control certain involuntary physiological responses (called biofeedback) such as blood vessel vasoconstriction, cardiac rhythm, and heart rate.
- Time management
- Problem-solving : apply the best solution to the problem situation and then review their progress with the therapist

Oral health is an integral and also a critical component of general health. Psychosocial factors are recognized as an essential and influential components in health and disease<sup>2</sup>.

Psychosocial factors encompass both psychologic issues (those that arise predominantly from within the individual) and sociologic issues (external factors).

It has been known for centuries that psychological / emotional factors are related to many physical illness. Traditionally we regard mind (psyche) and body (soma) separate but where and how do they interact? This was explained by Freud, who was the first to introduce the basic concept in psychosomatic medicine. He used the term “conversion hysteria” in describing the reaction in which emotional conflicts are converted into bodily or somatic symptoms<sup>3</sup>.

It is now well recognized that psychological states can produce somatic symptoms, anxiety rates are shown to cause autonomic arousal, heightened muscle tone and over breathing and hence a wide range of bodily symptoms. Depressive

illness can lead to weight loss, tiredness, loss of appetite and pain or an existing pain can aggravate.

However patients attribute these somatic syndrome to serious physical disease. The oral mucosa is highly reactive to psychologic influences and in some cases oral disease may be a direct expression of emotions or conflicts, while in other instances lesions of the oral mucosa may be the indirect result of an emotional problem. A wide spectrum of psychiatric disorders affects oral and para oral structures which have a definite psychosomatic cause, but unfortunately they remain unrecognized because of the common and limited nature of their presenting features

Changes in the psychological functioning in patients may be related to manifestation of pain in some patients with atypical odontoalgia, Temporomandibular disorders, chronic orofacial pain, burning mouth syndrome, aphthous stomatitis etc.<sup>4,5</sup>

In chronic pain syndromes, there is often a psychological or behavioral overlay of symptoms that are part and parcel of the disease. Treating the psychological and behavioral problems with physical aspect may increase the chances of a successful therapeutic outcome.<sup>6</sup>

Emotional or psychological factors have been emphasized as potential influences with respect to a person's health, resulting in an increased popularity of holistic medicine. Several studies relying on self reported patient information between psychological state and incidence or progression of disease and results have been interesting.<sup>7</sup>

### **Biopsychosocial Model of Illness:**

In prehistoric era the disease was supported to be a result of ill deeds of man or a effect of evil supernatural power and people generally relied upon with doctors, or natural resources. With civilization germ model or biological model of illness was proposed and it was believed that diseases arised due to germs and one germ one disease model of illness was unaptadised.

Gradually a psychosomatic aspect of disease was centralized and the disease was considered to be an interplay of bodily or somatic and psychogenic factors. This model led to conception of current biopsychosocial model of illness, which believes most of illness not be an interplay between some external biological factor and body's somatic factors such as immunity and psychologic factors.

In modern era, due to increased stress and anxiety and non inclination to spirituality there is an alarming rise in mental illness as well as physical diseases, as spirituality is an integral part of psychological aspect of man and plays a major role in disease manifestation.

### **Stress Anxiety and Oral Diseases:**

Though stress is one of the odd horses and psychiatry has been proposed to cause perception of trigger of psychiatric illness. Numerous domestic distress are also commonly linked with unpleasant thoughts and events or in other words, anxiety and depression and removal of these factors is frequently associated with the cessation of diverse physical symptoms.

The slipiness of the term "stresses" is both an advantage and a disadvantage.

It is an advantage because it is all embracing and allows a synthesis of many aspects of life's experience. It is disadvantageous because its references are diverse. Stress refers both to a subject and a predicate, an event and the consequences of that event.

For centuries physicians and patients have made an association between adverse life eventic illness. However there are no concrete evidence for studies regarding it. The conceptual push that has hindered progress in this field is the confusion of 'cause' and 'trigger' of illness.

The allegation that stress "caused" an illness is difficult to demonstrate in most human studies, as we impose a short term stresses and look for the resultant physiologic charges and hence positive results are difficult to establish.

The alternative hypothesis provides evidence that "stresses" triggers illness in individuals whose underlying illness is latent or subclinical and is evidenced routinely in psychophysiologic or psychosomatic studies. For instances, studies of

physiological response to stresses in normal individuals demonstrated long amplitude changes in physiologic levels of blood pressure, gastric motility and normal levels. When such psychophysiological studies are extended to patient groups, incontrovertible evidence is seen for the role of stressors as trigger events in eliciting pathophysiological phenomena.

Another conceptual problem that enters is the issue of stress vs coping.

Overall, following functions have been proposed showing stress related disorders by Richard Rahe in 1974.

Stress → Past experiences → Psychological defences →

Illness → Illness behaviour ← coping ← Psychological reaction

With the above background this book attempts to review the current available literature on “psychosomatic disorders in dentistry”.

## **HISTORY**

### **THE BEGINNINGS : PRIMITIVE CONCEPTS :**

The origins of most of psychiatry's scientific concepts are rooted in the past. The study of the primitive tribes of this day lends support to conjectures concerning the concepts of illness held by prehistoric men which are reflected in the myths and records of the early pages of history. The concepts of disease found among primitive people differ from those held by the scientific communities of today. For primitive people, all illnesses were attributed to forces acting outside the body.

The quest of the medicine man is often to find the lost or afflicted soul, to drive out the demon, and then to return the soul to the body. Throughout, one may recognize the primitive methods as beginning with simple cause and effect explanations and empirical observations, without recognition of the operation of internal forces of either a biological or a psychological nature. Nor does the medicine man direct his efforts to the individual man; rather, he directs his efforts to the individual but rather to a malignant invading force foreign to his primitive patient. The meanings and aims of primitive rites, while psychotherapeutic, hold no relationship to modern treatments which find the sources of illness within the biosocial organization and development of man.<sup>9</sup>

## **GRECO-ROMAN ERA :**

A significant move occurred in the sixth century B.C. as the Greek healer's interest turned toward observation and experimentation. This early scientific movement is best observed in the writings of Hippocrates (460-375 B.C.). He rejected the influence of the gods as causative of mental disease. High point of scientific observation during the Greco-Roman period was reached in the time of the Roman physician Galen (130-200 A.D.). Galen developed a theory of the rational soul as divided into external and internal parts. The former, in his system, consisted of the five senses; the functions of the latter were such things as imagination, judgment, perception, and movement. Galen concluded, as Plato thought but Aristotle denied, that the brain and not the heart was the seat of the soul.

The reactions of parts of the organism would be designated as physiological, while "mind" would be considered the integrated response of the organism to the complex physiological, psychological, and sociological forces that impinge upon it. The "mind", therefore, is merely one aspect – the psychological aspect – of biological functioning of the organism and not a metaphysical entity having an existence parallel to the body.<sup>9</sup>

## **THE MODERN ERA:**

### **Social Psychological Change:**

The interest in psychotherapy and humanitarian attitudes toward mental illness have undergone major revivals during the past half century. Various forms of psychotherapy now flourish worldwide. Varying from simple application of attitudes of acceptance toward the mentally and emotionally distressed, the modern psychotherapies are based upon a series of hypothetical propositions and operational tenets lacking in the earlier "moral therapy".

More or less coincident with the humanitarian reforms in treatment occurred the growth of medical interest in mental illnesses. Following a long series of observations by the brilliant clinicians in Europe, the German Emil Kraepelin (1856-196) gave to psychiatry the first comprehensive description of what he believed were

entitles of mental disease. Prior to his time, psychiatric attention had been directed to the symptom, which was regarded as the illness. Kraepelin assumed that mental disorders were definite disease entities analogous to the physical diseases and defined by etiology, symptomatology, course, and outcome. This led him to stress clinical observations and the search for physical origins for mental diseases. His system of classification was based on descriptions, symptoms, and outcome, since it was frequently impossible to make the diagnosis by laboratory examinations. Thus the classifications were not based on an understanding of etiologic factors, including those of psychodynamic processes.

Coincident with the successes that followed in the late nineteenth century with discoveries of the pathology and etiology of disease, scientists turned to similar attempts to understand the etiology of mental disorders just as institutes for the study of general medical illnesses were established.

In Western Europe, in 1896 the State of New York established the pathological Institute (now known as the New York State Psychiatric Institute) to study the etiology of the mental disturbances, then recognized and to develop therapeutic and preventive measures for them. This was the first research organization in which investigators from the biological, psychological and social sciences worked with integration. This was a team work of scientists from various fields of anatomy, histology, pathology, microbiology and cellular biology, psychology and anthropology. Within short duration, a worker attached to the Institute, in collaboration with another in the younger Rockefeller Institute, established the cause of paresis as the spirochete *Treponema Pallidum*.

It is presumed that Ira Van Gieson, the pathologist who was the first director of this Institute, derived many of his ideas from the great German pathologist Rudolph Virchow. Virchow had a broad perspective of the study of mankind, which superseded his extraordinary studies of organ pathology. He encouraged early archeological studies and involved himself actively in the social policies and political life of his nation.

Research institutes devoted to the field of psychiatry have spread throughout the world and vigorous investigative units have sprung up in universities and in many independent teaching hospitals. From these research efforts have evolved the enormous expansion of the knowledge of personality functioning, psychopathology, and brain structure and function. New therapeutic and preventive approaches and hypotheses with powerful, heuristic potentials have emerged.<sup>9</sup>

## **CLASSIFICATION OF PSYCHOSOMATIC DISORDERS**

### **International Classification of Diseases (ICD-10; WHO-1993)**

Depending on tissue damage

- ❖ Psychological malfunctioning not associated with tissue damage
- ❖ Psychological malfunctioning associated with tissue damage

**Zegarelli E.V., Kutscher A.H. and Hyman G.A. (1978) Classified psychosomatic disorders as ;<sup>11</sup>**

- 1) Psychoneurotic disorder
  - 2) Psychophysiologic disorder
  - 3) Personality disorder
  - 4) Psychotic disorder
- 1) Psychoneurotic – Basic Characteristic – is subjective feeling of anxiety.
- Type of Neurosis –    Phobic  
                                  Obsessive- Compulsive  
                                  Depressive  
                                  Conversion
- 2) Psychophysiologic – Distress - renders the individual to physiologic dysfunction and eventual tissue damage, rather than neurotic defenses or psychotic withdrawal.
- 3) Personality: The individual utilizes patterns of action or behaviour rather than mental, somatic or emotional symptoms.
- 4) Psychotic – Characterized by personality disintegration with failure in the ability to perceive, evaluate and test reality.

Psychosomatic oral medicine

Infancy - mouth plays a vital role in exploration, feeding and establishing the affectionate bond with the mother. (Bowlby, 1969)

Freud - oral stage of development determine important personality traits, but that problems at this stage lead to predisposition to certain depression in later life.

### **Classification of Oral Psychosomatic Disorders:**

#### **I) McCarthy P.L. and Shklar G. (1980)<sup>12</sup>**

- 1) Oral psychosomatic diseases
  - a) Lichen planus
  - b) Aphthous stomatitis
  - c) Glossitis and stomatitis areata migrans
- 2) Oral diseases in which psychologic factors may play some etiologic role
  - a) Erythema multiforme
  - b) Mucous membrane pemphigoid
  - c) Chronic periodontal disease
- 3) Oral infections in which emotional stress serves as a predisposing factor
  - a) Recurrent herpes labialis
  - b) Necrotizing gingivitis
- 4) Oral diseases induced by neurotic habits
  - a) Leukoplakia
  - b) Biting of oral mucosa (self mutilation)
  - c) Physical / mechanical irritation
  - d) Dental / periodontal disease produced by bruxism
- 5) Neurotic oral symptoms
  - a) Glossodynia (Glossopyrosis)
  - b) Dysgeusia
  - c) Mucosal pain

#### **II) Bailoor and Nagesh (2001) classified oral psychosomatic disorders as <sup>13</sup>**

- I. Pain related disorders
  - 1) MPDS
  - 2) Atypical facial pain
  - 3) Atypical odontogenic pain
- II. Disorders related to altered oral sensation
  - 1) Burning mouth syndrome

- 2) Idiopathic xerostomia
- 3) Idiopathic dysguesia

III. Miscellaneous

- 1) Oral lichen planus
- 2) Recurrent aphthous ulcers
- 3) Psoriasis
- 4) Erythema multiforme
- 5) Cancerophobia
- 6) ANUG
- 7) Anorexia nervosa
- 8) Bruxism

**III) Classification according to presentation of symptoms**

**A. PAIN**

**1. Facial Arthromyalgia**

- a) TMJ dysfunction syndrome
- b) Myofacial pain dysfunction syndrome
- c) Costens syndrome
- d) Recurrent subluxations
- e) Persistent trismus

**2. Atypical facial pain**

- a) Atypical facial neuralgia
- b) Idiopathic facial pain

**3. Tension headache**

**4. Atypical odontalgia**

- a) Idiopathic periodontalgia
- b) Phantom tooth pain

**5. Intractable pain**

**6. Psychotic pain (delusional pain)**

**7. Myalgic encephalomyelitis**

- a) Post viral fatigue syndrome
- b) Royal free syndrome
- c) Icelandic disease
- d) Epidemic neurasthenia

**C. Hysterical or Conversion Disorders**

#### **D. Somatopsychic Problems**

1. Dysmorphophobia ( morphodyshoria)
2. Cancerophobia
3. Hypochondriasis
4. Monosymptomatic hypochondrial psychosis
5. Mental retardation or Handicap.
6. Manhausen's Syndrome.

#### **E. Oral psychosomatic diseases**

1. Aphthous ulcers
2. Factitious ulceration- stomatitis artefacta
3. Lichen planus
4. Geographic tongue
5. Erythema multiforme
6. Mucous membrane pemphigoid
7. Periodontal diseases
  - a. Acute necrotizing ulcerative gingivitis
  - b. Atypical gingivostomatitis
  - c. Excoriative gingivitis (gingivitis artefacta)
  - d. Thegosis and somatization (parafunctional occlusal traumatism)
  - e. General adaptation syndrome
8. Herpes Labialis
9. Bruxism

#### **F. Anorexia Nervosa and Bulimia, Eating Disorders**

#### **G. Litigation, Compensation and the Post Traumatic Stress Disorder**

### **IV) Revised simple working type classification proposed for psychosomatic disorders pertaining to dental practice by Shamim (2014)**

#### **1. Pain related disorders:**

- a. Myofascial pain dysfunction syndrome (MPDS)
- b. Atypical facial pain
- c. Atypical odontogenic pain
- d. Phantompain

#### **2. Disorders related to altered oral sensation:**

- a. Burning mouth syndrome
- b. Idiopathic xerostomia
- c. Idiopathic dysgeusia
- d. Glossodynia
- e. Glossopyrosis

**3. Disorders induced by neurotic habits:**

- a. Dental and periodontal diseases caused by bruxism
- b. Biting of oral mucosa (self mutilation)

**4. Autoimmune disorders:**

- a. Oral lichen planus
- b. Recurrent aphthous stomatitis
- c. Psoriasis
- d. Mucous membrane pemphigoid
- e. Erythema multiforme

**5. Disorder caused by altered perception of dentofacial form and function:**

- a. Body dysmorphic disorder

**6. Miscellaneous disorders:**

- a. Recurrent herpes labialis
- b. Necrotising ulcerative gingivostomatitis
- c. Chronic periodontal diseases
- d. Cancerophobia
- e. Delusional Halitosis.

**LICHEN PLANUS**

Oral lichen planus is a common chronic immunologic inflammatory mucocutaneous disorder that varies in appearance from keratotic (reticular or plaque like) to erythematous and ulcerative.

According to most research studies, the average patient with lichen planus is of middle age, with men and women affected in equal number. Some studies report a slightly higher female population. The disorder has been found in people of all races, but a very high percentage of the affected people are white.

Although many cases are asymptomatic and discovered upon routine oral examination, roughly 2/3rds of patients report oral discomfort upon presentation of their disease.<sup>14</sup>

Oral lichen planus presents as white striations, white papules, white plaques, erythema, erosions or blisters affecting predominantly the buccal mucosa, tongue and gingivae, although other sites are occasionally involved. Lesions are typically bilateral and often appear as a mixture of clinical subtypes, white or grey streaks may form a linear or reticular pattern on an erythematous background.<sup>15</sup>

Desquamative gingivitis, a clinically descriptive term that encompasses many diseases, can apply to conditions characterized by clinically atrophic lesions with histologic oral lichen planus.<sup>15</sup>

Kovesi G. and Bancozy J. (1973)<sup>16</sup> diagnosed oral lichen planus in 326 patients between 1960-1969, and according to them, psychic stress appeared to be an important etiologic factor along with smoking. Smoking was also considered as a possible etiologic factor especially in cases where the patient had smoked more than 10 cigarettes/day for 3 years. Sedative therapy bromides, barbiturates and phenothiazine was attempted in patients with supposed psychic factors.

Shafer W.G. et al (1983)<sup>17</sup> stated that lichen planus was associated with number of stress related medical disorders such as diabetes and hypertension.

Lowental U., Pisontis (1984)<sup>18</sup> examined 49 patients with clinically diagnosed oral lichen planus. These authors stated that stressful events frequently preceded episodes of symptoms in patients with symptomatic erosive (ulcerous) or bullous OLP, whereas no such relationship was seen in patients with asymptomatic OLP.

Scully M. and El-Kom M. (1985)<sup>19</sup> quoted the relationship of lichen planus with stress and also neurogenic basis was suggested.

Hampt B. Goronc (1987)<sup>20</sup> investigated 56 patients with clinically and histologically verified oral lichen planus and 44 non-OLP patients for the degree of mental disturbance by means of the Cornell Medical Index psychological questionnaire. Most of the patients had the subjective feeling that the clinical appearance of OLP, including discomfort, become worse during times of mental stress.

Humphris G., Field E.A. (1992)<sup>21</sup> stated that the role of psychological factors in oral lichen planus could be the result of the condition of oral lichen planus influencing psychological distress.

Sebastian J.V. Bogan (1992)<sup>22</sup> conducted a clinical study on 205 patients with oral lichen planus. 66 patients had a history of stress, diabetes was found in 27, and chronic liver disease in 44. Both stress and diabetes were found in two patients, 3 cases involved stress, diabetes and chronic liver disease. Diabetes and liver disease were simultaneously present in eight cases, where as stress and liver disease were associated in 10.

McCartan B.E. (1995)<sup>23</sup> investigated 50 patients with oral lichen planus for current anxiety and depression and for related personality factors. Anxiety levels, as measured on the hospital anxiety and depression (HAD) scale, were elevated in 50% of cases, while depression scores, measured on the same scale, were low in all but a few.

Sugerman P.B. et al (1995)<sup>24</sup> assessed the potential role of stress derived HSP (Heat Shock Protein) expression using avidine biotina complex immunochemistry with an anti HSP-70 polyclonal antibody, in normal oral mucosa sections of OLP, non specific oral ulceration and dysplastic OLP. They found that there was statistically significant difference in vertical and horizontal staining distribution when other groups compared with OLP.

Scully C. et al (1998)<sup>25</sup> suggested that stress has been widely held to be an important etiological factor in OLP, but there have been remarkably few studies (Lowenthal and Pisonti, 1984). A statistically significant difference was found in the psychological profiles of patients affected by OLP as compared with those of controls in one study (Hary et al 1987) and others have found that patients with OLP had a tendency to be depressed (Bergdah et al, 1995).

Sugerman PB, Savage NW (2002)<sup>26</sup> stated exacerbation of OLP was linked to periods of psychological stress and anxiety.

Chaudary S (2004)<sup>27</sup> studied the importance of psychological stressors in patients with Oral lichen planus. The General Health Questionnaire version 28(GHQ-28) and the Hospital Anxiety and Depression Scale were used to evaluate psychological stressors in terms of stress, anxiety and depression respectively. Significantly higher stress, anxiety and depression levels were found in the OLP and positive control than the general population. They suggest that psychological stressors play an important role in the causation of OLP.

## **APHTHOUS STOMATITIS**

### **RECURRENT APHTHOUS STOMATITIS :**

#### **Definition :**

RAU is an inflammatory condition of unknown etiology characterized by painful recurrent, single or multiple ulcerations of the oral mucosa .<sup>26</sup>

The Greek term aphthi was initially used in relation to disorders of the mouth and is credited to Hippocrates (460-370 BC). Today recurrent aphthous ulceration, or recurrent aphthous stomatitis (RAS), is recognized as the most common oral mucosal disease known to human beings.<sup>29</sup>

Epidemiologic studies indicate that the prevalence of RAS is between 2% and 50% in the general population, most estimates fall between 5% and 25%. The peak age of onset for RAS is between 10 and 19 years. After childhood and adolescence it may continue throughout the entire human lifespan without geographic age, sex or race-related preference.

### **Clinical Manifestations :**

The most common presentation of RAS is minor RAS. Minor RAS manifests as recurrent, round, clearly defined, small, painful ulcers with shallow necrotic contents, raised margins, and erythematous halos. They are generally smaller than 10 mm in diameter and have a gray-white pseudomembrane. These lesions heal within 10 to 14 days without scarring. The most common location is on non-keratinized oral mucosa (the labial and buccal mucosa and floor of mouth).

Major RAS is occasionally referred to as Sutton's disease or periadenitis mucosa necrotica recurrens and is less common (approximately 10% to 15% of all RAS) yet more severe than minor RAS, they are larger than 10 mm in diameter, are deeper, often scar, and last for weeks to months. These lesions have a predilection for lips, tongue, soft palate and the palatal fauces and cause significant pain and dysphagia.

The least common form of RAS is herpetiform aphthous ulcers, which afflict 5% to 10% of patients characterize this rare form of RAS and they occur throughout the oral cavity. They tend to be small (2 to 3 mm) and numerous (ranging from 10 to 100 ulcers) but can become confluent to produce larger, plaque form, irregular lesions, lesions last 7 to 30 days and have the potential to scar.

### **Association between stress and oral ulcers**

**Psychological stress**

↓

**Increase number of leukocytes in the epithelium**

↓

**Degeneration of suprabasal epithelial cells**

↓

**Lymphocyte infiltrate in lamina propria**

↓

**Extensive edema**

↓

**Epithelial degeneration**



### **Frank ulceration**

**Miller M.F., Ship I.I. (1977)**<sup>30</sup> conducted, a 12 year retrospective investigation of 1,778 professional school students from the University of Pennsylvania and 651 proband subjects were available for the follow-up investigation. Techniques of subjective evaluation of disease status (mailed schedules describing disease and color photographs) were used in making an assessment of RAU, including both current disease and histories of prior disease.

The data presented suggested a trend toward decreased RAU prevalence and severity among physicians, dentists, veterinarians and nurses as compared to professional school students. Initially it has been suggested that the students may represent the highest levels of RAU and that special features of the life patterns of the students favor disease expression. But of late several factors could have contributed to this decrease.

**Buajeeb W. et al (1990)**<sup>31</sup> reported the relationship of recurrent aphthous stomatitis (RAS) to psychological factors. All new patients seen during May 1988 – November 1988 at the oral diagnostic clinic, completed the questionnaire regarding their history of RAS. For the measurement of anxiety, patients were given the self-rating anxiety scale (SAS). Of the 3,106 patients studied, 46.4% reported a positive history of RAS. In this population, females were significantly more than males. They concluded that patients with RAS were more anxious than patients without RAS.

**Peretz B. (1994)**<sup>32</sup> described a case of major recurrent aphthous stomatitis in a 11 year old girl to illustrate a disease which is relatively rare in children, emotional

stress was suggested as a possible etiological factor for the occurrence of major RA in this patient. Disappearance of these ulcers occurred after stress had been relieved.

**Mc Carton B.E. et al (1996)**<sup>33</sup> measured salivary cortisol levels in two groups of patients with recurrent aphthous ulcerations. One group of patients had persistent aphthae (Group 1) and other had been relieved of their aphthous following correction of detected haematinic deficiency states (Group 2). Anxiety was measured using the hospital anxiety and depression scale and radioimmunoassay of salivary cortisol. There was a statistically significant increase in proportion of borderline or clinically anxious patients in Group I compared to Group 2. It was concluded that stress plays a role in the etiology of recurrent aphthous stomatitis, particularly in patients who have an underlying anxiety trait.

**Natah S.S. et al (2004)**<sup>29</sup> in their study in which a relaxation / imagery treatment programme was used, found a significant decrease in the frequency of ulcer recurrence among all treated subjects.

## **BURNING MOUTH SYNDROMES**

### **DEFINITION :**

Burning mouth syndrome or more appropriately known as burning mouth disorder (BMD), is a painful oral condition featuring burning sensations of the tongue, lips, and mucosal regions of the mouth. Burning mouth syndrome is a distinct clinical entity of multifactorial etiology, in which no oral mucosal abnormality is evident on clinical examination. Any area of the oral mucosa can be affected, but the tongue and the denture bearing areas are most commonly involved.

The etiology of burning mouth have been considered to be multifactorial, it has been suggested that causative factors can be divided into 3 groups – local, system and psychologic.

### **Clinical Manifestations :**

Burning mouth disorder is characterized by an unexplained, usually persistent burning sensation of the oral soft tissues. Symptoms range in intensity from mild to severe, with most experiencing moderate levels of pain that appear on awakening or

later in the day. The tongue, typically the anterior 1/3<sup>rd</sup> of the 'dorsal surface, is most commonly affected, followed by the lips. The palate, gingiva and oropharynx are less commonly involved. Burning mouth syndrome mostly affects middle aged women.

Burning mouth disorder is accompanied by oral dryness and taste abnormalities (dysguesia) in at least 50% of cases. In patients with concomitant hyposalivation and/or dysguesia, examination often reveals fissuring of the tongue, dryness of and adherent saliva on the dorsum of the tongue, prominent fungi form papilla on the anterior one third of the tongue and taste abnormalities.<sup>34</sup>

Burning mouth is a condition that elicits a burning sensation in the oral cavity. When the oral mucosa is normal on clinical examination, these burning sensations are called burning mouth syndrome (BMS).

Multiple sites in the oral cavity may be affected, the most common being the tongue and is usually accompanied by a variety of complaints that may include dryness and an altered or disturbing 'taste'. The burning has been reported to be of moderate or severe intensity and may vary over the day.

The effect of cognitive therapy (CT) on 30 patients with resistant BMS after odontological and medical treatment was studied.<sup>35</sup>

**Ziskin D.E., Moulton R. (1948)**<sup>36</sup> considered that 13 out of 14 patients with burning orolingual pain suffered from emotional disturbance without organic pain.

**Quinn J.H. (1965)**<sup>37</sup> in his study of 54 patients with burning mouth, concluded that anxiety related in certain oral habits such as teeth clenching and tongue thrusting that explained their disorder, however no tongue lesions were evident.

**Ewalt J. (1966)**<sup>38</sup> reported that a common complaint in depression was a peculiar taste or a stinging or burning sensation around the teeth, gingivae, or tongue.

**Lescells R.G. (1966)**<sup>39</sup> in his study of patients with atypical facial pain, found a history of depressive illness in most cases, but he also found that depression was atypical.

**Schoenberg B. (1967)**<sup>40</sup> in their study of 55 cases of sore mouth, observed that 22% of the patients were overly depressed at the time of the interview and reported an association of psychological factors in burning mouth syndrome.

**Shoenberg B. et al (1971)**<sup>41</sup> reported 21 patients with idiopathic burning mouth who were studied by clinical interview and judged 81% to be currently depressed, with the other 19% showing some evidence of depression.

**Brooke R.I., Seganski D.P**<sup>42</sup> in their study of 55 cases of sore mouth, 22% of the patients were overly depressed at the time of the interview.

**Harris M., Davies G. (1980)**<sup>43</sup> stated that the association of emotional and mental suffering with symptoms in the mouth could be understood on the basis of the anatomic, physiological and developmental aspects of oral functioning. They also proposed that patients with burning mouth were suffering from either cancerophobia or reactive depression. A significant percentage (71%) patients health improved after 9 weeks of antidepressant treatment.

**Browning S. et al (1987)**<sup>44</sup> conducted study on 25 patients with a diagnosis of non organic burning mouth syndrome and 25 patients with organically based painful disorders of the mouth who were age and sex matched. All patients interviewed by a psychiatrist and completed the General Health questionnaire to screen for psychiatric disorders. The results of this controlled study of patients with burning mouth syndrome showed that a significantly higher proportion of patients in the burning mouth group had an associated psychiatric disorder when compared with the control group. The psychological disorders described in association with burning mouth syndrome included anxiety status, hypochondrial reactions, conversion reactions, tic and masochistic reaction.

**Grushka M. Sessle B.J., Hawley T.P. (1987)**<sup>45</sup> assumed that, in most of the patients with BMS, the causative organic factor was a functional disorder entailing psychologic, emotional and neurologic dysfunctions.

**Van der Ploeg H.M. et al (1987)**<sup>46</sup> reported results of psychological questionnaire survey of 184 patients who had burning mouth syndrome. They concluded that in large number of patients with glossodynia, psychological aspects such as anxiety, depression, and neurotic tendency were of great importance.

**Lamey P.J., A.B. Lamb (1989)**<sup>47</sup> applied anxiety and depression (HAD-hospital anxiety and depression scale) in 74 patients with burning mouth syndrome. From the results it can be concluded that more than one third of the study population, the majority of whom were females, have anxiety psychosis. Authors suggested that their somatic symptoms of burning mouth were partly due to the psychological result of restlessness, tension and an inheritant ability to relax .They concluded that the management of this group of patients will be improved by objective assessment of their psychological status by the HAD scale.

**Zilli C. (1989)**<sup>48</sup> assessed 31 consecutive subjects suffering from oral dysesthesia and without detectable organic disease with a screening test for psychiatric illness, the GHQ, 28 item version (GHQ-28). 12 subjects also completed the irritability, depression and anxiety Scale (IDA). The subjects with oral dysesthesia approved to have psychiatric illness more often than the other subjects with chronic pain. Their findings indicated that psychiatric illness, especially depression, plays an important role in this disorder.

**Attonasio Ronald (1991)**<sup>49</sup> stated that BMS was thought to be a psychological ailment and an individual with a lingual personality and most frequent cause being psychologic malfunctioning. They also stated that the beneficial effects of Tricyclic Anti depressants for reliving chronic pain have been corroborated in other related studies as well, which indicate that low doses of TCAs may act therapeutically as analgesics, separate from their action as antidepressants.

**Gorsky Meir et al (1991)**<sup>50</sup> conducted study on 130 patients with burning mouth syndrome for clinical characteristics and treatment responses. Most patients were postmenopausal women, the tongue was involved alone or with other oral sites

in 78% of the patients. They stated that psychogenesis was the most important etiologic factor.

**Bailoor D.N. et al (1992)**<sup>51</sup> in a South Indian study, reported this syndrome along with a high degree of depression predominantly in post-menopausal women. They suggested that psychiatric counseling and antidepressant medications were better modalities to treat such patients.

**D'Ambrosio A. Joseph and Fotos G. Peter (1993)**<sup>52</sup> recognized mood and personality changes are associated factors in BMS, to the extent that BMS was frequently labeled as psychological ailment. A psychogenic basis for BMS was derived from both psychological and drug therapy studies in BMS studies. Psychological tests and clinical interviews in numerous studies were used to demonstrate psychological dysfunction (eg depression, anxiety, irritability) in subjects with oral complaints, including mouth burning.

**Paterson A.J. et al (1995)**<sup>53</sup> They investigated 84 patients with burning mouth syndrome, using hospital anxiety and depression (HAD) scale questionnaire. A control group of 69 patients was also included. All patients interviewed regarding parafunctional habits and were subjectively examined for signs of occlusal wear of natural teeth or denture. There was a statistically significant relationship between parafunctional habits and anxiety as indicated by HAD scale but not with depression.

**Jerlong B.B. (1997)**<sup>54</sup> studied 20 women suffering from burning mouth syndrome (BMS) rated with regard to depressive symptoms and anxiety, values were compared to disability level assessed by interviews. The study included a psychological analysis of the communication pattern in the patient doctor relationship and concluded that somatic treatment dependence and helplessness may activate and defensive reactions in the dentist.

**Bogetto et al (1998)**<sup>55</sup> conducted a study on 102 patients with BMS in order to evaluate the prevalence and type of psychiatric disorders co-existing with burning mouth syndrome. They found that most prevalent concurrent diagnosis were

depressive disorders and generalized anxiety disorder and concluded that BMS has a high psychiatric co-morbidity but can occur in the absence of psychiatric diagnosis.

**Bergdahl M., Bergdahl J. (1999)**<sup>56</sup> surveyed 669 men and 758 men for oral complaints and salivary flow between the ages 20 and 69 years. 53 individuals, 11 men and 42 women were classified as having BMS. Various local, systemic and psychological factors have been found to be associated with BMS. The intensity of the burning sensations was estimated to be 4.6 on a visual analogue scale. It was concluded that BMS should be seen as a marker of illness and/or distress and the complex etiology of BMS demands specialist treatment.

**Reiss M., Reiss G. (1999)**<sup>57</sup> included hematological diseases, vitamin deficiencies, dental work, hormonal factors, or infections in addition to psychological disorders (such as neurosis, depression or phobias) as the primary etiological factors for glossodynia. They also mentioned that a multidisciplinary approach is required for the appropriate assessment of this disorder, i.e. the diagnostic procedure should involve dentistry, neurology, and internal medicine.

**Formaker B.K. and Frank M.E. (2000)**<sup>58</sup> evaluated seventy three patients with burning mouth syndrome (BMS), on oral pain disorder occurring primarily in post-menopausal women and frequently accompanied by taste complaints. This association of symptoms suggested an interaction between the mechanisms of nociception and gustation.

**Pokupec-Gruden J.S. et al (2000)**<sup>59</sup> researched upon the association between a psychogenic factor and stomatopyrosis as its consequence using the visual analogue scale for subjective assessment of the symptoms in the oral cavity. They took into account changes of depression, anxiety, adaptability and emotional stability. They also established a systematic and a psychiatric diagnosis that was necessary for making the right choices when treating people with stomatopyrosis and concluded that stomatopyrosis, a psychosomatic state can be cured or treated by appropriate treatment, which includes psychiatric treatment as well.

**Al Quron Firos A.M. (2004)**<sup>60</sup> studied 32 patients with burning mouth syndrome and 32 matched control subjects and were evaluated for their personality profile using a comprehensive, reliable, and validated inventory to measure domains of personality, namely neuroticism, extraversion, openness, Agreeableness and conscientiousness and some of the important traits or facts that define each domain. Many personality characteristics differentiate burning mouth syndrome patients from controls according to the Neo PI-R. They stated that psychotherapy could be initiated in BMS patients with psychological predisposing factors.

### **XEROSTOMIA**

Xerostomia or dry mouth is the abnormal reduction of saliva and can be a symptom of certain diseases or be an adverse effect of certain medications. The causes of xerostomia include disease of the salivary glands such as Sjogren's syndrome, uncontrolled diabetes mellitus, radiation to the head and neck region, chemotherapy and a number of commonly used medications. Injury to the head or neck can damage the nerves that are essential for the production and secretion of saliva by the salivary glands. Occasionally, xerostomia may be subjective, with no evidence of altered salivary flow. In these patients, xerostomia is often associated with psychological factor.<sup>61</sup>

The clinical consequences of long standing xerostomia are increased frequency of caries (cervical caries), productivity toward acute gingivitis, dysarthria, dysphagia, dysgeusia, proclivity toward candidal infection, burning tongue or depapillation of tongue, oral mucosal soreness, dry, sore, cracked lips and salivary gland enlargement.

The investigations of xerostomia centers upon a series of clinical, radiologic and laboratory based tests. Much can be elicited from the history and clinical examination alone, and on the basis of these and a knowledge of the possible causes of xerostomia, certain specific investigations can be undertaken to confirm the working diagnosis. The investigation can be grouped under the following headings : hematology, biochemistry, immunology, imaging, histology and others.

The different local and systemic methods for the management of xerostomia are used.

**Brown C.C. (1970)**<sup>62</sup> stated the conditions like depression may induce feeling of oral dryness (Brown C.C. : the parotid puzzle, a review of the literature on human salivation and its application to psychophysiology).

**Costa P.T. et al (1980)**<sup>63</sup> studied the stimulated flow rate, pH, osmolality and eleven composition variables in 390 normal men and correlated against eight personality dimensions, flow rate, pH, osmolality, and eight of the eleven salivary components were significantly correlated with four personality traits : consciousness, shrewdness and introversion. (Paul T. Costa, Howard H. Chauncey, Charles L. Rose and Krichan K. Kapur : Relationship of parotid saliva flow rate and comparison with personality traits in healthy men).

**Bergdahl H., Bergdahl J., Johansson I. (1997)**<sup>64</sup> assessed depressive symptoms in 94 healthy subjects with normal flow rates for unstimulated and stimulated whole saliva but with a subjective sensation of a dry mouth was assessed by the Beck Depression Inventory (BDI) and compared with healthy age – and gender matched controls. The subjects with a subjective dry mouth condition were significantly more depressive and also had a significantly higher frequency of depressive symptoms. Depression was found in 21.3% of the individuals with a subjective dry mouth sensation and in 3.2% of the controls. The results of their study indicate that, in some cases, subjective dry mouth may be of psychological origin. (Bergdahl M., Bergdahl J., Johansson I. : Depressive symptoms in individuals with idiopathic subjective dry mouth).

**Bergdahl M. and Bergdahl J. (2000)**<sup>65</sup> studied 1202 individuals divided into 3 study groups and controls. In their study of salivary flow and oral complaints, individuals were randomly selected from the public dental health service registers representing 48,500 individually living in places with different sociodemographic structures in the countries of North of Sweden, which included 655 women and 547 men. They used Beck Depression Inventory. The state-trait Anxiety Inventory and the General Perceived Stress Questionnaire for the assessment of depression, state-

trait Anxiety and General Perceived stress. Subjective oral dryness and unstimulated salivary flow  $>0.1$  mL/min were significantly associated with depression, trait anxiety, perceived stress, state anxiety, female gender and intake of antihypertensives. They found that age and medication seemed to play a more important role in individuals with hyposalivation, and female gender and psychological factors in individuals with subjective oral dryness.

### **BENIGN MIGRATORY GLOSSITIS**

[Erythema migrans, Geographic tongue, wandering rash of the tongue, erythema areata migrans, stomatitis areata migrans).

Erythema Migrans is a common benign condition that primarily affects the tongue. It is often detected on routine examination of the oral mucosa. The lesion occurs in 1% to 3% of the population. Females are affected more frequently than males by a 2:1 ratio.

Even though erythema migrans has been documented for many years, the etiopathogenesis is still unknown. Some investigators have suggested that erythema migrans occurs with increased frequency in atopic individuals, thus raising the possibility that it represents a type of hypersensitivity to an environmental factor. In addition, the lesions of erythema migrans in one female patient reportedly waxed and waned predictably with oral contraceptive therapy, suggesting that hormonal factors may be relevant.<sup>66</sup>

#### **Clinical Features :**

The characteristic lesions of erythema migrans are seen on the anterior two thirds of the dorsal tongue mucosa. They appear as multiple, well demarcated zones of erythema, concentrated at the tip and lateral borders of the tongue. This erythema is due to atrophy of the filiform papillae, and these atrophic areas are typically surrounded at least partially by a slightly elevated, yellowish white, serpentine or scalloped border.

Frequently, the lesion begins as a small white patch, which then develops a central erythematous atrophic zone and enlarge centrifugally. Often patients with fissured tongue are affected with erythema migrans as well. Some patients may have

only a solitary lesion, but this is uncommon. The lesions are usually asymptomatic, although, a burning sensation or sensitivity to hot or spicy foods may be noted when the lesions are active. Only rarely is the burning sensation more constant and severe.

Very infrequently, erythema migrans may occur on oral mucosal sites other than the tongue. In these instances, the tongue is almost always affected, however other lesions develop on the buccal mucosal, labial mucosa, and less frequently on the soft palate. These lesions typically produce no symptoms, and they can be identified by a yellowish-white serpentine or scalloped border that surrounds an erythematous zone.<sup>66</sup>

#### **Treatment and Prognosis :**

Generally, no treatment is indicated for patients with erythema migrans. Infrequently, patients may complain of tenderness or a burning sensation that is so severe that it disrupts their lifestyle. In such cases, topical corticosteroids, such as fluoroamide or betamethasone gel, may provide relief when applied as a thin film several times a day to the lesional areas. One uncontrolled study has recently suggested that zinc supplementation may be effective for symptomatic erythema migrans.

Zegarelli DJ (1984)<sup>67</sup> studied the burning complaint of each of 57 patients and psychogenesis was found to be the most frequent cause, followed by geographic tongue. The purely psychogenic group was composed mostly of postmenopausal women. The tongue and palate were the most frequently affected sites. There was some similarity among patients in the geographic tongue and psychogenesis groups.

Hauf G. (1987)<sup>68</sup> conducted a retrospective study of 64 patients with orofacial dysaesthesia. Special emphasis was laid on the patients symptoms and on the manipulative treatments they received before they were referred for psychiatric consultation. The patients had suffered from chronic orofacial pain or feelings of discomfort for periods ranging from 6 months upto to 25 years. Their study clearly showed that psychiatric consultations were still seldom made in patients with chronic orofacial dysarthesia, that many patients had mental disorder, and that most chronic psychosomatic pain disorders were treated as acute specific pain.

## ATYPICAL FACIAL PAIN

The term atypical orofacial pain, first used more than 60 years ago to describe a group of patients with an orofacial pain syndrome that did not conform to the standard anatomic or etiologic categories of facial pain and who responded poorly to the treatment, has often been used as a designation for any chronic pain that responds poorly to the treatment (eg. Atypical chest pain).

Atypical orofacial pain refers to pain that does not conform to recognized anatomic pathways in its distribution and hence includes orofacial pain that <sup>69</sup>

- Cannot be relieved by interruption of trigeminal, facial (accessory) or glossopharyngeal pathways.
- Has no identifiable neuropathic, extraneural or central focus or
- Is associated with a potential pain producing focus but is out of proportion to the focus or not strictly related to it in terms of recognized anatomic pathways and physiologic mechanisms.

Many authors refer atypical orofacial pain as a grab-bag category or a poorly defined syndrome with multiple etiologies.

Psychologic factors are also prominent in this group of patients, and it is difficult to distinguish the category of atypical facial pain clearly from what other authors may refer to as psychogenic or psychologic pain.<sup>69</sup>

TMJ myofascial dysfunction, orofacial pain of vascular origin, and referred pains in the head and neck all show some resemblance to atypical facial pain, and this term was used on occasion to include these conditions.

Atypical facial pain must be distinguished from atypical trigeminal neuralgia on the basis of the ability to respond to the symptoms of steady aching pain. Orofacial pain of neuropathic origin possess no one quality and may be either episodic as in the doulourux or a steady aching pain.

Clinical Features :

The feature that most commonly suggests a diagnosis of atypical facial pain is the patients inability to define a precise location and quality of the pain. The patient

frequently uses description such as “deep dull ache”. A tendency to discursive wondering replies is often noted in these patients, adding significantly to the clinical frustration when trying to document a clear history of the patient’s pain problem.<sup>69</sup>

Patients with these atypical orofacial pain described other oral sensory problems such as burning, dryness, and taste aberrations. When these patients are followed for many years, one chronic oral symptom often replaces another with diagnosis and treatment of one time focused on pain and at another on suspected salivary glands disease and glossodynia.

As a group, patients exhibiting the features of atypical facial pain (or psychogenic or somatoform pain) are frequently middle aged female (female : male ratio is 19:1), and have a long history of chronic facial pain or dysesthesia. Most often, the pain is described initially as unilateral, although 20% to 35% patients, subsequently develop bilateral symptoms. The quality and location of pain are poorly defined and the patient often has recourse to symbolic language when attempting to characterize the pain verbally.<sup>69</sup>

**Paulson G.W. (1977)**<sup>70</sup> mentioned the use of antidepressant and psychotropic agents as worth considering in the treatment of atypical facial pain, but the patient’s state along with the emotional concomitants of the illness requires special attention.

**Maier C. and Hoffmeister B. (1989)**<sup>71</sup> suggested a more complete approach with 4 treatment modalities for the management of patients with atypical facial pain, which included Transcutaneous electric nerve stimulation (TENS), Sympathetic nerve block, Drug therapy, and Psychotherapy .

**Reher P. and Harris M. (1998)**<sup>72</sup> mentioned that occlusal forces are less important in its etiology and psychological and biochemical factors are more recognized. They also suggested that it is essential to take complete history including the psychological and social aspects in order to arrive at accurate diagnosis.

**Viekers E.A., Covering M.J., Woodhose A.(1998)**<sup>73</sup> assessed pain description and intensity ratings, gender differences, prevalence of concurrent conditions, and interinstrument relationships of the McGill pain center study in 120 consecutive chronic orofacial pain patients. There were significantly higher total pain

scores of the McGill pain questionnaire in patients with multiple conditions as compared with single condition.

**Junpier R.P. and Glynn C.J. (1999)**<sup>74</sup> in their study on 83 patients have explained atypical facial pain as dull and unrelenting and its site ill defined. They found that it generally affects younger people, with women predominating and sometimes difficult to distinguish this entity from psychogenetic or psychologic pain since most patients in this group also had a prominent psychologic factor. They stated that rating scales should also confirm the existence of any anxiety or depression.

**Woda A., Pionohom P. (2000)**<sup>75</sup> et al found that the presence of psychological factors was a common feature, but it was not known whether these were causal or whether the pain induced the psychosocial problem.

**McNeil D.N. et al (2001)**<sup>76</sup> examined whether fear of pain, dental fear, general indices of psychological distress, and self-reported stress timely differed between 40 orofacial pain patients and 40 gender and age matched control general dental patients. They also explored how fear of pain, as measured by the fear of pain questionnaire III relates to established measures of psychological problems in their sample of patients. Their results indicated that fear of pain and anxiety related distress broadly defined, were particularly elevated in orofacial pain patients relative to matched controls.

## **ATYPICAL ODONTALGIA**

### **(IDIOPATHIC OR PHANTOM TOOTH PAIN)**

Atypical odontalgia, and idiopathic odontalgia or periodontalgia, and phantom tooth pain describe tooth ache with no detectable causes (ie. Persistent pain in a single tooth or group of teeth that exhibits no abnormality on percussion, thermal or electrical diagnostic testing or radiographic examination). Characteristically, the pain is unaffected by endodontic therapy or extraction of the tooth and persist at the extraction site or moves to an adjacent tooth. Like atypical facial pain, this diagnosis is usually made by exclusion, and in number of cases, the cause of previously unexplained pain becomes apparent with time. With an exception of the rather well-localized character of pain, atypical odontalgia is difficult to distinguish from the

atypical facial pain and most authors assume it is a variant of atypical facial pain or psychogenic pain.<sup>69</sup>

Features shared by the two conditions include age distribution, female predominance, onset usually following a dental procedure with persistence of pain despite a variety of endodontic or surgical procedures, associated emotional and mental problems, and response to treatment with antidepressant medication.

An association between a history of migraine and atypical odontalgia has been reported and vascular spasm of alveolar blood vessels postulated as an alternative explanation. The association with depression is far stronger in most series of cases, and classification of the condition as a form of atypical, psychogenic or somatoform facial pain seems better justified.

As with these conditions restorative, endodontic periodontal and surgical procedures should be avoided in atypical odontalgia unless clearly indicated by physical examination / or radiographic findings.

This is a variant of atypical facial pain or psychogenic pain since it also shares similar age distribution and female predominance with the latter. It is described as a persistent tooth or teeth pain with no exhibiting abnormalities on percussion, thermal, electric diagnostic testing or radiographic examination and also responds poorly to the treatment. The incidence of atypical odontalgia varies from 3-6% in general population as studied by Marbach J.J. et al with a female predominance.<sup>77</sup>

The average age for the patients with atypical facial pain is in the mid-forties but, has ranged from 20 to 82.

**Bates Robert Edward Jr. and Stewart Carol Marie (1991)**<sup>78</sup> studied 30 cases of atypical odontalgia and clinical characteristics of these cases were compared with other cases reported in literature. The resulted pain could then be the result of a vascular mechanism, psychological aspects such as stress and/or emotional disturbance, or even damage or sensory nerve.

**Schnurr R.F., Brooks R.I. (1992)**<sup>79</sup> studied 120 patients of atypical odontalgia which included women about 81% between the ages of 23 and 60. They stated that psychological disturbance may play a less significant role than initially thought and antidepressant medication as the treatment of choice for this condition.

**Graff-Radford S.B. and Solberg W.K. (1993)<sup>80</sup>** found that their findings failed to support psychological dysfunction as a primary condition associated with patients suffering from atypical odontalgia.

**Nicolodi M. and Sicuteri F. (1993)<sup>81</sup>** have related the cause of atypical odontalgia to many factors, including psychological ones.

**Lilly Jeffrey P. and Law Alan S. (1997)<sup>82</sup>** reported atypical odontalgia in among females in 74% to 100% of cases. They stated that, the mechanisms for atypical odontalgia include psychological, vascular and neural differentiation and the most effective reported treatments for atypical odontalgia were pharmacologic, with the drug of choice being tricyclic antidepressants.

**Vickers E.R. et al (1998)<sup>83</sup>** in their study, evaluated 50 patients diagnosed with odontalgia by pharmacological procedures including topical anesthetic application and phentolamine infusion. Each patient was diagnosed by the pain center oral surgeon in collaboration with other pain center personnel (pain specialist, psychologist, psychiatrist, physiotherapist). Early evidence based treatment of AO like long-term tricyclic antidepressant medication with adjunct psychological interventions were also tried. Result of their pharmacological procedures suggested that atypical odontalgia was a neuropathic pain of the oral cavity that may have a component of sympathetically maintained pain.

## **IDIOPATHIC DYSGEUSIA**

### **Definition :**

Dysgeusia is defined as a persistent abnormal taste. Dysgeusia is less tolerated than hypoguesia or hyposmia.

Most cases of dysgeusia are produced by or associated with an underlying systemic disorder such as radiation therapy to the head and neck region. Trauma, tumors, or inflammation of the peripheral nerves of the gustatory system usually produce transient hypoguesia rather than dysgeusia. In contrast, relatively common upper respiratory infections produce a temporary and mild dysgeusia in almost 1/3<sup>rd</sup>

of cases, although they seldom produce hypogeusia. CNS neoplasms predominantly produce dysgeusia.

The perception of a particular taste depends on its concentration in a liquid environment. Hence, persons with severe dry mouth may suffer from both hypogeusia and dysgeusia. In addition, more than 200 drugs are known to produce taste disturbances. 40% of persons with clinical depression complain of dysgeusia.

Affected patients may describe their altered taste as one of the primary ones, but many describe the new taste as metallic, foul or rancid. The latter two are more likely to be associated with aberrant odor perception (parosmia) than with dysgeusia. The altered taste may require a stimulus such as certain foods or liquids, in which case the taste is said to be distorted. If no stimulus is required, the dysgeusia is classified as a “phantom” taste.

If an underlying disease or process is identified and treated successfully; the taste function should return to normal. For idiopathic cases there is no effective pharmacologic or surgical therapy. Idiopathic dysgeusia is less of a problem for the patient, but tends to slowly become worse overtime.

**Steiner J.E. et al (1969)**<sup>84</sup> suggested that taste dysfunction was another accompanying complaint along with idiopathic xerostomia and also has been considered a manifestation of depression.

**Deems D.A. et al (1991)**<sup>85</sup> agreed on the fact that depression frequently accompanies chemosensory distortion.

**Mott A.E. et al (1993)**<sup>86</sup> stated that clinically significant taste loss was less common than abnormal taster (dysgeusias) and both were caused by a previous viral upper respiratory infection, head trauma, iatrogenic causation, neurologic or psychiatric disorders, toxic chemical exposure, systemic conditions, xerostomia, severe nutritional deficiency and some oral or dental disorders.

**Osaki T. et al (1996)**<sup>87</sup> investigated 14 patients with abnormal taste sensation (dysgeusia) and found that abnormal taste sensation may be induced by many oral and

systemic disturbance. They found that the treatment of depression on many occasions reduced the severity or completely eliminated these subjective complaints.

### **ACUTE NECROTIZING ULCERATIVE GINGIVITIS (ANUG)**

Description of acute necrotizing ulcerative gingivitis (ANUG) have been recorded of hundreds of years, and the disease has been assigned a multitude of names.

Xenophon stated in 401 BC that many of his soldier's; on their retreat from Persia; were plagued with sore, ulcerated and foul smelling mouths. John Hunter in 1778 is credited with making the first clinical differential diagnosis between gingival lesions now recognized as representing ANUG and the oral symptoms of scurvy.

He noted swelling and sponginess of 'gingiva between the teeth', along with tenderness, bleeding and ulceration over the inflamed gingiva. Hirschfeld et al cited Bergerom, who, while serving with French troops in 1859, also described a similar disease with both acute and chronic forms. Hirschfeld in 1886, added the diagnostic features of ropy saliva, enlarged submaxillary lymph glands, fever and malaise to the already known pathognomonic signs of fetid breath, bleeding gums, painful gums and pseudomembraneous ulcers.<sup>88</sup>

Acute necrotizing ulcerative gingivitis is an endogenous oral infection that is characterized by necrosis of the gingiva.

ANUG became known notoriously as "trench mouth" during World War I because of its prevalence in the combat trenches, and it was incorrectly considered a highly contagious disease. The organisms most frequently mentioned as working symbiotically to cause the lesions are the fusiform bacillus and spirochetes.

Classic ANUG in patients without an underlying medical disorder is found most often in those between the ages of 16 and 30 years, and it is associated with 3 major factors.

1. Poor oral hygiene with pre-existing marginal gingivitis or faulty dental restorations.
2. Smoking
3. Emotional stress

Systemic disorders associated with ANUG are disease affecting neutrophils (such as leukemia or aplastic anaemia), marked malnutrition, and HIV infection. Malnutrition associated cases are reported from emergent countries where the untreated disease may progress to noma, a large necrotic ulcer extending from the oral mucosa through the facial soft tissues.<sup>89</sup>

### **CLINICAL MANIFESTATIONS :**

The onset of acute forms of ANUG is usually sudden, with pain, tenderness, profuse salivation, a peculiar metallic taste, and spontaneous bleeding from the gingival tissues. The patient commonly experiences a loss of the sense of taste and a diminished pleasure from smoking. The teeth are frequently thought to be slightly extruded, sensitive to pressure, or to have a “woody sensation”. At times they are lightly movable. The signs noted most frequently are gingival bleeding and blunting of the interdental papillae.

The typical lesions of ANUG consists of necrotic punched out ulcerations, developing most commonly in the interdental papillae and the marginal gingivae. These ulcerations can be observed most easily on the interdental papillae, but ulceration may develop in the cheeks, the lips and the tongue, where these tissues come in contact with the gingival lesions or following trauma. Ulcerations also may be found on the palate and in the pharyngeal area. When the lesions have spread beyond the gingivae, blood dyscrasias and immunodeficiency should be ruled out by ordering appropriate laboratory tests, depending upon associated signs and symptoms. The ulcerative lesions may progress to involve the alveolar process with sequestration of the teeth and bone when gingival hemorrhage is a prominent symptom, the teeth may become superficially stained with a brown color, and the mouth odor is extensively offensive.

**Pindborg J.J. (1951)**<sup>90</sup> examined 9577 men in the Danish defence forces, and concluded that after some months of service, there was a considerable increase in the

number of ANUG cases. **Grupes H.E. and Wilder L.S. (1956)**<sup>91</sup> reported that ANUG was present in 2.2% of a newly inducted army personnel population. The coincidence of ANUG with nail biting suggested a psychosomatic etiological factor.

**Giddon D.B. et al (1963)**<sup>92</sup> in his epidemiological study of a University population, reported that the monthly prevalence of ANUG appeared to have some relation to situational factors such as academic examination or vacation periods. **Formicola A.J. et al (1970)**<sup>93</sup> investigated personality traits of student naval aviators, who were undergoing preflight training. Comparing students with ANUG with a healthy control group they found a significant positive correlation between dominance and ANUG, and a significant negative correlation between abasement and ANUG. The investigators suggested that suppression of dominance during military training could create emotional disturbance and a subsequent increase in ANUG incidence for a dominant type of individual. **Cohen Cole S.A. et al (1983)**<sup>94</sup> investigated the role of psychosocial factors and immunosuppression in ANUG. Initially 35 patients showing ANUG and 35 controls, matched for age, sex and dental hygiene, completed rating questionnaires, gave blood for tests of immune and edocrine function and collected overnight and spot urine. Compared to controls the patients with ANUG were in more state of anxiety before disease resolution, while trait anxiety was high both during ANUG and after its resolution.

**Johnson B.D., Engel D. (1986)**<sup>88</sup> suggested that stress, associated with the disease, play a role through induction of increased cortisol and catecholamine levels. They stated that the treatment modalities should involve attempts at controlling significant psychological and other physical factors.

**Da-Siva-A.M. et al (1995)**<sup>95</sup> suggested that emotional stress was one of the predisposing factors to ANUG. They also stated that psychological factors may be involved in the etiology of inflammatory periodontal diseases, which in turn would relate to clinical management of these conditions.

## **INFLAMMATORY PERIODONTAL DISEASE**

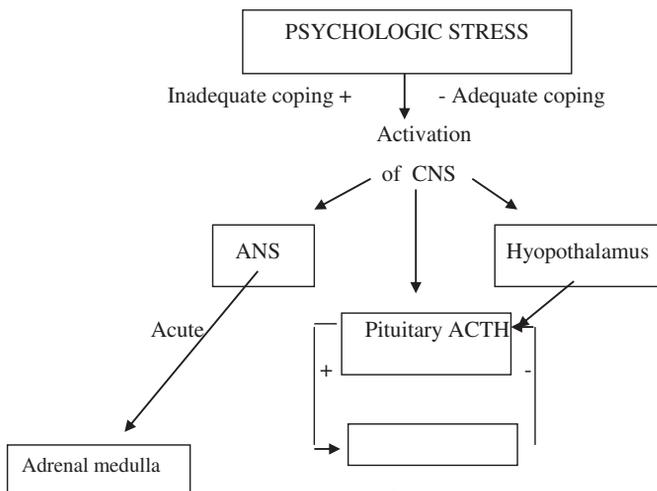
The aetiology of inflammatory periodontal disease is complex. There are many processes at work, and probably, no single one of these is the causative factor in all cases. The aetiological significance of biological and behavioural risk factors,

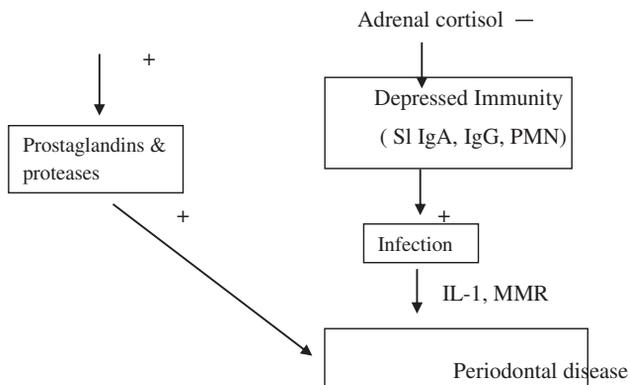
including systemic conditions, smoking, oral cleanliness and age, has been demonstrated.

The bacteria are the triggering agents, but host defence mechanisms within the gingival / periodontal tissues seem to be responsible for most of the tissue damage and for the outcome and progression of the disease.

However, a significant proportion of the variation in disease severity cannot be explained taking only these factors into consideration. The remaining variance, at least in part, may be explained by important psychosocial factors. Seymour (1991) presents a model of chronic inflammatory periodontal diseases in which genetic factors divide the population into susceptible and non-susceptible individuals. In general, the periodontal tissues of susceptible individuals are in balance with their oral flora and any lesion of the periodontium is present in its stable form. Progressive disease results when this balance is disrupted, and this may involve a depression of immune responsiveness as a result of factors such as physical and mental stress (Ballieux 1991).

However, if those patients resistance is lowered by their inability to cope with stressful life events, then overt inflammatory periodontal disease may be manifested. Several workers in the field have pointed out a possible association between psychological factors and inflammatory periodontal disease on the basis of their clinical observations<sup>96</sup>





**Moulton R. et al (1952)**<sup>97</sup> reported that severe cases of ANUG were preceded by acute anxiety arising from a conflict about dependency and/or sexual needs. In addition, severe chronic periodontitis cases presented (i) a background of longstanding, less acute conflict, mainly related to dependency needs, and (ii) significant marital conflict and psychosomatic symptoms.

**Baker E.G. et al (1961)**<sup>98</sup> found significant correlations between periodontal status and such factors as age, broken home, marital adjustment, hysteria scores and somatization (the tendency to develop psychogenic physical complaints or psychosomatic disorders).

**Davis C.H. and Jenkin D. (1962)**<sup>99</sup> investigated possible associations between what they called “psychological measures of stress” and periodontal disease, again in psychiatric patients. They found that anxiety was significantly correlated with periodontal index.

**Vogel R.I. et al (1977)**<sup>100</sup> evaluated possible relationships between neuroticism/introversion and inflammatory periodontal disease / plaque scores in 50 subjects registering for treatment at a dental school clinic. Significant correlations were found between introversion and plaque, and between introversion and inflammatory periodontal disease as measured both clinically and radiographically. There was also a significant correlation between neuroticism and radiographic measures of inflammatory periodontal disease.

**Ludenia K. and Donham G.W. (1983)**<sup>101</sup> examined the relationship between health locus of control and the following variable : age, depression, trait anger, trait anxiety, and dental ratings of oral hygiene and inflammatory periodontal disease using the multidimensional health locus of control scale (NHLC). They found that trait anxiety, depression and trait anger were correlated negatively and significantly to health internality.

**Green L. et al (1986)**<sup>102</sup> investigated 50 male veterans for gingival and periodontal pathology, stressful life events and somatic symptomatology. A significant association was evident between life events stress and periodontal status.

**Mareenes et al (1993)**<sup>103</sup> investigated possible associations between eight specific negative life events and self reported oral symptoms, namely, toothache or trouble with the gums. After the authors adjusted for the other variables studied, marital or family problems remained significantly associated with self reported acute and chronic oral symptoms.

**Breivik T. et al (1996)**<sup>104</sup> they suggested that emotional or psychological load (stress) influence immune activities directly via nerve messenger substances or indirectly via neuroendocrine substances (Hormones).

**Monterio da Silva A.M. et al (1996)**<sup>105</sup> Investigated more formally possible associations between a number of relevant psychosocial factors and RPP. The significance of the psychosocial variables was assessed by comprising 3 groups : 50 patents with RPP, 50 patients with routine chronic adult periodontitis (RAP) and 50 patients without significant periodontal destruction (controls). It was anticipated that the RPP group could show higher levels of psychosocial malalignment than the RCAP and control groups. 2 psychosocial factors, depression and loneliness were significant in distinguishing between groups. The RPP group significantly increased depression and loneliness compared to the RCAP and control groups.

**Hildebrand H.C. et al (2000)**<sup>106</sup> reviewed studies that investigated the association between psychological stress and periodontal disease. They found that

psychological stress represents a risk indicator for periodontal disease and should be addressed before and during treatment.

## **ORAL PSORIASIS**

Psoriasis is a chronic inflammatory skin disease affecting 10% of the population and making its first appearance generally in the second and third decades of life.

Dark skinned persons are seldom affected. The cause of the disease is unknown, but stresses and anxiety as well as winter weather, may increase its severity.

Clinically, it is characterized by the presence of popular squamous lesions, their sizes varying from a few millimeters to large plaques. Itching is a common feature and the elimination of the plaques may result in tiny bleeding points referred to as Auspitz's sign. The disease follows a chronic course with remissions and exacerbations.

Since the existence of oral lesions is a controversial matter, it has been suggested that the diagnosis of oral psoriasis should be conditional upon parallel skin. Manifestations of the disease and HLA typing. It is of relevance that psoriatic patients have a higher tendency for a number of oral pathological conditions such as geographic and/or fissured tongue ectopia geographic tongue, gingivitis and periodontitis.<sup>107</sup>

**Devrimci – Ozguven H. et al (2000)**<sup>108</sup> examined 50 psoriasis patients, dermatologically and psychiatrically. Psoriasis patients reported significantly higher degree of depression than controls. In addition, the risk for developing psoriasis increased significantly in patients with moderate and severe depression. They also found a relationship between symptom severity and low affective expression.

**Naldi L. et al (2001)**<sup>109</sup> studied patients with a finer diagnosis ever of acute gustate psoriasis, made by a dermatologist. Controls were patients newly diagnosed as having dermatologic conditions other than psoriasis. Inclusion of cases and controls was restricted to patients older than 16 years. The Holmes and Rahe Social

Readjustment Rating Scale was used to assess stressful life events during the 6 months before diagnosis. A total of 73 cases (Median age 26 years) and 430 controls (Median age, 28 years) were included in the analysis. It was documented that the strong association between gattate psoriasis and a family history of psoriasis. The study added evidence to the belief that stressful life events may represent risk factors for the onset of psoriasis.

**Garg A. et al (2001)**<sup>110</sup> stated that a large number of skin diseases including atopic dermatitis and psoriasis, appear to be precipitated or exacerbated by psychological stress. They investigated 27 medical dental, dental and pharmacy students for relationship between psychological stress and epidermal permeability barrier function, without coexistent skin disease. Their psychological state was assessed with the perceived stress scale and the profile of blood states. They found that stress-induced derangements in epidermal function as precipitations of inflammatory dermatoses.

**Perrott S.B. et al (2000)**<sup>111</sup> studied 58 men and 43 women living with psoriasis by completing questionnaires assessing quality of life and feeling of stigmatization. Physician ratings of disease severity were used in conjunction with these variables to account for psychosocial impact. Results showed that ratings of severity were poor predictors of quality of life and stigmatization. It was concluded that attempts to understand the psychological impact of psoriasis in terms of current measures of disease severity and demographic characteristics were limited.

**Onder M. et al (2000)**<sup>112</sup> investigated skin problems of 117 musicians working in a professional orchestra. The results of their survey suggested a significant incidence of occupational and stress-related skin problems in musicians such as hyperhidrosis, lichen planus, psoriasis, seborrheic dermatitis and urticaria. It was thought that emotional factors exacerbated their problems. They also discussed importance of psychiatric consultations in dermatological problems.

## **TEMPOROMANDIBULAR JOINT DISORDERS**

Temporomandibular joint disorders, is an all inclusive term referring to a heterogeneous group of psychophysiological disorders with the common

characteristics of orofacial pain, masticatory dysfunction and both. The primary symptoms of TMD are preauricular pain, limited mandibular functioning and joint sounds (such as clenching, popping or grinding).<sup>113</sup>

It is reported that TMD is a female disease with female to male ratios ranging from 3:1 to 6:1.<sup>114</sup>

Women tend to seek care more often than do men because of psychophysiological stress. This may result from higher stress hormone levels and the presence of estrogen receptors that are absent in men.<sup>115</sup>

**Greene C.S., Olson R.E. and Laskin D.M. (1982)**<sup>116</sup> reviewed the psychologic factors like stress, anxiety and depression in etiology, progression and treatment of MPD syndrome. They concluded that although psychological factors were coexistent with MPD syndrome, their etiological role could not be confirmed, and no one personality profile necessarily predisposes development of MPD syndrome, but the disorders were perpetuated by psychological factors.

**Eversole L.R., Stone C.E., Matheson D. et al (1985)**<sup>117</sup> conducted psychometric, study to compare the subgroups of temporomandibular patients i.e. TMD with internal derangement, myofascial and myogenic facial pain (MFP), and atypical facial pain, myofascial and myogenic facial pain (MFD). Using the Minnesota Multiphasic personality inventory (MMPI) as their primary psychometric measures, they found that MFP and AFP groups had more extensive psychopathology.

**Goss Alastair N. et al (1985)**<sup>118</sup> in their retrospective study of a pain clinic population found 43 patients who had pain in the TMJ region. The clinical presentation of these patients did not differ greatly from that observed with typical response. They found that there was high incidence of major psychiatric problems in the past histories (30%) involving length in patient treatment.

**Ronald Attonario (1991)**<sup>119</sup> postulated that diverse conditions such as marked depression, hysterical conversion, psychosis, obsessional neurosis, anxiety disorders,

stress, loss and learned pain behaviour are all implicated in TMD. They also stated that function of TMJ patients with myofascial pain dysfunction, commonly considered a stress related illness. (Ronald Attanasio : Physiologic considerations in TMD, A Biopsychosocial view of symptom formation. Temporomandibular Disorders and orofacial Pain. DCNA. January 1991, vol.35, No.1.)

**Tuersky J. et al (1991)**<sup>120</sup> assessed the role of a depressive illness in the outcome of the treatment of patients with TMJ pain – dysfunction syndrome. One group was considered psychiatrically normal and the other had a concurrent depressive illness. The latter group was subdivided equally to produce 3 treated groups. One undergoing occlusal splint therapy, one receiving antidepressant medication, and 3<sup>rd</sup> having a combination of occlusal and antidepressant therapy. The results showed clearly that there was a significant difference in response in the nonpsychiatric and combined therapy in comparison with the two depressed groups treated either with occlusal splint or with antidepressant therapy.

**Zach and Andreason (1991)**<sup>121</sup> compared the psychological profiles of 98 patients with signs and symptoms of temporomandibular disorders with a control group having no signs and symptoms of such disorders. They used the crown crisp experimental index (a 48 item self-administered questionnaire) and found that TMD patients were more anxious than their normal counterparts. Low scores were noted for TMD patients in the profile of hysteria. The authors formed an opinion that this could be a reflection of TMD patients perception of their "locus of control".

**Dworkin S.F. (1994)**<sup>122</sup> conducted a series of studies examining the course of TMD pain in relation to diagnosis, clinical signs and the level of psychosocial function. They assigned a clinical TMD diagnosis using the published diagnostic criteria of Eversole and Machado of 232 clinical cases referred for TMD treatment. They emphasized the multidisciplinary treatment and self management approaches that focus on the cognitive thought processes and behaviours that influence subjective symptom.

**Phillips Jennifer M. et al (1994)**<sup>123</sup> assessed 233 patients (161 women, 72 men) with acute TMD symptoms with a battery of biopsychosocial measures.

Patients were diagnosed as having TMD on the basis of research diagnostic criteria or RDC for TMD. Women who developed chronic TMD exhibited significantly more psychosocial distress and impairment than women who did not develop chronic TMD. Men who developed chronic TMD differed significantly from men who did not develop chronic TMD.

**Morris S. et al (1997)**<sup>124</sup> studied 97 patients from a potential 138 patients satisfying the diagnostic criteria for PDS (pain Dysfunction syndrome). Patients were assessed with a range of socio-demographic, dental and psychosocial measures including a psychiatric interview. Patients with PDS and a mental disorder were compared with those without a mental disorder. Among 97 patients, 32 (33%) had a mental disorder. They observed that those with a mental disorder complained of more pain associated with PDS.

**Pankhurst C.L. (1997)**,<sup>125</sup> postulated that among individuals with TMD, myogenic patients have increased severity of pain and suffer enhanced psychological distress.

**Turk C.Dennis et al (1997)**<sup>126</sup> suggested that several psychosocial and behavioral factors, in addition to physical pathology, play a role in pain and disability.

**Goldstein H., Burton (1999)**<sup>127</sup> stated that a variety of physical and psychologic factors are implicated in chronicity such as oral habits, radiographic changes, secondary gain, coping skills, and higher levels of pain and disability on specific psychologic tests. They also stressed that a wide range of associated factors including depression, anxiety, and gum chewing may propagate TMD symptoms on the basis of physical, emotional and/or neurobiologic factors. Pain, muscle tension, head ache, and chronic pain in the head, neck and jaws predispose to TMD via neuroanatomical and neurobiologic mechanisms. They recommended that prognosis should be assessed by behavioral / psychologic assessment

**Kight M., Gatchel R.J., and Wesley L. (1999)**<sup>128</sup> analysed the data of 277 acute and chronic temporomandibular disorder patients to determine if there was a

relationship between psychological and physical diagnosis. A significant relationship existed among muscle disorder and considered part of current mood disorder, personality disorder, combined current mood, anxiety, or substance use disorder. Psychopathology was significant in muscle disorders as compared to disc or joint disorders.

**Rollman G.B. and Gillespie J.M. (2000)**<sup>129</sup> stated that strong emphasis should be placed on psychosocial variables in both assessment and management of TMD patients.

**Auerbach S.M. et al (2001)**<sup>130</sup> investigated the role of psychological factors in TMD. Orofacial pain patients pretreatment levels of depression, disability caused by pain, and exposure to stressful life events were measured and differences on these variables between patients with TMJ disease and those with pain of muscular origin were evaluated. Before undergoing treatment 258 patients were administered the Beck depression, Inventory (BDI), the pain disability index (PDI) and the social readjustment rating scale (SRRS). Follow-up data on pain disability, current level of pain, depression and satisfaction with treatment were obtained on 48 of these patients who were contacted at varying intervals after completing treatment. They concluded that the findings were consistent with previous research indicating a link between emotional dysfunction and TMD and were largely supportive of the conclusion that psychological factors play a more pronounced role when pain was of muscular origin.

**List T., Wahlund K., Larsson B. (2001)**<sup>131</sup> examined the influence of psychosocial functioning and dental factors in adolescents with TMD and compared them with healthy subjects. They found that psychosocial factors such as increased levels of stress, somatic complaints and emotional problems played a more prominent role in adolescents with TMD than the dental factors.

**Ferrando Maite et al (2004)**<sup>132</sup> analyzed 425 patients for the psychological variables of distress, personality, and coping that are related to the diagnosis based on the Research Diagnostic criteria for TMD. The MANCOVA (Multiple Analysis of Variance) between the muscular, articular and control groups showed that the muscular group differed from the control group, in having higher levels of distress,

anxiety, and depression, and minor use of positive reinterpretation and humor as coping strategies. The articular group also showed higher distress, less positive reinterpretation and a lower interest in the search of instrumental social support than control group. The coping predictor of distress in both TMD groups was behavioural disengagement, however, the personality predictors differed. Neuroticism and depression were present in the muscular group, whereas conscientiousness and self-discipline were in the articular group.

## **BRUXISM**

Bruxism is the term applied to either the static or dynamic contact or occlusion of the teeth at times other than for normal functions such as mastication or swallowing. It is therefore considered a parafunctional habit. It usually occurs unconsciously and spontaneously and may be repetitive at varying intervals. It is practiced almost universally, usually during sleep, either biometrically (clenching) or isotonicity (grinding). Because of its necessary relation to the occlusion it has the potential for being responsible for more dentally related problems than any other oral habit. For the habit to occur, psychological, muscular, and dental factors are necessary.

Bruxism has been shown to be linked to psychological stress as a necessary component. While mental tension provides the spark for the initiation of this habit and the fuel for its continuation, the original source of this energy comes from the genetically determined drives and needs of the individual. Other causes such as systemic disease (epilepsy) and local factors (high restorations) have been implicated, but their relation to psychological tension should be obvious.

Since the mouth is the means of receiving food and the earliest means of exploring the environment, it is intimately tied to emotions such as satisfaction, frustration, anxiety and anger.

Freud's teaching seems to be tailored towards explaining the presence of bruxism in the individual. The oral stage is the first in the child's psychosexual development. The life drive and the need to aggress the two forces operating in the child are both part of the habit of bruxism.

**Pierce CJ, Christmas K, Bennett ME, Close JM (1995)**<sup>133</sup> examined the relationships between electromyographic measured nocturnal bruxism, self-reported stress, and several personality variables and the relationship between belief in a stress-

bruxism relationship and self-reported stress. 100 adult bruxers completed a battery of personality questionnaires indicated whether they believed in a stress bruxism relationship, presented for a dental examination, and had dental impressions taken. Subsequently electromyographic measurements of bruxing frequency and duration were recorded for 15 consecutive nights. Correlations between electromyographic measures and self-reported stress were statistically significant for eight individual subjects. Further, subjects with high levels of stress reported more anxiety, irritability and depression, and less denial. Subjects who believed in a stress bruxism relationship reported greater stress.

**Hagberg C, Hagberg M, Kopp S. (1994)**<sup>134</sup> compared general musculoskeletal symptoms and emotional stress situations in terms of psychosocial stresses at work and sleeping disturbances between patients craniomandibular disorders (CMD) (56 women, 24 men) and a random population sample (88 men, 86 women in the Stockholm music study). A multiple choice questionnaire was used. In comparison with the CMD men the CMD woman had an increased rate of tooth clenching and muscular pain in the face. The CMD men differed in reporting higher scores for psychologic demands at work and also in having more sleeping disturbances.

**Thompson BA, Blount BW, Krumholz TS (1994)**<sup>135</sup> stated that bruxism, or the grinding and clenching of teeth, occurs in approximately 15% of children and in as many as 96% of adults, because of its nonspecific pathology, and may be difficult to diagnose. In addition to complaints from sleep partners, signs of teeth grinding include masticatory pain or fatigue, headaches, tooth sensitivity and attrition, oral infection and temporomandibular joint disorders. They suggested adults may be managed with stress reduction therapy, alteration of sleep positioning, drug therapy, biofeedback training, physical therapy and dental evaluation.

**Fischer WF, O'toole ET (1993)**<sup>136</sup> randomly selected adults from a periodontal practice to participate in research to determine whether the personality traits of people who chronically brux (were examined by the periodontist, who determined which were chronic bruxers grind their teeth) diverge significantly from the personality traits of those who do not do so. All participants completed a

personality questionnaire and out of which 28 of the men and 46 of the women were diagnosed as bruxers. Their personality trait scores differed significantly from those of the non bruxers. In general, and regardless of gender, chronic bruxers were found to be shy, stiff, cautious and aloof, preferring things rather than people, avoiding compromises, rigid in their ways, affected by feelings of inferiority, impeded in expressing themselves, apprehensive, and given to worrying.

**Biondi M, Picardi A. (1993)**<sup>137</sup> formed an opinion that temporomandibular joint pain dysfunction (TMJPD) syndrome and bruxism have a major psychosomatic component. They reviewed these entities in an integrated manner, both medical and psychological aspects. Two etiological models have been developed; the structural model emphasizes the role played by malocclusion or alterations of the maxillomandibular relationship, while the functional model underscores the role of stress, emotional tension, and personality characteristics. They concluded that treatment strategy can also be based on psychotherapeutic and relaxation treatment.

**Pingitore G, Chrobak V, Petrie J. (1991)**<sup>138</sup> investigated whether the combination of physical abnormalities, type A behaviour pattern, and the perceived desirability and controllability of life stress are related to bruxism. Study included 125 dental patient who were classified as bruxers or non bruxers by a licensed dentist and who completed two measures, the Jenking activity survey, and a modified version of the Holmes and Rahe life events scale. The linear combination of physical abnormalities, type A behaviour and stress was significant, and suggested that it was the best predictor of bruxism.

**Restrepo, Alvarez E, Jaramillo E, Velez C, Valencia I. (2001)**<sup>139</sup> studied 4 main causes of bruxism, high anxiety level, malocclusion, TMD and oral habits.

The aim of their study was to investigate the effectiveness of psychological techniques in children with bruxism. A total of 33 children, 3-6 years of age with normal occlusal features, without oral habits, rate in the conner's parent rating scale (CRPS) and more than 0.75% in Conner's teacher rating scales (CTRS), and one or more TMJ disorders registered in the Bernal and Tsomtstouris examination, were selected from 188 children. Two psychological techniques, directed muscular relaxation and competence reaction, were applied for 6 months. The results were

analysed with a Wilcoxon rank sum test. They concluded that psychological techniques were effective in the reduction of signs of bruxism in children with primary teeth.

## **CANCEROPHOBIA**

The term phobia, which comes from the Greek word for fear, denotes a number of psychological and physiological conditions that can range from serious disabilities to common fears to minor quirks.

It is a persistent fear in patients that they have controlled oral cancer. These are usually well read educated patients, who constantly change their tooth pastes, often use a multitude of mouth washes and are in general very finely about the oral hygiene, but at the same time they go from dentist to dentists seeking reassurance that all is fine. This has been noted to be associated with depression. It is a type of monosympathetic hypochondriacal psychosis (MHP), which is a chronic disorder characterized by a single hypochondriacal illusion, a false, unshapable belief which is out of keeping with the individuals social and cultural background and is not amenable to reason.

There are two subtypes which are of relevance to dentistry. First is phantom bite syndrome, the patient holds the illusionary belief that his / her dental bite is abnormal and the other is dysmorphophobia present with delusion that some part of their jaw or face is deformed. They believe that this deformity is noticeable to others, despite evidence to the contrary and blame it for all problems in their life. The monograph of such patient including exclusion of organic disease and any other primary psychiatric disease. Referred to a psychiatrist is helpful. Patients who do not respond to psychological causality may need Pinazide, a dopamine antagonist. The daily dose varies from 2 to 12 years and is best given in many as it may cause insomnia.

Remion RA and Blasberg B (1985), Yontchev E et al (1986), Grosky DMD et al (1991) reported cancerophobia to be a frequent finding in patient with atypical facial pain, glossodynia and burning mouth syndrome. It is a persistent fear in the patients mind that they have contracted oral cancer. There are usually well read, educated patients who constantly change their tooth pastes, often use a multitude of

mouth washes and one in general very finicky about the oral hygiene, but at the same time go from dentist to dentist seeking reassurance that all is fine. This has been noted to be associated with depression.

**Gorsky Meir (1991)**<sup>140</sup> studied clinical characteristics and treatment responses in 130 patients with burning mouth syndrome. Most patients were post menopausal women, and the tongue was the most frequently afflicted site. Although 395 of the patients complained of dry mouth, no causative factors were evident. Therefore BMS is assumed to be a functional disorder. This was at least partially confirmed because the most effective management was in response to moods – altering drugs.

In their study, they confirmed previous observations of the primary recurrence in postmenopausal women, the tongue as the most frequent site, and lack of evident causative systemic explanation. Although about 1/3<sup>rd</sup> benefited from salivary gland stimulation with a sialogogue, most patients did not benefit. Because causative organic factors have not been consistently identified, it is assumed that BMS, atleast in most patients is a functional disorder entailing psychologic, emotional and neurologic dysfunctions.

**Yontchev Eutim et al (1986)**<sup>141</sup> studied 113 patients with facial and general complaints which they assumed were caused by metallic dental restorations and/or oral galvanic cements. An extensive case history was taken by means of a questionnaire and an interview and results showed that patients presented with varying oral and general symptoms. It is probable that many general factors, besides oral findings, alone or in causation, eg. general health problems, sided effects of medication, psycho-social problems, including stressful life events, and complications due to the chronicity of pain, may be associated with the oral and general complaints of these patients.

**Creagon ET (1999)**<sup>142</sup> reviewed of the relationship between psychosocial, emotional and attitudinal factors and aggravation of malignancy. They left the debate open with a note that the strong effect of emotions on different medical conditions cannot be ignored.

**Rogers SN et al (1999)**<sup>143</sup> have determined that edentulous patients after cancer treatment have more psychological disturbances and they may complicate compliance with prosthetic appliances.

**Bocca M. et al (1999)**<sup>144</sup> in their study of 28 oral cancer patients found almost all subjects revealed the presence of anxiety symptoms and 60% of subjects were affected by minor depression. Many patients exhibited loss of interest in family, job and sex.

**Malt UF et al (1997)**<sup>145</sup> have mentioned 99 patients who felt that dental amalgam was causing multiple somatic symptoms. This study revealed that 62% of them suffered from chronic anxiety disorder and 47% suffered from major depression as compared to none in 93 of alternative group.

#### **Eating Disorders : (Anorexia Nervosa / Bulimia):**

Eating disorder should be considered in the differential diagnosis of unexplained occlusal and palatal enamel erosion, particularly in younger female patients.

Self induced vomiting is a frequent problem in patients with morbid fear of obesity, so it may be present in anorexia nervosa and is of diagnostic significance in bulimic nervosa, when the patient enters the cycle of binge eating and vomiting. Persistent vomiting may lead to enamel erosions and attrition through the effects of gastric juice. Females outnumbered male by 16 to one. In addition to binge eating a purging the bulimic patient may engage in alcohol or drug abuse, shapflifting, promiscuity, and aberrant sexual practices.

Pathological avoidance of food where the subject has a delusional body image. Characterized by extreme loss of weight (15%), abnormal attitudes towards food, distorted body image with morbid fear of fatness. Common in females of adolescence

#### **Etiology:**

**Psychodynamic theories:** means of avoiding maturation or as a means of acquiring independence and/or a sense of achievement, through strict control of diet and weight.

**Cultural theories :** *social and media pressures urging women to be slim and diet-conscious*

#### **Clinical features:**

Loss of weight by dietary restriction, self induced vomiting, laxatives or excessive exercising.

Disturbance of fluid or electrolyte imbalance. Bone fractures secondary to osteoporosis.

- ✓ Bulimia nervosa, described by Russell (1979)
- ✓ Powerful and intractable *urges to overeat*
- ✓ Efforts to *avoid the fattening effects of food by inducing vomiting or abusing purgatives*
- ✓ *Morbid fear of fatness*
- ✓ Bouts of eating vast quantities of food (bingeing) occur in response to an uncontrollable psychological urge. Self-induced vomiting often follows such episodes.

#### **Oral manifestations:**

**Mucosal lesions-** atrophic glossitis, erythematous lesions on the palate, glossodynia

**Periodontal** – poor oral hygiene, gingival inflammation and predisposition to periodontitis

Vitamin C deficiency leads to gingival bleeding, ulcerations and tooth mobility

**Teeth-** dental erosion, increased caries incidence, dental sensitivity to episodes of pain

**Salivary-** swelling of major salivary glands (sialadenosis), necrotizing sialometaplasia

Increased predisposition to opportunistic infections

Treatment:

**Psychotherapy:** psychodynamic psychotherapy, family therapy, behavioral therapy, and group therapy.

#### **Pharmacotherapy:**

- ✓ Hospitalization if weight loss becomes severe
- ✓ Fluoxetine (20-60 mg per day)
- ✓ Imipramine (Tofranil) or desipramine (Norpramin) at a low dosage (50 mg per day),  
increasing by 50-mg increments every 3-4 days, to a daily dose of 150 mg

## **FACTITIOUS ULCERATION OR STOMATITIS ARTEFACTA**

- ✓ **Self Injurious Behaviour (SIB)** is a deliberate harm to the body without suicidal intent which may occur with a series of psychiatric disorders, development deficiencies or syndromes.
- ✓ Consists of repetitive movements that produce tissue damage and may be observed in normal or mentally impaired individuals
- ✓ Prevalence is 750 per 100,000
- ✓ 7.7% to 22.8% in mentally disabled
- ✓ Oral structures such as gingiva, oral mucosa, tooth support structures, or teeth are affected.

**Consists of :**

- ✓ Putting fingernails or foreign objects in the gingival sulcus, digital pressure on oral structures or biting of tissue.
- ✓ Factitial gingivitis,
- ✓ Factitial periodontitis,
- ✓ Factitial ulcer,
- ✓ Self-extraction
- ✓ Wide areas of peeling, macerated, hyperkeratinized epithelium of the buccal mucosa

**Classification of self inflicted injuries** (Stewart and Kernmohan)

Type	Description
Type A	Injuries superimposed upon pre-existing lesion
Type B	Injuries secondary to another established habit
Type C	Injuries of unknown and/or complex aetiology

**Theories proposed:**

**Biological theory:** expression of an underlying genetic defect that may produce alteration of neurotransmitters

**Functional theory:** as a means of escape or attention seeking and may arise in stressful situations

Associated with lesch nyhan syndrome, Munchhausen, Familial Dysautonomia, XXY syndrome, trisomy 18, mental retardation, hereditary sensory neuropathies

- ✓ Lip biting- fissures, areas of hyperkeratosis or mucous extravasation cyst.
- ✓ In older anxious or agitated patients lip chewing produced varicosities so the vermillion border appears cyanotic in appearance.

- ✓ Rubbing of alveolar mucosa with a finger leaves an elongated erythematous patch.

**Management:**

- Behavioural modification techniques
- Pharmacological treatment
- Physical restraints

Behavioural modification techniques:

- ✓ Positive reinforcement (use of a positive reinforcer each time the desired behaviour is observed),
- ✓ Extinction (lack of attention when the undesired behaviour is exhibited)
- ✓ Time-out (removing the child from the place or situation when the undesired behaviour is exhibited)

**Oral restraints include:**

Fixed or removable acrylic horseshoe appliance, soft mouth guards, buccal or lingual shields,

Thermoplastic appliances in combination with intraoral and extraoral elastics

Accessories such as facemasks, chin-cups, lip separators, special clothing or belts

**Pharmacotherapy:** Selective Serotonin Reuptake Inhibitors

**CONCLUSION**

It is not uncommon to see the patients diagnosed with “Oral Psychosomatic Disorders”, so there is a growing need to accurately diagnose and treat such patients.

Management of illness is based on the knowledge of its specific and non-specific aspects. The influence of psychosocial and environmental factors on the appearance of the illness must be recognized and dealt with. So the doctor must recognize the influence exerted by the illness itself- through pain, fear, depression, or paralysis which are its manifestations on the patient and his environment. The handling of the sick person depends on our awareness of these aspects, our knowledge and experience of them, on our patience and our flexibility. In practice this means that the doctor must listen to his patient, get to know him, his background and present life; must examine him physically, it is the care and the confidence with which it is done that

matters. The doctor must encourage questions, and must answer them to the best of his ability; must seek the patient's view of himself, of his illness, and sometimes of his medical experiences. There is no comprehensive up to date account of psychosomatic medicine in dentistry.

As the stress is increasing in day today life due to cut throat competition in every field. So there are more chances of a dental practitioners encountering patients with psychosomatic disorders. Hence one should be familiar with such manifestations and if accounted with such patients should try to manage them with psychiatrist consultation whenever needed.

To conclude we can say that many diseases manifesting in the oral cavity have a psychological component in their etiology or have some effect of psychologic factors. Similarly psychiatric disorders have an influence upon health of oral tissue.

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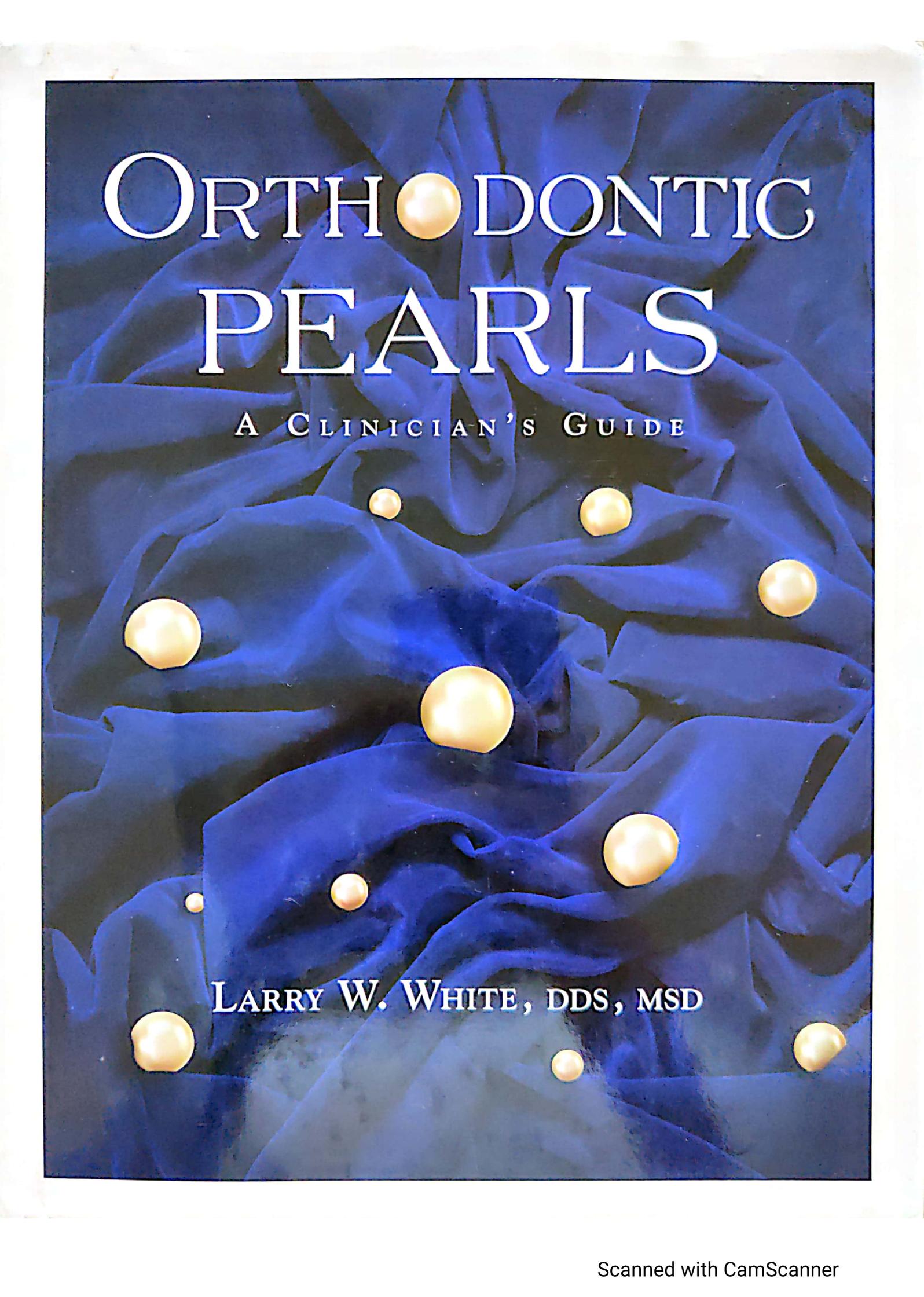
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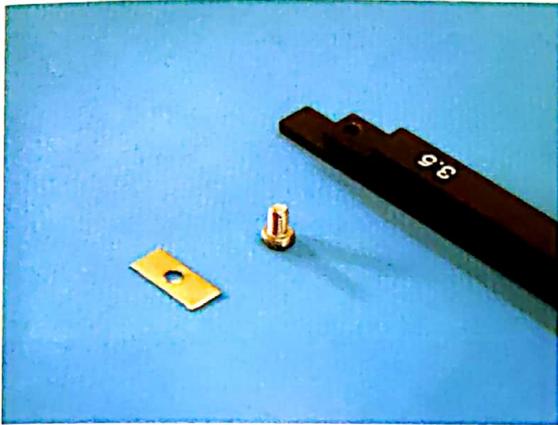
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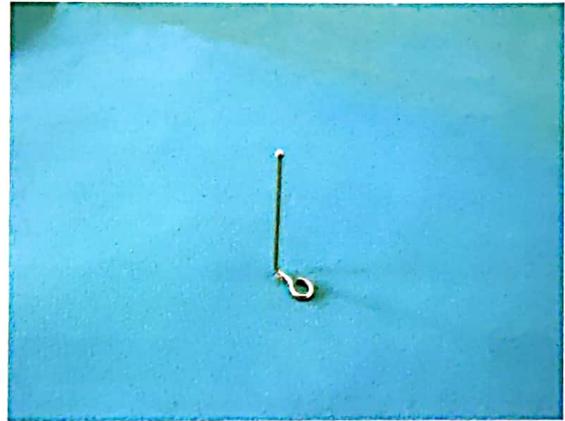
Vacuum Retainers	Tom Barron	Page 74
Bonding Kits	Tom Barron	Page 74
Bonding Aids	Tom Barron	Page 75
Cross Bite Turbos	Bud Luecke	Page 77
Retention Relapse	Marvin Kastrop	Page 77
Ribbon Arch	Editor's Cache	Page 78
Bonding Technique	Barry Mollenhauer	Page 79
Mandibular 3-3 Technique	Loring Ross	Page 79
Axiograph Procedure	Carlos Peraldi	Page 80
Class III Tx with TADs	Carlos Peraldi	Page 80
Direct Bonding Aid	Clark Coville	Page 81
Bite Opening	Julia Harfin	Page 82
Functional Therapy	Julia Harfin	Page 83
Deimpaction of Molars	Richard Bach	Page 84
Individual Tooth Torquing	Giorgio Fiorelli	Page 85
Alignment of Rotated Molars	Carlos Coelho	Page 86
Mandibular Protraction Appliance	Carlos Coelho	Page 87
Impression Aids	Editor's Cache	Page 89
TurboMax	Raintree	Page 89
Incisor Augmentation	Hilton Goldreich	Page 90
Mousetrap	Silberstein & Hohit	Page 91
Topical Anesthetic	Phil Campbell	Page 92
Crossbow Appliance	Robert Miller	Page 93
Opal Sealant	Robert Miller	Page 94
Bite Turbos	Robert Miller	Page 94
Bracket Gauge	Rohan Hattarki	Page 95
Chlorhexidine Use	Editor's Cache	Page 96
Separators	Editor's Cache	Page 96
Apthous Ulcer Rx	Editor's Cache	Page 97
Indirect Mandibular 3-3	J. Farill-Guzman	Page 98
DentaPop	Maryam Barnes	Page 99
Face Shield	Maryam Barnes	Page 99
Invisalign Auxiliaries	Bayer & Curtis	Page 100
Staff Bonuses	Bayer & Curtis	Page 100
Staff Recognition	Bayer & Curtis	Page 100
Three-prong Pliers Design	Keith Hilliard	Page 100
Canine Retraction	Bill Wyatt	Page 101
Interproximal Enamel Reduction	Editor's Cache	Page 101
Slenderizer	Orthomatic Co.	Page 103
Treating Fearful Patients	Weinstein et al	Page 104
Mandibular Protraction Appliance	Carlos Coelho	Page 105
Cantilever Applications	Giorgio Fiorelli	Page 106
Direct Bonded 3-3	Irelia Machado	Page 107
MARA Adjustments	Piet Botha	Page 108
Direct Bonding Tips	Piet Botha & Bertus van Niekerk	Page 108

Ceramic Bonding	Paul Gange	Page 157
Bite Openers	Phil Corbin	Page 158
Office Music	Phil Corbin	Page 160
Intra-arch Activation	Phil Corbin	Page 160
RPE Auxiliary	Phil Corbin	Page 161
Instant Nance Arch	Phil Corbin	Page 162
Referring Doctor Cards	Phil Corbin	Page 163
Brodie Bite Corrector	Phil Corbin	Page 163
Therapy for Avulsed Incisors	Phil Corbin	Page 165
Welding Technique	Phil Corbin	Page 166
Interproximal Enamel Reduction	Phil Corbin	Page 167
Soldering Technique	Phil Corbin	Page 167
Impression Technique	Phil Corbin	Page 168
Impression Tray Cleanup	Phil Corbin	Page 169
Insurance Letters	Phil Corbin	Page 170
Arch Wire Construction	Phil Corbin	Page 171
Closing Arch Wire Design	Phil Corbin	Page 171
Ectopic Mandibular Molars	Phil Corbin	Page 172
Impacted Canine Strategy	Phil Corbin	Page 173
Sideswipe	Phil Corbin	Page 174
One-to-one Images	Phil Corbin	Page 175
Bite Register	Phil Corbin	Page 175
Essix Polishers	Phil Corbin	Page 176
Electric Lab Motor	Phil Corbin	Page 177
Mandibular 3-3	Phil Corbin	Page 178
Wilckodontics	Robert Orr	Page 179
Forsus for Class III Treatment	Robert Orr	Page 181
Ectopic Erupting Molar Strategy	Richard Bach	Page 182
Interceptive Class II Therapy	Paola Merlo	Page 184
Nonsurgical Mucosal Spring Retrieval	Collins & Shellinck	Page 186
True Unilateral Crossbite	David Alger	Page 187
Functional Correction	Giorgio Fiorelli	Page 188
Molar Uprighting Appliance	Mike Steffen	Page 192
Cetacaine for Gagers	Mike Steffen	Page 193
Resin Stops for Arch Wires	Editor's Cache	Page 193
SeLECT Defense Sealant	Jim Reynolds	Page 194
Special Water Faucet	Greg Cohlma	Page 195
Air-water Vacuum Syringe	Greg Cohlma	Page 195
Elastomer Dispenser	Greg Cohlma	Page 195
Difficult Bracket Ligation	Rohan Hattarki	Page 196
Impacted Canine Ligation	Emile Rossouw	Page 197
Shower Floss	Mary Robb	Page 198
Maxillary Second Molar Extractions	Claudia Tatis	Page 199

**Dr. Rohan Hattarki** of Mumbai, India, has adapted a bracket gauge that he buys from Denticon Dental Instrument Co. ([www.denticon.in](http://www.denticon.in)) to help him position brackets correctly in the vertical dimension.



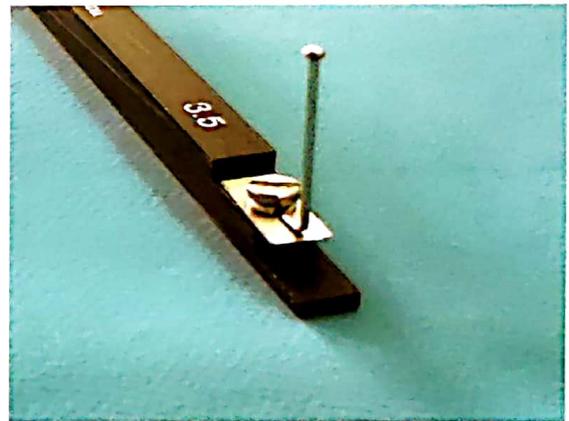
Disassembled parts.



Vertical guide made from a ball clasp wire.



Screw fitted on the vertical wire.



Assembled instrument.



Using the gauge to position bracket.



Centering the bracket on the tooth.

**Dr. Rohan Hattarki** of Belgaum, India, has developed a nifty solution to the problem of ligating a badly rotated tooth while simultaneously depressing the arch wire into the bracket slot. He attaches an elastic adjacent to the rotated surface and stretches it to the other side. This force engages the wire completely into the rotated bracket slot and allows the easy ligation of the wire. This method offers simplicity and thorough bracket engagement and requires only one person to do it. After completing the ligation, he cuts the elastic and removes it.



Stretching the elastic from the wire distal to the canine on the other side.



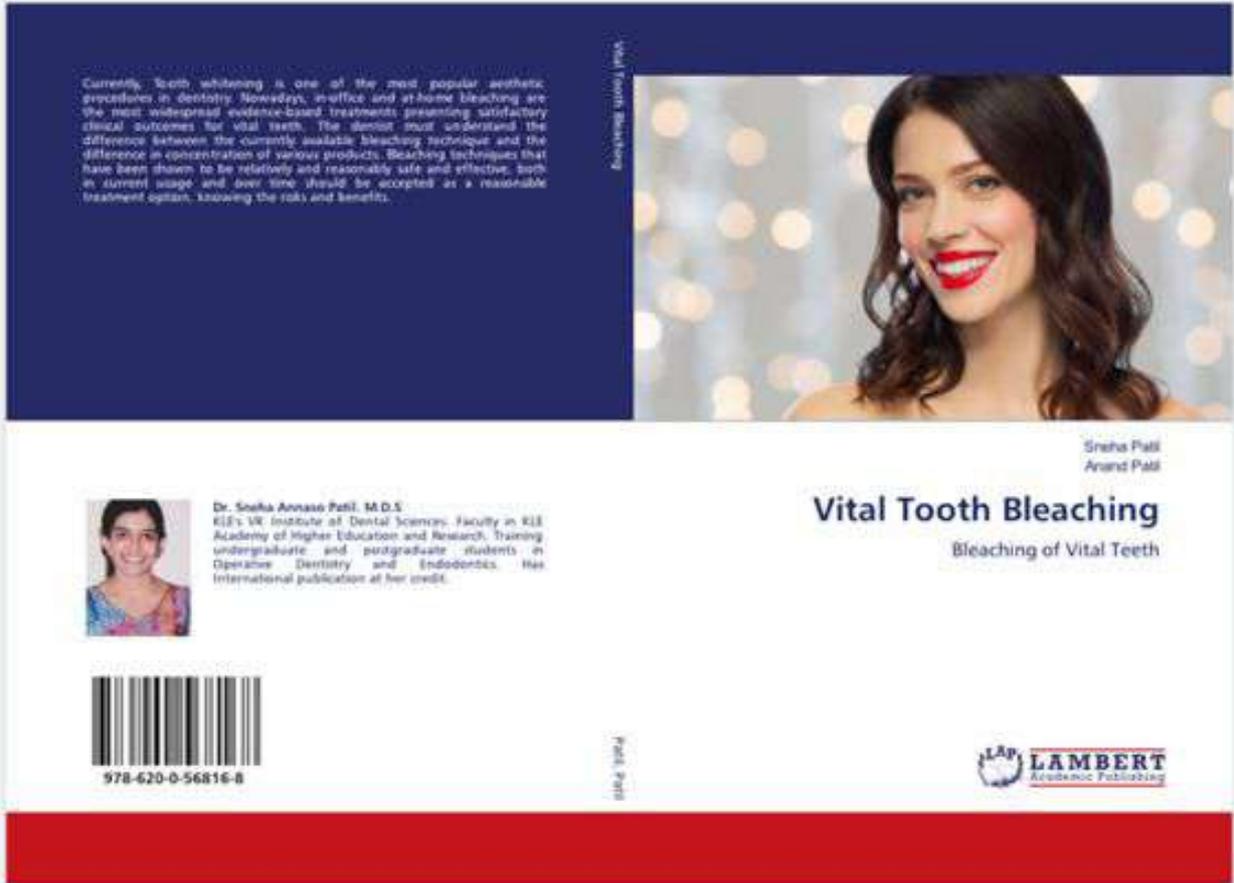
Attaching the elastic to the premolar and canine brackets on the opposite side.



Arch wire ligated into the bracket of the rotated canine.



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Currently, tooth whitening is one of the most popular aesthetic procedures in dentistry. Nowadays, in-office and at-home bleaching are the most widespread evidence-based treatments promising satisfactory clinical outcomes for vital teeth. The dentist must understand the difference between the currently available bleaching technique and the difference in concentration of various products. Bleaching techniques that have been shown to be relatively and reasonably safe and effective, both in current usage and over time should be accepted as a reasonable treatment option, knowing the risks and benefits.

Vital Tooth Bleaching

Sneha Patel  
Anand Patel

## Vital Tooth Bleaching

Bleaching of Vital Teeth



**Dr. Sneha Anand Patel, M.D.S.**  
 KJ Somaiya Institute of Dental Sciences, Faculty in KJ Somaiya Institute of Higher Education and Research, Training undergraduate and postgraduate students in Operative Dentistry and Endodontics. Has international publication at her credit.



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# Contents

Chapters	Page No.
1. Metal Ceramics Alloys <i>(Dr. Priyanka Priyadarshni)</i>	01-24
2. Dental Ceramics: A Basic Review <i>(Dr. Priyanka Priyadarshni)</i>	25-46
3. Clinical Features of Oral Squamous Cell Carcinoma <i>(Dr. Ritesh Vatsa)</i>	47-68
4. Concepts of Radiographic Justification <i>(Dr. Rathi Rela and Dr. Daya Shankar)</i>	69-80
5. Equipment Factors in Reduction of Radiation Doses to Patients <i>(Dr. Rathi Rela and Dr. Daya Shankar)</i>	81-92
<b>6. Bruxism and Its Current Treatment Modalities</b> <i>(Dr. Hema Kanathila, Dr. Ashwin Pangi and Dr. Bharathi Poojary)</i>	<b>93-105</b>
7. 2D and 3D Planning in Orthognathic Surgery <i>(Dr. Abhishek Kumar)</i>	107-122
8. Efficacy of Conchal Auricular Cartilage Graft in the Treatment of Orbital Floor Blow out Fractures <i>(Dr. Ritesh Vatsa and Dr. Priyanka Priyadarshni)</i>	123-133



**Chapter - 1**  
**Metal Ceramics Alloys**

**Author**

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Tutor, Patna Dental College & Hospital, Patna, Bihar, India



# Chapter - 1

## Metal Ceramics Alloys

Dr. Priyanka Priyadarshni

### Abstract

The metal ceramic crown system still is selected the most frequently because of its strength and versatility. The ability to select metals for color or strength for single unit or fixed partial dentures gives great flexibility. As the occlusal forces become more of a factor, selection of a restorative system will depend more on strength than esthetics demand. When greater strength is required metal ceramic crowns are preferred. Metal ceramic core materials like alcerams and inceram provide greater flexibility and compressive strength. The main drawback of metal crowns are poor esthetics especially in anterior region.

**Keywords:** cast metal ceramic restoration, swaged metal ceramic restorations, metal ceramic

### Introduction

The introduction of metal ceramics as restorative material produced restorations comparable to natural teeth. The metal ceramics are stronger, wear resistant and impervious to oral fluids and absolutely biocompatible with long term color stability and ability to be formed into precise shapes. Although it has some drawbacks like poor esthetics, the metal ceramics are highly used in dental clinics because of low cost.

Also called- Porcelain Fused to Metal (PFM)

- Metal Bonded Restoration
- Ceramometal

Jacket crowns made entirely of porcelain entirely had poor tensile strength and the crown breaks easily under abnormal occlusal conditions. So, to get the benefits of metal for strength & porcelain for esthetics, these two were combined to get the metal ceramic.

1962-Weinstein developed porcelain composition for metal ceramics. 1994 survey reports that 90% of ceramic restoration were porcelain fused to metal.

The development of metal ceramics was possible because of

1. Development of a metal and porcelain that could bond to each other
2. Raising the CTE of ceramic to make it more compatible to that of metal

### **Types of metal ceramic restorations**

1. Cast Metal Ceramic restorations
  - a) Cast noble metal alloys
  - b) Cast base metal alloys
  - c) Cast titanium-ultra low fusing
2. Swaged metal ceramic restorations
  - a) Gold alloy foil coping
  - b) Bonded platinum foil coping

### **Cast metal ceramic restorations**

This is one of the commonest ways of constructing a ceramic restoration. Because of strong metal frame, it is possible to make long span bridges. It can also be used when all ceramic is not possible because of high stresses & reduced preparation depth.

### **Uses**

- Single anterior & posterior crowns
- Short & long span anterior & posterior bridges

### **Metal ceramic alloys**

Metal ceramic alloys are compatible with porcelain and capable of bonding to it. A layer of porcelain is fused to the alloy to give it a natural tooth like appearance.

Also called Porcelain Fused to Metal (PFM). Ceramometal Alloys, porcelain Bonded to Metal (PBM).

### **Requirements of alloys for porcelain bonding**

In addition to the general requirements of alloys, metal ceramic alloys have some special requirements to be compatible with porcelain veneering.

1. Alloy's melting temperature should be higher than the porcelain firing temperature
2. It should be able to resist creep or sag at these temperatures

3. Its CTE (Coefficient of Thermal Expansion) should be compatible with that of porcelain
4. They should be able to bond with porcelain
5. It should have a high stiffness (modulus of elasticity)
6. Should not stain or discolor porcelain

### Uses

1. Intended for porcelain veneered restorations (crowns & Bridges)
2. Also be used as an all metal restorations

### Classification of metal ceramic Alloys: (Types)

1. High Noble - Gold-palladium-platinum alloys
  - Gold-palladium-silver alloys
  - Gold-palladium alloys
2. Noble  
(Palladium alloys)
  - Palladium-Silver alloys
  - Palladium-Gallium alloys
  - Palladium-Gold alloys
  - Palladium-Gold silver alloys
  - Palladium-Copper alloys
  - Palladium-Cobalt alloys
3. Base Metal - Nickel Chromium Alloys
  - Nickel-Chromium-Beryllium alloys
  - Cobalt Chromium Alloys
  - Pure Titanium
  - Titanium-Aluminum-Vanadium

### High noble metal ceramic alloys (Gold based)

Contains more than 40 wt% gold and so-called Gold based alloys.

### Properties

1. Most expensive crown & bridge alloys.
2. Color ranges from white to gold.
3. Melting temperatures ranges from 1149-1304 C.
4. High density 13.5-18.3 gm/cm-cast to cast

5. Hardness 182-220 VHN-softer when compared to base metal alloys easy to cut grind & polish.
6. Percent elongation 5-20%.
7. Porcelain Bonding-Presence of an oxide layer on the surface of alloy. 1% of base metals like tin, Iridium, Iron etc are added to the metal ceramic alloys assists in chemical bonding of porcelain to the alloy to induce formation of oxide layer.
8. Less sag resistant
9. Do not tarnish easily and extremely stable in the oral environment.
10. Biocompatible & easier to solder.

### **Gold-palladium-platinum alloys**

**(Jelenco "O", SMG-3 (Ney))**

BY-Dr. Ritesh Vatsa.

#### **Composition**

Gold-80 to 88 wt%

Palladium-5 to 11 wt%

Platinum-6 to 8 wt%

Silver-0 to 4.9 wt% (rarely present)

Base metals-Around 1%

These alloys have lower sag resistance, hence long span bridges are avoided with this alloy.

### **Gold-Palladium-Silver Alloy [Whilbond 75 (Wilkinson)]**

#### **Composition**

Gold-39-77 wt%

Palladium-10-40 wt%

Silver-9-22 wt%

Base metals-1 wt%

Silver has a tendency to discolor some porcelain

### **Gold-palladium alloys olympia (Jelenko)**

#### **Composition**

Gold-44-55 wt%

Palladium-35-45 wt%

Base metals-1 wt%

Absence of Silver eliminates the discoloration problem

The Noble (Palladium Based Alloys) Metal Ceramic Alloys These alloys must contain at least 25% of noble metal alloy. These are mostly Palladium based alloys.

Common Features of Palladium based alloys:

1. Cost ranges between that of gold alloys & base metal
2. Color-White
3. Density-less dense than gold alloys 10.5-11.5gm
4. Easy to work with easy to cut grind & polish
5. Melting range 1155-1304 C
6. Yield strength 462-685 Mpa
7. Hardness 189-270 VHN slightly harder than the high noble metal ceramic alloys
8. Percentage elongation 10-34%
9. Porcelain bonding-like the gold alloys, base metals like tin, Iridium, etc. are added to assist porcelain bonding
10. Resistant to Tarnish & corrosion
11. Scrap value is good. Safe & biocompatible

## **Types**

Palladium-Silver alloys

Palladium-Copper alloys

Palladium-Cobalt alloys

Palladium-Gallium-Silver alloys

Palladium-Gold alloys

Palladium-Gold-Silver alloys

## **Palladium-silver alloys**

Introduced in 1970's as alternative to gold & base metal alloys.

## **Composition**

Palladium 53-60 wt%

Silver 28-40 wt%

Base metals balance

**Greening problem:** high silver content causes the most severe greening problem (greenish-yellow discoloration) among all the metal ceramic alloys. Gold metal conditioners & coating agents are added to minimize this effect.

### **Palladium-copper alloys**

#### **Composition**

Palladium	74-80%
Copper	5-10%
Gallium	4-9%
Gold	1-2%
Base Metals	1%

Copper produces slight discoloration of the porcelain. These alloys are most technique sensitive produces black oxide layer-masked with opaquer.

### **Palladium-cobalt alloys**

#### **Composition**

Palladium	78-88%
Cobalt	4-10%
Gallium	upto 9%
Base metals	1%

Here cobalt can cause some discoloration. Dark oxide layer can be masked with Opaquer.

Most sag resistant of all noble alloys.

### **Palladium-gallium alloys**

2 Types

1. Palladium-Gallium-Silver
2. Palladium-Gallium-Silver-Gold

Composition:

Palladium	75%
Gallium	6%
Silver	5-8%
Gold	6%
Base metals	1%

Oxide layer though dark is somewhat lighter than the palladium copper & palladium cobalt alloys.

Silver content does not cause any greening.

### **Base metal alloys for metal ceramic alloys**

Contains little or no noble metals. Introduced expensive noble metal ceramic alloys.

The first noble metal Alloys were the Cobalt-Chromium alloys.

Nickel chromium alloys were introduced later.

### **Base metal alloys used for metal ceramics are**

1. Nickel-Chromium alloys
2. Cobalt-Chromium alloys
3. Pure Titanium
4. Titanium-Aluminium-Vanadium Alloys

### **Nickel-chromium alloy**

Composition

Nickel	61-81%
Chrome	11-27%
Molybdenum	2-9%
Beryllium	0.5-2%

Some alloys may contain occasionally one or more minor elements like Aluminum, Iron, Silicon, copper, manganese, Cobalt & Tin

### **General features of nickel-based alloys**

1. Cheapest of Casting Alloys
2. White in color
3. Melting Range 1155-1304 °C
4. Density 7.8-8.4 (half the density of Gold Alloys)
5. Hardness 75-360 VHN-harder than high noble metal alloys & difficult to work with.
6. Yield Strength 310-828 MPa-stronger than Gold and Palladium based alloys.
7. Modulus of Elasticity 150-210 MPa (x 10<sup>9</sup>) twice stiff as gold alloys. Thinner & lighter castings can be made metal copings can be reduced to 0.3-0.1 mm

8. Percent elongation 10-28%
9. Porcelain bonding-forms adequate oxide layer for porcelain bonding
10. Sag resistance-Higher sag resistance
11. Esthetics-a dark oxide layer may be seen at the porcelain metal junction
12. Highly resistant to tarnish & corrosion due to property of passivation  
It is the property by which a resistant oxide layer forms on the surface of Chrome containing alloys. This oxide layer protects the alloy from further oxidation & corrosion. So these alloys can maintain their polish for many years
13. They have higher casting shrinkage than the gold alloys.
14. Bio compatibility-Nickel may produce allergic reactions in some individuals. It is also a potential carcinogen
15. Beryllium also potentially toxic-Causes 'Berylliosis'

### **Titanium & Its alloys**

Because of its excellent biocompatibility light weight good strength and ability to passivity, these Titanium alloys are well adapted in dentistry.

### **Uses**

1. Metal ceramic restorations
2. Dental implants
3. Partial denture frames
4. Complete denture bases
5. Bar connectors

Also used as an alternative alloy to those allergic to Nickel.

### **Pure titanium**

Titanium has the ability to passivate itself.

Excellent corrosive & tarnish resistant against mineral acids & chlorides

Highly Biocompatible & non-toxic

### **Mechanical properties**

1. Density-4.5 gms/cm<sup>3</sup> (light weight)
2. Modulus of elasticity-110 GPa
3. Melting point -1700°C
4. Thermal expansion-8.4x10/C

{Lower than porcelain-so low fusing porcelain have been developed}

5. Pure Titanium exists in alpha & Beta forms
6. The alpha forms exists at room temperature with lower strength & high ductility
7. Above 830 °C it is converted into the Beta phase which is stronger and more brittle

### **Titanium alloys**

Titanium is alloyed with Aluminum, Vanadium and Palladium. Commonly used Titanium alloy is Ti6 Al4V.

Alloying the Titanium increases the strength & stabilizes the alloy. These alloys cannot be heat treated and amenable to brazing and soldering.

### **Chapter 8-Metal ceramic bond**

BY-Dr. Priyanka Priyadarshni

The primary requirement for the success of a metal ceramic prosthesis is development of a durable bond between the porcelain & the alloy along with the thermal compatibility of the alloy & porcelain.

### **Theories of metal-ceramic bonding**

1. Mechanical interlocking between porcelain & metal
2. Chemical bonding across the metal porcelain interface
3. Compression

### **Mechanical bonding**

Good wetting of the metal surface or metal oxide surface by the porcelain is essential to achieve mechanical bond. Surface tension provides intimate contact of porcelain with all the micro surface irregularities of the metal surface and some mechanical interlocking occurs when fired. Metal coping is sand blasted and cleaned. This roughened surface provides an easily wettable surface assisting in mechanical retention.

### **Chemical bond**

Heating to 1000 °C in vacuum for 10 min. degases the metal first. Then air cooled slowly. This will remove gases from the surface of the metal & induce some age hardening of the alloy. At the same time the base metal atoms will diffuse to the surface of the metal & form an oxide film (Tin, Indium or Zinc). This oxide film will provide chemical bond when porcelain is applied over it and fired. On further heating to maturing temperature of porcelain (950 °C), shrinkage & pore elimination will occur.

## Compressive bond

On cooling, the metal will contract faster than porcelain & this itself will put metal under tension and porcelain under compression. This will make the porcelain bond to metal firmly.

## Bonding of porcelain to metal using electrodeposited substrates

A new method of bonding porcelain to metal-by forming an additional oxide layer deliberately over the metal surface by using electro deposition. Deposition of a layer of pure gold onto the cast metal & then a layer of tin over it improves the wetting of porcelain onto the metal and to reduce the amount of porosity at the metal porcelain interface the electrodeposited layer acts as a barrier between the metal casting and porcelain to inhibit diffusion of atoms from the metal into the porcelain during normal firing cycles-limits buildup of oxide layer. Produces light color of the oxide-enhances vitality of porcelains and blocks the dark metal oxide color.

Alloys & metals like cobalt chromium, stainless steel, Palladium-silver, high & low gold content alloys & titanium have been successfully electroplated & tin coated to achieve satisfactory ceramic bonding.

## Metal-Porcelain bond failure

Bonding failures in metal ceramics occurs at 3 sites

1. Along the interfacial region between the opaque porcelain & the interaction zone (metal oxide)
2. Within the Interaction zone (metal oxide)
3. Between Metal & Interaction zone (metal oxide)

## Brein's classification of bond failure

1. **Porcelain metal:** This fracture occurs when the metal is devoid of oxides

Metal surface leaves a clean surface.

2. **Metal oxide-porcelain:** oxide is firmly attached to the metal seen in base metal alloys
3. **Cohesive within porcelain:** Seen in Gold alloys Bond strength is higher than the tensile strength so bond failures occur within the porcelain
4. **Metal-metal oxide:** Metal oxide is attached to the porcelain. Seen in base metal alloys due to formation of Nickel and Chromium oxides

5. **Metal oxide-metal oxide:** fracture occurs through metal oxide resulting from over production of oxides. Metal oxide is found attached to both metal and porcelain
6. **Cohesive within the metal:** This type of fracture usually occurs in crown and bridge but rarely seen in single crowns

## **Manipulation & technical considerations of cast metal ceramic restorations**

### **Construction of cast metal coping or framework**

A wax pattern of the intended restoration is constructed & cast in metal. Sharp angles or pits on the veneering surface of metal are to be avoided to avoid internal stress in final porcelain so convex surfaces & rounded contours are produced.

The intended metal ceramic junction should be as definite & smooth as possible-90° angle. Metal should be of sufficient thickness to prevent distortion during firing.

0.3 mm for Noble metal alloys.

0.2 mm for base metal alloys

The metal ceramic interface must be at least 1.5 mm from all centric occlusal contacts and must be distinct to facilitate removal of excess porcelain.

### **Metal preparation**

A clean metal surface is essential for good bonding. Oil impurities from fingers can contaminate. Surface is finished with ceramic bonded stones or sintered diamonds.

Final texturing done by sandblasting with an alumina air abrasive which aids in bonding. Finally it is cleaned ultrasonically, washed and dried.

### **Degassing & Oxidizing**

A controlled oxide layer must be created on the metal surface to establish the chemical bond between metal & porcelain. Oxide layer obtained by raising the temperature, exceeding the firing temperature of porcelain. A vacuum created in the firing chamber eliminates any adherent gases-hence the term 'degassing'.

High gold content ceramic alloy held at oxidizing temperature for several minutes. Low gold content alloys contain high base elements resulting in thick oxide layer. so air abraded lightly with alumina or placed in hydrofluoric acid.

## **Opaquer**

Dense yellowish white powder supplied with a special liquid -used to cover the metal frame. The metal framework is held with a pair of locking forceps. Opaquer powder is dispensed on to a ceramic palette & mixed with special liquid to a paste like consistency. It is carried & applied to the metal framework with a brush & condensed. Excess liquid is blotted with a tissue. Opaquer is built with 2 thickness. Casting with opaquer placed in furnace & fired at approximate temperature.

## **Condensation**

The process of packing powder particles together & removing excess water is known as condensation. This helps to minimize the porosity & reduce firing shrinkage.

## **Condensation techniques**

### **Vibration**

Use light vibration to spread the material thinly and evenly. Moving the serrated instrument back and forth over the handle of the tweezers will create the necessary disturbance. Excess moisture that comes to the surface can be blotted off with a clean tissue. Vibration may not be as necessary with the so-called paint opaques. An ultrasonic vibration is also used.

### **Spatulation**

A small spatula is used to apply and smoothen the wet porcelain which brings out excess water.

### **Dry powder**

Dry powder placed on the side opposite a wet increment. The water moves towards the dry powder pulling the wet particles together.

### **Whipping method**

Surface of the wet paste is tapped lightly with a spatula few times causes water to come on the surface. Excess water removed by blotting paper.

### **Gravitation method**

Gravity will bring the water off the paste to the surface- removed with blotting paper.

All these methods aim at bringing the water to the surface. Surface Tension of water is the driving force for condensation and the porcelain must never be allowed to dry out until condensation is complete.

## **Before firing, inspect the opaque application to see that it satisfies the following criteria**

The entire veneering surface is evenly covered with a smooth layer that masks the color of the metal.

There is no excess anywhere on the veneering surface.

There is no opaque on any external surface adjacent to the veneer. There is no opaque on the internal aspect of the substructure.

## **Firing and sintering of porcelain**

The thermochemical reaction between the porcelain powder components are virtually completed during the original manufacturing process. So, the purpose of firing is simply to sinter the particles of powder together properly to form the prostheses. Firing is done in a porcelain furnace. Modern furnaces are computer controlled & have built in programs to control the firing cycle. Programs can also be changed by the operator.

## **Firing cycle**

The entire program of preheating firing, subjecting to vacuum subjecting to increased pressure, holding & cooling is known as firing cycle. The firing cycle vary depending on the stage-opaquer firing dentin firing glaze firing etc. Opaquer has the highest temperature and the glaze the lowest.

**Preheating:** The condensed mass should not be placed directly into the hot furnace. This can cause rapid formation of steam which can break up the mass. Modern furnaces-work is gradually raised into the furnace this is preheating.

## **Vacuum firing**

During firing a vacuum is created in the furnace-air pressure reduced by 1/10 of atmospheric pressure by vacuum pump. As the temperature rises, the particles sinter together & closed voids are formed in the porcelain mass. At a temperature of about 55° c below the upper firing temp, the vacuum is released so pressure increased from 0.1 -1 atm. as pressure is increased by 10 folds, the voids are compressed to 1/10" of their original size and the total volume of porosity is reduced. The vacuum is not activated during the Glaze firing.

## **Cooling**

Cooling of fired porcelain should be well controlled. Rapid cooling causes porcelain to crack or, it can induce stresses which weaken the

porcelain Cooling is done slowly and uniformly and usually computer controlled. Thermal expansion will increase after slow cooling, because additional (high-expansion) leucite will crystallize. In general, alloys with high thermal expansion coefficients require more rapid cooling than alloys with low coefficients.

### **Evaluation of the opaque porcelain**

Small cracks and fissures are common after the first firing. This problem can be resolved by applying moisture, followed by a thin mix of opaque carefully condensed into the fissures. When correcting a thin area where the color of the metal has not been masked completely, the surface should be moistened before a second coat is applied.

### **After firing, check that the opaque application meets the following criteria**

Relatively smooth even layer masking the color of the framework.

Eggshell appearance.

No excess on any external or internal surface of the restoration (which would prevent it from seating fully on the die).

### **Dentin & Enamel porcelain**

After the opaquer is fired & cooled-dentin powder mixed with distilled water or liquid supplied with glass spatula Bulk of the tooth is built up with dentin a portion of dentin in the incisal area is cut back and enamel porcelain can be added. After build up & condensation is over-returned to the furnace for sintering.

### **Additions**

Not necessary to build up the restoration in one step. Large restorations are built up in 2 or 3 stages. After each firing porcelain is shaped by grinding & additional porcelain placed in deficient areas. Each additional firing is done at a lower temperature Caution-avoid too many firings, as this may give rise to a over translucent, lifeless restoration.

To compensate for the firing shrinkage that result when the particles fuse, slightly overbuild the porcelain. A typical metal-ceramic anterior crown will shrink 0.6 mm at the incisal edge and 0.5 mm mid facially.

### **Gingival and Transparent porcelain**

Enamel of natural teeth at incisal edges appear transparent, so a transparent porcelain is used for this. Depending on the desired appearance,

make a cut-back for the more translucent incisal powder. Whether the cut-back is made with a razor blade, scalpel, or modeling instrument, condensing the body buildup well before cutting back is necessary. This will minimize the risk of fracture during the process. Furthermore, to minimize the chance of damaging the unsupported incisal portion of the buildup, the cut-back should be made from incisal to cervical.

The cervical portions of natural teeth may appear more darker (more yellow). Cervical porcelain or gingival/neck porcelain are used to duplicate this effect.

### **Surface staining, characterization & effects**

Staining & characterization helps make the restoration look natural and helps it to blend with adjacent teeth. Internal or intrinsic characterization or staining may be accomplished by incorporating colored pigments in the opaque, body, or incisal powder. Stain powders are mixed with a special liquid applied and blended with a brush. To recreate natural look of teeth, special techniques were used to create effects like cracks defects & other anomalies within the enamel. Highly colored glazes, commonly used as surface stains, may be layered within the buildup powders to create special effects.

Colored opaque modifiers that can be selectively mixed with the opaque to increase the saturation of the desired pigment. A variation of this approach is to use opacified dentin powders that produce a finished restoration with a slightly higher chroma than one prepared with the more translucent dentin powders. Similarly, a translucent powder can be used to enhance incisal translucency.

The surface texture of a metal-ceramic restoration should resemble that of the adjacent teeth, including selected characterizing irregularities that exist on those teeth.

Several rules of light reflection must be remembered when attempting to accomplish this:

1. A flat surface will reflect primarily parallel light bundles
2. A convex surface will result in divergence of reflected light, whereas a concave surface will create a convergent light bundle
3. Sharp transitions (e.g., geometric line angles) will result in line reflections, but smooth, gently flowing curved surfaces will create a reflection pattern with greater surface area

## Glazing

Glazing is a process by which the restoration is given a smooth glossy surface. Before final glazing restoration is tried in the mouth checked and adjusted by grinding. Restoration is smoothed prior to glazing.

### Objectives of glazing

1. Glazing enhances esthetics
2. Enhances Hygiene
3. Improves strength-stronger than unglazed porcelain. It inhibits crack propagation
4. Reduces the wear of the opposing teeth

### Types of glazing

1. **Over glaze:** Glaze powder is mixed with special liquid & applied on to the restoration. Firing temperature lower than body porcelain. Firing cycle does not include vacuum. Chemical durability is less because of high flux content
2. **Self-glaze:** instead of a separate glaze layer, the restoration is subject to a controlled heating at its fusion temperature, this causes only the surface layer to melt and flow to form a vitreous layer resembling glaze.

Glazing is superior to conventional polishing

### Other metal ceramic Systems

#### 1. Swaged gold alloy foil

-ceramic crowns (burnished foil copings)-Captek.

Captek-capillary casting technology Based on principle of capillary attraction to produce gold composite material without having to cast it. Comes in fluted form & is adapted to the die by swaging & burnishing Foil coping is carefully removed & flame sintered. An interfacial alloy powder is applied and fired which helps to bond the ceramic & metal Porcelain is the condensed and fired to form the crown.

### Advantages

Thinner foil alloy allows greater thickness of ceramics -improving esthetics.

Underlying alloy is gold colored-gives more warmth & life to the restoration.

## 2. Bonded platinum foil ceramic crowns

A platinum foil coping is constructed over the die to improve the bonding of the ceramic to the platinum foil coping an electro deposition technique is used.

### Electrodeposition technique

This is used to improve both esthetics & bonding. A layer of pure gold is electrodeposited onto the metal, followed by a quick minimal deposition of tin over the gold.

### Advantages

1. Gold color enhances vitality of the porcelain
2. Tin helps in chemical bonding
3. Good wetting at gold porcelain interface reducing porosity

Electrodeposition also done with other alloys Co-Cr. Stainless steel. titanium, low gold & non-gold alloys.

## 3. Cast metal ceramics with labial margins

When esthetics is of prime importance, a collar less metal-ceramic crown is considered Collarless crowns have a facial margin of porcelain and lingual & proximal margins of metal.

### Advantages

1. Esthetic improvement
2. Plaque removal easier when gingival tissues are in contact with vacuum fired glazed porcelain than the finished gold

### Disadvantages

1. Marginal adaptation-slightly inferior cast metal
2. Fracture of unsupported margin-during try in or cementation due to careless handling
3. Time consuming more costly

**Indication:** when conventional metal ceramic esthetic result.

**Contraindication:** when an extremely smooth 1 mm wide shoulder cannot be prepared in the area of ceramic veneer.

**Methods of Fabrication:** Includes

1. Platinum foil matrix technique
2. Direct lift (cyanoacrylate) technique
3. Porcelain wax technique

## Advantages & disadvantages of each technique

	Method	Advantages	Disadvantages
1	Platinum Foil	No shoulder porcelain Good marginal adaptation Smooth surface. Low plaque accumulation.	Time consuming & Technically Difficult
2	Wax suspension	Separates easily	Shoulder porcelain needed. Less accurate fit
3	Direct lift	Least time Consuming	Shoulder porcelain needed. Rougher margins

## Common reasons for failure of metal ceramic

### Restorations

	Failure	Reason
1.	Fracture during Bisque bake	1. Improper condensation 2. Improper moisture control 3. Poor frame work design 4. Incomplete metal-porcelain combination
2.	Bubbles	1. Too many finning 2. Air entrapment during building of restoration 3. Improper moisture control 4. Poor metal preparation 5. Poor casting Technique
3.	Unsatisfactory Appearance	1. Poor communication with technician 2. Inadequate tooth Reduction 3. Opaque too thick 4. Excessive firing
4.	Clinical fracture	1. Poor Framework design 2. Centric stops too close to metal ceramic interface 3. Improper metal preparation

## Cast metal ceramic restoration

### Indications

1. Esthetics
2. If all-ceramic crown is contraindicated
3. Gingival involvement

### Contraindications

1. Large pulp chamber
2. Intact buccal wall
3. When more conservative retainer is technically feasible

## **Advantages**

1. Better fracture resistance because of metal reinforcement
2. Better marginal fit because of metal frame
3. Superior esthetics as compared to complete cast crown

## **Disadvantages**

1. Less esthetic when compared to all porcelain. Reduced because of underlying metal & opaque translucency
2. Margins may appear dark because of the metal. Sometimes shows through the gingiva causing it appear dark and anesthetic
3. Removal of substantial tooth structure
4. Subject to fracture because porcelain is brittle
5. Difficult to obtain accurate occlusion in glazed porcelain
6. Expensive

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**Chapter - 2**  
**Dental Ceramics: A Basic Review**

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# Chapter - 2

## Dental Ceramics: A Basic Review

Dr. Priyanka Priyadarshni

### Abstract

Dental ceramics are nonmetallic inorganic structures containing oxides of one or more metallic or semi metallic elements. They are able to mimic the appearance of natural teeth, have color stability, wear resistant, and excellent biocompatibility. Despite having excellent esthetics they are prone to fracture under tensile or flexural loading. By enrolling the amount and type of component used in manufacturing ceramics broadly classified as silicate ceramics, oxide ceramics, non-oxide ceramics, and glass ceramics. Basic structure of all dental ceramics contain a crystal phase and silicate glass matrix phase. Dental porcelain is manufactured by heating ingredients at high temperature to form a glassy mass which is then rapidly quenched in water to this glassy mass. This process is called fritting and the product formed is frit.

**Keywords:** dental ceramics, excellent esthetics, silicate glass matrix phase, frit

### Introduction

#### What are ceramics?

The word 'ceramic' is derived from the Greek word Keramikos'-meaning Burnt Earth. A ceramic is therefore an earthy material usually of a silicate nature and may be defined as "Nonmetallic, inorganic structures primarily containing compounds of oxygen with one or more metallic or semi metallic elements (Aluminum, calcium, lithium, magnesium, phosphorus, potassium, silicon, sodium, titanium & zirconium) that is formulated to produce the ceramic based dental prosthesis. "They may be crystalline, non-crystalline, or both including crystalline phase in a glassy amorphous matrix.

#### What are porcelains?

The name porcelain is said to have been coined by Marco Polo in the 13th century from the Italian term porcellino. This was the name of the

translucent cowrie shell (also called the Venus shell) which looked like a little pig or, in Italian, porcelain. He likened Chinese porcelain to this translucent white shell. The characteristics most admired in porcelain are its white color, the thinness of the vessels that can be created with it, its high density and its innate strength. To quote a tenth century European reflecting on his journey through China. "A ceramic so white that it was comparable only to snow, so strong that vessels needed walls only 2-3 mm thick and consequently light could shine through it. So continuous was the internal structure that a dish, if lightly struck would ring like a bell. This is porcelain!"

The two major components in ceramics are a refractory (non-meltable) crystalline structure and glass Pottery was the first, and is still the foremost ceramic. It contains both of the major ceramic components and is made from clay. Clay bodies are further subdivided into three groups: earthenware, stoneware and domestic porcelain. Each classification, from earthenware to porcelain contains increasing percentages of glass and decreasing percentages of alumina. Dental porcelain is a further subdivision of domestic porcelain

The modern traditional ceramic articles are made with clay (kaolin), silica, quartz, and feldspar Dental ceramics also contains the same but for little or no kaolin and feldspar as the major component.

	<b>Dental Porcelain</b>	<b>House Hold Porcelain</b>
Feldspar	81%	15%
Quartz	15%	14%
Kaolin	4%	70%
Metallic Pigments	<1%	1%

In dentistry, we use three different types of porcelain composition depending on their application. One is for denture teeth, one is for ceramo-metal applications and another is for all porcelain restorations (PJs, veneers and inlays).

Denture tooth porcelain begins as a mixture of powders of feldspar, clay and quartz. This is referred to as high-temperature porcelain in some dental materials textbooks.

Feldspathic dental porcelain, used for ceramo-metal restorations, begins as a mixture of powders of potassium feldspar and glass. This type of porcelain composition can also be used for fabricating porcelain veneers and inlays.

Aluminous porcelain, used in PJC's, is composed of mixtures similar to that of feldspathic dental porcelain with increased amounts of aluminum oxide.

These three types of dental porcelain also contain pigments and opacifying agents to create various shades and translucencies. After baking, all three types of porcelain contain similar components: small crystals (leucite and/or other alumino-silicate crystals) embedded in a silicate glass (a non-crystalline, amorphous matrix) of crystal and glass depend on the specific type of porcelain in question Leucite (a reaction product of potassium feldspar and glass) is a particularly important component in dental porcelain because it affects the optical properties, thermal expansion, strength and hardness of the porcelain.

Uses and applications of Dental Ceramics:

1. Inlays and onlays
2. Esthetic laminates (veneers) over natural teeth
3. Single (all ceramic) crowns
4. Short span (all ceramic) Bridges
5. As veneer for cast metal crowns and bridges
6. Artificial denture teeth-for CD & RPD's
7. Ceramic orthodontic brackets
8. Implant Superstructures and biodegradable implant material

Ceramics are the earliest group of inorganic materials to be structurally modified by man. He transformed clay into ceramic articles of utility.

The origin of glazing technique is of importance in dental field

- 4000B.C.-earliest glazing technique by Sumerian invention is Egyptian Blue Faience -bluish green hues from metal oxides added during firing
- 100 BC stonewares were produced in China
- 1774 A.D. a Parisian apothecary Alexis Duchateau, with assistance of a Parisian dentist Nicholas Dubois de Chemant, made the first successful porcelain dentures at the Guerhard porcelain factory.
- 1789 De Chamant (French Scientist) patented first porcelain tooth material
- 1808-Fonzi (Italian dentist prepared porcelain teeth baked with Platinum posts or pins. Fonzi called these teeth "terra metals

incorruptibles" and their esthetic and mechanical versatility provided a major advance in prosthetic dentistry

- 1817-Plateau (French dentist) introduced porcelain teeth to the U.S.
- 1822-Peale an artist developed a baking process in Philadelphia for these teeth
- 1844 Mass production of porcelain teeth by S.S. White company.
- 1886-Dr. Charles Land introduced first ceramic crowns to dentistry. Using platinum foil matrix and high-Fusing Feldspathic Porcelain. Low Flexural strength, and increased firing shrinkage resulted in high incidence of failures. The same technique was again described by Land (1903) and much later by Pincus (1937) for the fabrication of artificial ceramic veneers.
- 1958-Vines metal introduced finer porcelain powder for vacuum firing or low-pressure firing. Had better packing densities that facilitated the carving and layering of the green porcelain.

### **Metal ceramics**

- 1962-Weinstein and Weinstein-porcelain compositions for metal ceramic restorations were introduced (Patented) K20 level was increased to produce high expansion glasses suitable for bonding to metal.
- 1963-First commercial metal ceramics by Vita Zahnfabrik and later Ceramco was introduced
- 1965-McLean and Hughes-development of Aluminous core and veneer porcelain-upto 50% wt of Alumina crystals were added. Restricted use-in maxillary anteriors only with high Fracture rate in posteriors. Large sintering shrinkage 15-20% Strength of upto 180MPa were achieved
- 1976-first commercially viable foil-reinforced (vita-pt) crown system was developed by McLean and Scad-Here surface of platinum foil was coated with upto 2.0 um of tin provided mechanism for bonding of porcelain.
- 1979-Rogers reported gold copings made by electroforming and use of tin oxide coatings for attachment of conventional metal bonding porcelain

## **Fluorescence**

- During development of Aluminous veneer porcelain radio active Fluorescein sodium uranium septoxide (Na<sub>2</sub>U<sub>2</sub>O<sub>7</sub>) was used. It produced a strong greenish-yellow color.
- When small amounts of cerium oxide were added a bluish-white Fluorescence similar to human teeth was achieved. -But Radioactive Fluorescers have been banned.

## **Glass ceramics**

- Glass ceramics-Mac Culloch described methods for making artificial teeth, veneers, & crowns in glass ceramic in 1968, But with little recognition.

1984-Grossman and Adain-controlled crystallization of glass was demonstrated -Dicor.

Glass was melted and cast into a refractory mold and then crystallized. The glass ceramic material contained Tetrasilic Floor Mica crystals (K<sub>2</sub>Mg<sub>5</sub>Si<sub>10</sub>F<sub>4</sub>) to give added strength and resistance to fracture propagation. Mac Culloch reported shade modification achieved with surface colorants which eroded over time. Dicor high translucency has a chameleon-like effect and merges with surrounding teeth. Dicor-MGC-with 70% tetrasilic Floor Mica crystals is a machinable glass ceramic version.

- 1990-pressable glass ceramics (IPS Empress) containing 34% Leucite was introduced which did not require crystallisation as Dicor-developed by Wohlwend
- Late 1990's-IPS-Empress 2-pressable glass ceramic containing 70% lithium disilicate crystals was introduced-more fracture resistant
- 1993-procera-All ceramic system was introduced All ceramic crowns composed of a coping of densely sintered, high purity alumina-Andersson and Oden
- Procera copings are manufactured by compacting high purity alumina powder (A1203 > 99.9%) with a dry pressing technique against enlarged models of tooth preparation

## **Slip cast alumina ceramics**

- 1989 Sadown refined slip casting technique to produce high strength coping-In Ceram (Vita ZahnFabrik). He showed that a lightly sintered alumina powder could be infused with low fusing sodium lanthanum glass to produce dense composite ceramic of

very high strength. High concentration of Alumina 72% were used to obtain strength upto 700MPa.

### **Supplied as 3 core materials**

In Ceram Alumina

In Ceram Spinell

In Ceram Zirconia-Al<sub>2</sub>O<sub>3</sub>-ZrO<sub>2</sub> ceramic.

- **Bonded porcelain restorations:** 1983 Simonson & Calamia reported the concept of bonding composite resin to acid etched porcelain. Fabrication of porcelain veneers with this system was reported by Horn in the same year
- **CAD CAM ceramics:** CEREC (Sirona) was introduced in 1986
  - I) Generation could mill only inlays
  - II) Generation (1994) inlays, onlays & crowns were made
  - III) Generation increased overall acceptance with improved computer technology
- Other CAD CAM Systems includes Duret, Minnesota, DCS, Procera, & Cicero Classification of Dental Ceramics

### **According to firing temperature**

1. High Fusing-1300 °C-denture teeth
2. Medium fusing-1101-1300 °C-denture teeth
3. Low fusing-850-1100 °C-crown & bridge use
4. Ultra low fusing-<850 °C used with Titanium

### **According to use or indications**

Ceramics for

1. Artificial teeth
2. For crowns & inlays
3. For veneer over a cast metal crown
4. Anterior Bridge porcelain
5. Posts and cores Stain & Glass ceramics

### **According to composition/type**

1. Feldspathic or conventional porcelain
2. Aluminous porcelain

3. Leucite reinforced porcelain
4. Glass infiltrated alumina
5. Glass infiltrated Spinell
6. Glass ceramic

**According to processing method**

1. Sintered porcelain
2. Cast porcelain
3. Machined porcelain

**According to application while building a crown layer by layer**

1. Core porcelain
2. Dentin or body porcelain
3. Enamel porcelain
4. Neck porcelain

**Based on substructure or core material used**

1. Porcelain fused to metal alloy
2. All ceramic restorations

**Classification & Description of ceramic systems**

Ceramic systems classified based on *substructure* or core material as

- i) Metal bonded
- ii) All Ceramic restorations

**i) Metal bonded (PFM) or Metal ceramic restorations**

- A) Cast metal ceramic restorations
  1. Cast noble metal alloys
  2. Cast base metal alloys
  3. Cast Titanium (ultra-low fusing)
- B) Swaged Metal ceramic restorations
  1. Swaged gold alloy foil ceramic crowns
  2. Bonded platinum foil ceramic crowns

**ii) All ceramic restorations**

1. Conventional Porcelain Jacket Crown
2. Aluminous Porcelain Crown

3. Leucite reinforced feldspathic porcelain-OPTEC-HSP
4. Magnesia based core material
5. Glass ceramics
  - a) Castable glass ceramics-Dicor
  - b) Hydroxy apatite-based Glass ceramics-Cerapearl
  - c) Lithia based Glass Ceramics
6. Hot pressed Injection molded Ceramics
  - a) IPS Empress I-Leucite reinforced
  - b) IPS Empress II-Lithia disilicate reinforced
  - c) Al Ceram-Spinell based
7. Slip cast Ceramics
  - a) In Ceram-Alumina
  - b) In Ceram Spinell
  - c) Ceram zirconia
8. Machinable ceramics
  - a) CAD CAM ceramics-CEREC system
  - b) Copy milled ceramics
    - Cercon & lava zirconia core ceramics
    - Celay system

## **Current dental ceramics**

### **A. Feldspathic porcelain (low leucite content)**

1. Condensed and sintered
2. Veneers, anterior crowns, low-stress inlays and onlays, crowns (PFMs)

Metal. ceramic fixed partial dentures (FPDs)

### **B. Leucite-reinforced porcelain**

1. Powder processed and sintered, pressure molded
2. Anterior crowns, low-stress posterior crowns
3. Examples
  - 1) Optec HSP-powder processed (Pentron-no longer available)
  - 2) IPS Empress (injectable porcelain system)-pressable (Ivoclar)

- 3) OPC (Optimal Pressable Ceramic)-pressable (Pentron)
- 4) Finesse All-Ceramic-pressable (Ceramco)

### **C. Alumina-reinforced porcelain**

1. Powder processed and sintered
2. Anterior crowns; low-stress posterior crowns
3. Examples:
  - 1) Vita VMK Hi-Ceram (Vita Zahnfabrik)
  - 2) Viladur-N (Vita Zahnfabrik)
  - 3) Vitadur Alpha (Vita Zahnfabrik)

### **D. High density alumina (Al<sub>2</sub>O<sub>3</sub>) core**

1. Powder processed, machined in "green-body" state and sintered
2. Anterior & posterior crowns, anterior FPDs; low-stress posterior FPDS
3. Examples:
  - 1) *Procera ALL Ceram* (Noble Biocare)

### **E. High density zirconium (ZrO<sub>2</sub>) core**

1. Powder processed, machined in "green-body" state and sintered
2. Posterior crowns anterior and posterior FPDS
3. Examples
  - 1) *Lava* (3M-ESPE)
  - 2) *Cercon* (Dentsply-Ceramco)
  - 3) *Denzir* (Dentronic)

### **F. Glass-infiltrated core**

1. Slip-cast, sintered, and infiltrated with glass
2. Anterior & posterior crowns, anterior FPDs, posterior FPDs (*In-Ceram Zirconia* only)
3. Example: In-Ceram ("infused ceramic")
  - 1) *In-Ceram Alumina* [Al<sub>2</sub>O<sub>3</sub>] (Vita Zahnfabrik)
  - 2) *In-Ceram Spinell* [MgAl<sub>2</sub>O<sub>4</sub>]-enhanced translucency, mechanical properties inferior to In-Ceram Alumina-anterior use only (Vita Zahnfabrik)

- 3) In-Ceram Zirconia ( $ZrO_2$ )-enhanced mechanical properties (VitaZahnfabrik)

### **G. Glass-ceramic core ceramic**

1. Cast and creamed; pressure molded
2. Anterior & posterior crowns; anterior FPDs (Empress 2)
3. Example:
  - 1) *Dicor* "Dentsply International/Corning Glass"-mica based, no longer available
  - 2) *IPS Empress 2*-lithia disilicate core/(Ivoclar)

### **H. Ceramics for CAD-CAM (*CEREC*; *CEREC 2*) and copy milling (Celay)**

1. Milled or ground
2. Anterior & posterior crowns; 3-unit anterior FPD (In-Ceram Alumina)
3. Examples
  - 1) *Dicor* MGC machinable glass-ceramic" mica based, no longer available
  - 2) *Vita Mark II*-machinable feldspathic porcelain (Vita Zahnfabrik)
  - 3) *In-Ceram Alumina* and *In-Ceram Spinell*-crowns & bridges (Vita Zahnfabrik)
  - 4) *Pro CAD*-modified "machinable" version of IPS Empress (Ivoclar)

### **Composition & manufacture of dental ceramics**

Dental porcelain is a glass like ceramic material containing mixture of feldspar, silica, kaolin, alumina & other oxides, it is formed as a fine refractory powder on heating.

This powder is mixed with liquid or distilled water to form a plastic mass, which is molded or shaped into a desired size & shape it is then fired (sintered) at high temperature to fuse the particles together and forms a hard smooth solid.

Many dental ceramics contains a crystal phase and a glass phase based on the silica structure. Silica structure is characterized by a Si-O tetrahedron in which a Si<sup>4+</sup> is positioned at the centre of tetrahedron with O-anions at each four corners. The SiO<sub>4</sub> tetrahedron are linked together by sharing their corners.

The glass obtains porcelain like qualities when the Silica network is broken by alkalis like sodium & potassium. These chemicals along with alumina and boric oxide acts as a glass modifiers & fluxes to lower the fusion temperature.

The composition of different dental porcelains are essentially the same, the principal difference being the proportion of the primary ingredients and firing procedures.

### **Feldspathic porcelain**

Basic constituents includes

- Feldspar - Basic glass former
- Kaolin - Binder
- Quartz - Filler
- Alumina - Glass former & flux
- Alkalis - Glass modifiers
- Color pigments - Modified color
- Opacifiers - Reduce transparency

### **Feldspar**

Naturally occurring mineral which forms the basic constituent of feldspathic porcelain. Most of the components needed to make dental porcelain are found in feldspar which occurs as potassium feldspar and sodium feldspar in nature containing potash, soda, alumina & silica. Feldspar is the basic glass former. When fused at high temperatures during manufacture it forms a feldspathic glass containing potash feldspar ( $K_2O \cdot Al_2O_3 \cdot 6SiO_2$ ) and soda feldspar ( $Na_2O \cdot Al_2O_3 \cdot 6SiO_2$ ). Pure feldspar is colorless & transparent. So various glass modifiers & opacifiers are added to alter its sintering temperature, viscosity, CTE and appearance. CTE-less than 10 ppm/c. Feldspar when heated between 1150 °C & 1530 °C undergoes incongruent melting & forms crystals of Leucite which is potassium aluminum silicate minerals with large CTE 20-25 ppm/°C.

### **Kaolin**

White clay like material-hydrated aluminum silicate. Acts as a binder & gives opacity to the mass. Kaolinite is found in nature a relatively pure form known as kaolin (China clay). It derives its name from the Chinese term for "high ridge", the place where the Chinese first discovered this purest form of kaolinite. The chemical formula for kaolinite is  $Al_2O_3 \cdot 2SiO_2 \cdot 2H_2O$ .

## Quartz

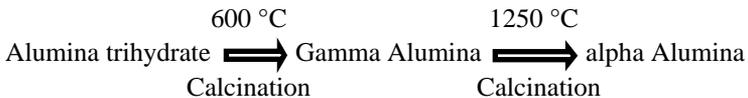
Quartz is a form of silica. Silica exhibits polymorphism- exist with more than one crystal structure.

Quartz 867 °C, tridymite 1470 °C, cristobalite 1713 °C fused quartz.

Quartz with hexagonal structure is most stable form of silica. Ground quartz acts as a refractory skeleton providing strength & hardness to porcelain during firing. The quartz remains as separate, unmelted particles dispersed throughout the glassy phase produced by the melting of the feldspar. Quartz is part of the refractory crystalline structure in ceramic bodies, and helps the body to retain its shape in the kiln while the feldspathic glass melts around it. It remains relatively unchanged during and after firing. Insoluble in water and acids.

## Alumina

Alumina oxide replaces some of the silica in the glass network. It gives strength and opacity to the porcelain. It alters the softening point & increases the viscosity of porcelain during firing Alumina is oxide of aluminum  $Al_2O_3$  extracted from mineral bauxite mainly hydrated aluminum oxide. Alumina Trihydrate is formed when the ore is treated with caustic soda



Alpha form is used in ceramics. Generally ball milled & commercially supplied as fine powder 10-20 microns size. Prefabricated profiles or reinforcements used for dental purpose includes rods, tubes or sheets (alumina powder mixed with a binder methyl cellulose & a releasing agent).

## Glass modifiers

Potassium, sodium & calcium oxide ( $K_2O$ ,  $Na_2O$ ,  $CaO$ ) are used as glass modifiers and act as fluxes by interrupting the integrity of  $SiO_4$  network Purpose of flux is to lower the softening temperature of a glass by reducing the amount of cross linking between oxygen & glass forming elements- silicon for e.g. Soda  $Na_2O$  is introduced into a silicate melts to produce sodium silicate glasses.

The greater the number of  $Na^+$  ions are added, the more the Si-O-Si bridges are broken &  $Na^+$  ions incorporated into the silicate forming the sodium silicate structure. This linear chains of silica tetrahedra are able to move easily at lower temperatures- thereby lowers softening temp. & increases thermal expansion & reduces viscosity

Too high concentration of glass modifiers is also not advisable because it reduces chemical durability of the ceramic may cause the glass to crystallize (devitrify). Other glass modifiers includes Lithium oxide & Boric oxide Manufacturers employ glass modifiers to produce dental porcelain with different firing temperatures as-High fusing, medium fusing, low fusing, & ultra-low fusing

### Opacifiers

Pure feldspathic porcelain is colorless so opacifiers like oxides of Zirconium, Titanium, Calcium & tin are added to increase its opacity-to stimulate natural teeth.

### Color modifiers

Natural teeth exist in various shades also it acquires external stains from the environment so color modifiers are added to adjust the shades. These are fused together with regular feldspar & then reground and blended to produce the colors.

Uranium oxide was used to provide fluorescence but because of the radioactivity, lanthanide earths are used.

Pigments	
Zirconia, alumina, silica	white
Titanium oxide	yellow brown
Cobalt oxide	blue
Iron or Nickel Oxide	brown
Nickel oxide	brown
Manganese oxide	lavender
Copper oxide	green
Chromium oxide	green

### Types of feldspathic porcelains

- **Opaque porcelain:** Feldspathic glass loaded with opacifiers zirconium/Titanium oxide
- **Body dentin porcelain:** Colored feldspathic glasses with high translucency
- **Gingival dentin:** Colored feldspathic glasses with reduced translucency
- **Overlay enamel:** Highly translucent feldspathic glasses containing sub-micron opacifiers or crystalline material to create special color effect.

## Composition of low & medium fusing feldspathic porcelain

Ingredient	Low fusing %	Medium fusing
SiO <sub>2</sub>	69.36	64.2
B <sub>2</sub> O <sub>3</sub>	7.53	2.8
CaO	1.85	-
K <sub>2</sub> O	8.33	8.2
Na <sub>2</sub> O	4.81	1.9
Al <sub>2</sub> O <sub>3</sub>	8.11	1.9
Li <sub>2</sub> O	-	2.1
MgO	-	0.5
P <sub>2</sub> O <sub>5</sub>	-	0.7

### Manufacturing

Traditional porcelain powder is manufactured by a process called Fritting. Various components are mixed together and fused.

#### 2 Different phases are formed

- A) *vitreous or glassy phase*-amorphous & has properties typical of glass like brittleness, high surface tension in fluid state. This phase is provided by feldspar
- B) *crystalline or mineral phase* includes silica & other metal oxides Vitreous phase is prominent as it binds the crystalline particles together

Fusion Temperature of main Ingredients

Feldspar - 1100 °C

Silica - 1713 °C

Kaolin - 1770 °C

Fused mass after heating is called FRIT. While it is still hot it is quenched in water which causes the mass to crack & fracture making it easier to powder. They are again fired with appropriate color pigments to give color & shades to match natural tooth. Then after cooling, the mass is grinded to produce powder porcelain.

**Fritting:** Process of blending melting & quenching the ceramic components

**Vitrification:** Formation of glassy phase due to melting and cooling of ceramic ingredients-non-crystalline & amorphous

**Devitrification:** If the vitreous glassy phase, crystallizes due to disruption of silica tetrahedron network is known as Devitrification.

Most of the chemical reaction takes place during the manufacture. During subsequent firing in dental lab there is not much of chemical reaction the porcelain powder simply fuses to form the desired restoration.

**Composition of porcelain used in metal ceramic systems**

Metal ceramics must fulfill certain requirements

1. CTE must be slightly less than that of metal ( $14.5 \times 10^{-6}/^{\circ}\text{C}$ ) to avoid undesirable tensile stresses developing in the ceramic on cooling
2. The mineralogical structure of porcelain must be maintained during successive baking of metal ceramic crowns to avoid problems of devitrification or hydrolytic instability
3. The soda & potash content is increased to raise the thermal expansion compatible with metal substructure
4. Some porcelain contains Leucite (K<sub>2</sub>OAl<sub>2</sub>O<sub>3</sub>SiO<sub>2</sub>) as a crystalline phase CTE of leucite ( $20 \times 10^{-6}/^{\circ}\text{C}$ ) matches higher gold alloys

**Opaque porcelain**

The opaque porcelain is applied directly to the metal surface. These are heavily loaded with opacifiers to mask the metal sub structure & reduce the thickness of the porcelain to minimum. Modern paint on opaques, effectively mask the metal when applied in thickness as low as 100µm.

**Composition of opaque porcelain**

Contents	Action	%
Silica SiO <sub>2</sub>	Glass Former	48-59%
Alumina Al <sub>2</sub> O <sub>3</sub>	Intermediate	16.3-20%
Potash K <sub>2</sub> O	Alkali Fluxes	8.4-10.3%
Soda Na <sub>2</sub> O	Alkali Fluxes	5.7-7%
Calcium Oxide	Fluxes	1.2-1.45%
Boric Oxide	Fluxes	1.2-1.45%
Titania TiO <sub>2</sub>	Nucleating Agent	2.7-3.3%
Tin Oxide SnO <sub>2</sub>	Opacifiers	4.3-5.25%
Zinc Oxide		1.2-1.5%
Ferric Oxide		Trace
Fluoride		Trace

**Low fusing metal ceramic-enamel & dentin porcelain**

The dentin & enamel porcelains for metal veneering which covers the opaque layer also consists of feldspathic glasses, but for higher Alkali content to raise the CTE.

## Composition of low fusing metal ceramic-enamel & dentin porcelain

	Dentin	Enamel
SiO <sub>2</sub>	59.20%	63.50%
Al <sub>2</sub> O <sub>3</sub>	18.50%	18.90%
Na <sub>2</sub> O	4.80%	5%
K <sub>2</sub> O	11.80%	12.30%
B <sub>2</sub> O <sub>3</sub>	4.60%	0.10%
ZnO	0.60%	0.10%
ZrO <sub>2</sub>	0.40%	0.10%
Firing temp	900°C	900°C

### Metal ceramics supplied as

Typical kit which consists of

- Opaquer powders in various shades together with a liquid for mixing
- Dentin powders in various shades (bottles)
- Enamel powders in various shades
- Gingival porcelain powder in various shades
- Transparent porcelain powder
- Liquid for mixing Enamel, dentin, gingival & transparent porcelains
- Variety of stain powders
- Glaze powder
- Special liquid for mixing stains & glaze

### Aluminous porcelain

Mclean & Hughes developed the PJC with an alumina reinforced core in 1965. Alumina is added as filler in high % to strengthen the porcelain by interruption of crack propagation Flexural strengths of upto 180MPa were achieved with this porcelain High Alumina Ceramics generally contain a minimum of 95% pure alumina.

### Composition of aluminous porcelain

Composition	Aluminous core	Dentin porcelain	Enamel porcelain
Silica SiO <sub>2</sub>	35%	66.50%	64.70%
Alumina Al <sub>2</sub> O <sub>3</sub>	5.80%	13.50%	13.90%
Calcium oxide CaO	1.12%	-	1.78%

Soda Na <sub>2</sub> O	2.80%	1.20%	4.80%
Potash K <sub>2</sub> O	4.20%	7.10%	7.50%
Boric Oxide B <sub>2</sub> O <sub>3</sub>	3.2	6.60%	7.30%

## Glazes

Special type of colorless porcelain applied to the surface of the completed ceramic restoration to give a glossy life like finish. They must have a lower fusion temperature & so contains lot of glass modifiers - makes them less chemically durable. They do not contain opacifiers.

Metal (PFM) to milled and pressed brand-named processes with one firing. Nova Ceramic Spray Glaze is formulated to increase efficiency and productivity by allowing technicians to stain, add-on contacts and glaze in a single bake and can be applied to single or multiple units in less than 10 seconds to one or multiple units without distorting characterization stains or anatomical details.

## Stains

Porcelain powder containing high concentration of color modifiers Lower fusion temperature- by increased glass modifiers Stains are used to provide individual color variation in the finished restoration

## Other reinforced core porcelains

- MgAL<sub>2</sub>O<sub>4</sub> (spinel)
- Leucite (leucite reinforced porcelain)
- These reinforced porcelain are stronger than regular feldspathic porcelains & used to create a stronger inner core which imparts strength to the ceramic

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**Chapter - 3**  
**Clinical Features of Oral Squamous Cell  
Carcinoma**

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# Chapter - 3

## Clinical Features of Oral Squamous Cell Carcinoma

Dr. Ritesh Vatsa

### Abstract

Cancerous lesions do not produce unique symptoms. The majority are asymptomatic in the early stages. Clinical symptoms may vary from lump, pain, ill-fitting denture, teeth mobility, paraesthesia, to neck swellings, restricted mouth opening and restricted tongue movement. Clinically squamous cell carcinoma present as exophytic, leukoplakic, erythroplakic. An exophytic lesion typically has a surface that is irregular, fungating, papillary, or verruciform. The endophytic growth pattern has a depressed, irregularly shaped, ulcerated, central area with a surrounding rolled border of normal, red or white mucosa. The leukoplakic and erythroplakic examples are probably early cases that have not yet produced a mass or ulceration

**Keywords:** neck swellings, exophytic, leukoplakic, erythroplakic

### Introduction

Neoplasia refers to new growth. A neoplasm, as defined by Willis, is an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissue and persists in the same excessive manner after the cessation of the stimuli which evoked the change <sup>[1]</sup>.

Tumors of the head and neck comprise an important group of neoplasms, the incidence of which is increasing in many parts of the world <sup>[2]</sup>.

Among head and neck neoplasms, oral cancer is the eleventh most common cancer world-wide; with an especially high incidence reported in the Indian subcontinent, Australia, France, Brazil, and south Africa <sup>[2]</sup>.

Approximately 94% of all oral malignancies are squamous cell carcinomas <sup>[2]</sup>. They account for about nine of every ten oral malignancies <sup>[3]</sup>. They constitute a major health problem in developing countries, representing a leading cause of death <sup>[4]</sup>.

Squamous cell carcinoma is defined as-a malignant epithelial neoplasm exhibiting squamous differentiation as characterized by the formation of

keratin and/or the presence of intercellular bridges (Pindborg JJ *et al.*, 1997) [1].

Squamous cell carcinoma of the oral cavity accounts for approximately 3% of all cancers in men and 2% in women [4]. It ranks 6<sup>th</sup> most common cancer in men after lung, prostate, colorectal, stomach and bladder and liver and 12<sup>th</sup> most common cancer in women [4].

Oral Squamous cell carcinoma (ICD CODE: 8070/3) displays a strong and synergistic association with tobacco smoking and alcohol abuse [5]. Other etiological factors discussed in the literature are alcohol, viruses, diet, immune deficiency, Candidal infection, syphilis and family history of HNSCC [6].

Basic pathology behind the occurrence of SCC is the genetic mutation in the squamous cells induced by suppression of tumour suppressor genes and promotion of oncogenes. Factors suggested to be responsible for this mutation are the carcinogenic agents (example nitrosamines in tobacco) [7].

The resultant effect of this mutation is, uncontrolled and uncoordinated growth of cells presenting clinically most often as a nonhealing ulceroproliferative growth [7].

Even in the present era, gold standard methodology for the diagnosis of SCC is histopathological examination. Histopathologically, this tumor shows proliferation of squamous cells displaying architectural and cytological atypia with or without invasion of the deeper structures. Based on the distinct clinical and histopathological features, SCC has been classified in the literature, into various variants like Verrucous carcinoma, basaloid squamous cell carcinoma and so on [7].

Depending on the clinical presentation and histopathological features, staging and grading of the lesion is done. This procedure of staging and grading aids in formulating the treatment plan and predicting prognosis on a long term, since SCC, similar to any other malignant neoplasm can undergo invasion and metastasis leading to secondary tumors [7].

As per the literature, SCC is usually preceded by potentially malignant disorders such as leukoplakia and erythroplakia. Hence, prompt early diagnosis and routine screening for these premalignant disorders can prevent the occurrence of more dreadful SCC [8].

Routine treatment for this fatal disease is surgical excision with or without radiotherapy and subsequent submission of the specimen for assessing surgical margins and final diagnosis which will aid in determining the prognosis [8].

“Prevention is better than cure”

## **Clinical features**

OSCC is most common in elderly men. Cancerous lesions do not produce unique symptoms. The majority are asymptomatic in the early stages. Symptoms of oral cancer, most of the times mimic the symptoms of lesions produced by common oral diseases. The common signs and symptoms of oral cancer are <sup>[9]</sup>:

- Lump or swelling
- Rough spot
- Crust
- Pain or tenderness
- Bleeding
- Change in bite
- Loose tooth or teeth
- Malfitting denture
- Neck lump or swelling
- Restriction of the tongue
- Change in jaw movement
- Dysgeusia
- Hyperesthesia, paraesthesia, or anesthesia
- Paresis or paralysis
- Diplopia
- Chronic cough
- Speech change
- Voice change
- Dysphagia
- Symptoms of distant primary

## **Clinical presentation**

Oral squamous cell carcinoma has a varied clinical presentation, including the following <sup>[10, 11]</sup>:

- Exophytic (Fig 1)
- Endophytic (Fig 2)
- Leukoplakic (Fig 3)

- Erythroplakic (Fig 4)
- Erythroleukoplakic

An exophytic lesion typically has a surface that is irregular, fungating, papillary, or verruciform, and its color may vary from normal to red to white, depending on the amount of keratin and vascularity. The surface is often ulcerated, and the tumor feels hard on palpation <sup>[11]</sup>.

The endophytic growth pattern has a depressed, irregularly shaped, ulcerated, central area with a surrounding rolled border of normal, red or white mucosa. The rolled border results from invasion of the tumor downward and laterally under adjacent epithelium. This appearance is not unique to oral carcinoma because granulomatous lesions, such as deep fungal infections, tuberculosis, tertiary syphilis, oral lesions of Wegener's granulomatosis or Crohn's disease, and chronic traumatic ulcers, may look similar <sup>[11]</sup>.

The leukoplakic and erythroplakic examples are probably early cases that have not yet produced a mass or ulceration. These mucosal surface changes typically are destroyed by the developing exophytic or endophytic mass, but many cases are diagnosed before their complete destruction and show residual precancerous lesions involving adjacent mucosa <sup>[11]</sup>.

### **Differential diagnosis**

- Traumatic ulcer
- Ulcer from odontogenic infection
- Major aphthous ulcer
- Low grade mucoepidermoid tumor
- Metastatic tumor
- Keratoacanthoma
- Necrotizing sialometaplasia
- Systemic mycosis
- Chancre
- Gumma
- Ulcers secondary to systemic diseases

Squamous cell carcinoma is the most common malignant ulcer of the oral mucosa. A lesion is most likely a squamous cell carcinoma, however, if <sup>[12]</sup>

- The patient is over 40 years of age, male and smokes or drinks heavily

- There is no evidence, that the lesion is related to trauma or systemic disease
- The serological findings are negative and presence of spirochetes cannot be demonstrated
- The lesion is not located in the posterolateral region of the hard palate

Rupture of cystic area in a low grade mucoepidermoid tumor may reveal a striking resemblance to squamous cell carcinoma; but if the lesion is situated in the posterolateral region of region of hard palate, it is most likely to be a minor salivary gland tumor <sup>[9]</sup>.

If the lesion in question is painless, the possibility that it is a traumatic ulcer, a chancre, an ulcer secondary to systemic disease, or major aphthae is eliminated <sup>[9]</sup>.

If an odontogenic infection cannot be found, the probability that it is an odontogenic ulcer is lessened <sup>[9, 12]</sup>.

Intraoral gummas occur more commonly in the midline of the palate or tongue and are rare in industrialized countries <sup>[9, 12]</sup>.

Ulcers secondary to systemic diseases are usually short term, but they may persist if the predisposing systemic disease is not corrected. They may be confused with any of the shallow persistent ulcers. Usually systemic problems become apparent through the history or clinical examination and prompt proper diagnosis. These ulcers are usually painful and have minimal bases <sup>[9, 12]</sup>.

A traumatic ulcer can be generally ruled out by establishing the absence of physical. Injury <sup>[1, 9, 11, 12]</sup>

Necrotizing sialometaplasia is basically a self-limiting disease that usually heals in 6-12 weeks. The lesion is usually a nodule of slight elevation, and the surface may be ulcerated. During its ulcerated stage, it very much resembles a squamous cell carcinoma and an ulcerated mucoepidermoid carcinoma. Biopsy is indicated to establish the diagnosis <sup>[1, 11, 9, 12]</sup>.

Keratoacanthoma is similar to ulcerative types of squamous cell carcinoma. It rarely occurs in the oral mucosa but often is seen on the lower lip, where it may look identical to a squamous cell carcinoma. Its rapid growth may help differentiate it from carcinoma, but excision is necessary. Histopathological differences between keratoacanthoma and squamous cell carcinoma are not significant and established, thus not reliable for differentiation <sup>[1, 9, 11]</sup>.

Major recurrent aphthous ulcer is a persistent ulcer that may closely resemble a squamous cell carcinoma on clinical examination. However, two striking features help the clinician to rule out malignancy.

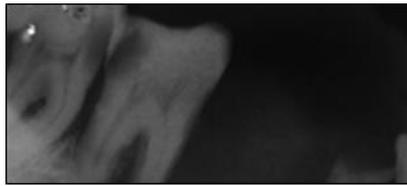
They are <sup>[9, 12]</sup>:

- Severe pain
- Broad inflammatory (non-velvety red) border

### **Radiographic features**

Destruction of underlying bone, when present, may be painful or completely painless and it appears on radiographs as a moth-eaten radiolucency with ill-defined or ragged margins <sup>[11]</sup>.

Intraoral and dental radiographs (Fig 5), in combination with orthopantomography, may help in identifying involvement of the underlying bone. Three-dimensional imaging with computed tomography (CT) and magnetic resonance imaging (MRI) is frequently used to supplement the clinical evaluation and staging of the primary tumour and regional lymph nodes <sup>[8]</sup>.



**Fig 5:** Intra-oral periapical radiographs showing ill-defined radiolucency, displacement and resorption of apical parts of roots of teeth in the areas of lesion

CT scan or MRI gives more information about the local extent of the disease and can also help to identify lymph node metastases. CT scanning is useful in evaluating involvement of cortical bone. MRI is more informative when evaluating the extent of soft tissue and neurovascular bundle involvement. The combination of soft tissue characterisation and anatomical localization afforded by CT and MRI make them valuable tools in the preoperative assessment of patients with oral or oropharyngeal cancers <sup>[8, 11]</sup>.

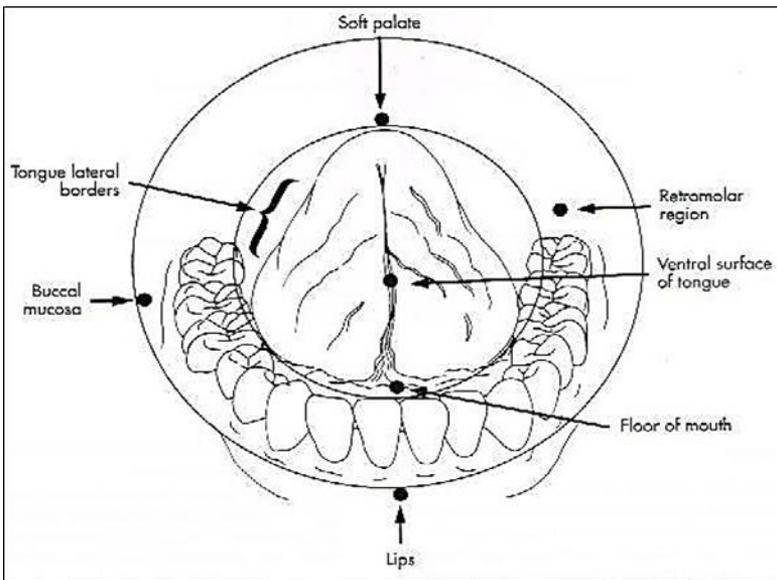
Distant metastasis from oral and oropharyngeal cancer is uncommon at presentation. At minimum, a routine radiograph of the chest is performed to rule out lung metastases <sup>[8]</sup>.

## Site specific clinical features

Squamous carcinoma can occur in any of the following oral sites (Fig 6):

- Lip (C 00)
- Buccal mucosa (C 14)
- Gingiva (C 03)
- Retromolar trigone (C 06)
- Floor of the mouth (C 04)
- Tongue (C 01 & C02)
- Palate (C 05)

Site specific clinical features are as follows:



**Fig 6:** High risk oval-site of poor prognosis

## Carcinoma of lip

### Incidence & Prevalence

The incidence of carcinoma of lip varies from series to series. It represents about 24-30% of oral cancers <sup>[13, 14, 15]</sup>, 12% of head and neck cancers & less than 1% of all human malignancies <sup>[15]</sup>.

### Age & Gender predilection

This anatomical location is more frequently involved in women than in

men (50-80 years). The relative overall paucity of lip cancer in women has been attributed to the use of lipstick, which acts as a sunscreen, and to less outdoor exposure both of which makes females less susceptible to the cumulative effects of actinic damage. The carcinoma of upper lip grows rapidly than those of the lower lip. The vermilion border that is, exposed strip of modified mucosa between the mucocutaneous junction and the point of contact of the lips is most commonly affected <sup>[16]</sup>.

## **Race**

Lip cancer is virtually unknown in blacks and other dark-complexioned races <sup>[16]</sup>. This apparent immunity is presumably due to the protection against actinic radiation afforded by the large amounts of melanin inherently present in these individuals <sup>[7]</sup>. Carcinoma of lip is quite rare in Asians <sup>[18]</sup>.

## **Clinical presentation**

The lower lip is affected in from 85 to 98% of cases and most patients are men in all lip cancers. Upper lip accounts for 1.8 to 7.7% of all lip cancers <sup>[19]</sup>.

The early lesion is described as a focus of thickening<sup>1</sup> and a generalized variegated area, with a red and white blotchy appearance; an area that imparts a dry atrophic appearance, with foci of whitish thickening; an area of persistent chapping, with localized flaking and crusting <sup>[20]</sup>; or a fissure that refuses to heal <sup>[21]</sup>.

As lesion progresses it may present as an exophytic, infiltrating or fungating mass <sup>[21]</sup>. However the most typical appearance is that of an ulcer <sup>[1, 20]</sup>. An important diagnostic feature is induration, which can be palpated at the periphery of the tumor <sup>[22]</sup>.

Carcinoma of lip is usually associated with actinic cheilitis. SCC, usually well differentiated is seen in 6-10% of patients with actinic cheilitis. Such malignant transformation seldom occurs before 60yrs of age, with resulting carcinoma typically enlarging slowly and metastasizing only at a late stage <sup>[11]</sup>.

Carcinoma of upper lip grow rapidly, those of lower lip generally tend to progress slowly <sup>[23]</sup>. Usually, perineural spread is limited to within 15 mm of the primary tumor, but extension along the inferior alveolar nerve, through foramen ovale and into the skull, accompanied by multiple cranial nerve palsies or meningeal spread has been documented <sup>[24]</sup>.

Usually perineural spread is limited within 15 mm of primary tumour. In such conditions, patient might present with numbness of chin, or in cases of spread to cranial nerves through inferior alveolar nerve, patient might present with paralysis of cranial nerves <sup>[19]</sup>.

## **Carcinoma of buccal mucosa**

### **Incidence & prevalence**

Krolls & Hoffman found 245 examples which represented 2% of the 14,253 cases of all oral-oropharyngeal cancers in the files of the Armed Forces Institute of Pathology <sup>[25]</sup>. Other authors have observed an incidence of 1-10% <sup>[26]</sup>. In India, where chewing betel nuts and tobacco is a common practice, it constitutes 44% of all squamous cell carcinomas of the oral cavity <sup>[27]</sup>.

### **Age**

Most cases occur in the sixth and seventh decades of life, with over 90% developing after the age of 40 years <sup>[19]</sup>.

### **Race**

Leffal and White mentioned in their study that squamous cell carcinoma of buccal mucosa is infrequent in blacks <sup>[28]</sup>.

### **Clinical presentation**

According to Waldron's description <sup>[28]</sup>, early carcinoma may present as an area of leukoplakia, an irregular erythematous patch erythroplakia or a papillomatous exophytic mass with a roughened surface that is white or pink. In its fully developed form, squamous cell carcinoma exhibits one of the three clinical patterns:

- Exophytic
- Ulcerative or infiltrative
- Verrucous

All the foregoing varieties of carcinoma usually develop along or inferior to the line opposing the plane of occlusion and most often affect the middle or posterior compartment of the buccal mucosa <sup>[29, 30]</sup>.

Martin & Pflueger <sup>[31]</sup> reported that extension beyond the mucosa of the cheek had taken place by the time of admission in 61% of their patients, region wise extension as follows (Table 1):

This propensity for extension beyond the buccal mucosa appears to be related to the size of the tumor <sup>[32]</sup>.

Invasion of the lateral pharyngeal wall, anterior tonsillar pillar, retromolar trigone or the palate is a frequent occurrence in patients in whom the tumor originates in the posterior portion of the buccal mucosa <sup>[29]</sup>.

**Table 1:** Extension percentage of carcinoma of buccal mucosa

<b>Region of extension</b>	<b>Percentage (%)</b>
Upper jaw	7
Lower jaw	18
Both upper & lower jaw	8
Mucosa overlying ascending ramus of mandible	11
Upper jaw & Mucosa overlying ascending ramus of mandible	4
Lips	13

Lymphnode metastasis is limited to the ipsilateral submandibular group and characteristically occurs only late in the course of the disease [33].

## **Carcinoma of gingiva**

### **Incidence & prevalence**

Carcinoma of gingiva constitutes approximately 1% of all cancers and from 4 to 16% of all oral cancers. If the lips are omitted, carcinoma of the gingiva is the third most common intraoral malignancy, exceeded only by cancer of the tongue and floor of the mouth [34]. The most common attributed etiological factor for gingival squamous cell carcinoma in India is the use of mishri (smokeless tobacco rubbed over the gingiva) [11]. Carcinoma of gingiva is also termed as Indian oral cancer because of increased occurrence in India [9].

### **Age**

It is primarily a disease of elderly, with the vast majority of cases occurring in individuals 50 years of age or older. This disease usually involves the mandibular region and affects women more frequently [19].

### **Race**

Krolls & Hoffman have found that gingival carcinoma represents the most frequent malignancy in blacks [34].

### **Clinical presentation**

Gingival carcinoma presents as an area of erythema, an ulcer, or an exophytic, proliferative mass. Rarely, the tumor may present as a pigmented mass [35, 36]. Fixed gingiva is more frequently affected than free gingiva and edentulous ridges more often than dentulous regions [36].

Soreness or gingival pain is the predominant manifestation. In advanced lesions additional signs and symptoms include toothache, induration and fixation of tissue. Typically this cancer extends along the periodontal

membrane, with destruction of the supporting bone, resulting in loosening of the teeth <sup>[37]</sup>.

### **Clinical differential diagnosis**

- Epulis fissuratum
- Advanced Periodontitis
- Endodontic-Periodontics lesion

On the alveolar ridge the carcinoma often grows in the form of a flat, elongated ulcer <sup>[38]</sup>. Lateral spread of a maxillary lesion eventually involves the mucobuccal fold and soft tissues of the cheek, whereas median extension results in invasion of the hard palate or tonsillar pillar. In the mandible, cancer of the buccal-labial aspects of the gingiva can spread into the vestibule, cheek, lower lip and chin, those arising from the lingual surface extend into the floor of the mouth and ventral surface of the tongue <sup>[39]</sup>. Because of its close relation to the gingiva and alveolar mucosa, the underlying bone is usually involved early in the course of the disease <sup>[19]</sup>. If this process reaches the mandibular canal, the inferior alveolar nerve may become involved and paresthesia may develop <sup>[39]</sup>. In the maxilla, penetration of the antrum is a frequent occurrence. A foul odor becomes apparent, and bleeding may ensue <sup>[39]</sup>.

Location of the lesion determines the probability of metastasis. Eric *et al.* mentioned that in about 30-32% of patients with mandibular carcinomas, lymphnode metastasis was present compared to 9-14% of patients with maxillary bone involvement <sup>[40]</sup>.

Soo *et al.* evaluated cervical metastasis in 109 cases, and accordingly concluded that incidence of nodal metastasis was <sup>[37]</sup>:

- T1-24%
- T2-36%
- T3-21%
- T4-63%

### **Carcinoma of alveolar ridge**

#### **Incidence & Prevalence**

SCC of the alveolar ridge constitutes from 7% to 18% of all intraoral cancers, including cancer of the lip <sup>[41]</sup>.

#### **Clinical presentation**

Tumors at this site may be ulcerating or exophytic. As they occur at sites naturally firmly connected to bone, tumors at this location are always fixed to

the bone. Radiographs are needed to assess the extent of bone involvement, which may be either by erosion, resorbing bone over a broad front, or penetration through Haversian canals and marrow spaces, the former growth pattern known as expansive and the latter as infiltrative. There are some indications that initially, when only the alveolar ridge is involved, SCC exhibits an expansive growth pattern, whereas the infiltrative pattern is associated with growth of the tumor into the basal bone, which is less easily resorbed. The variation in patterns of bone involvement have until now not be shown to have any relationship with metastatic rate or other established clinicopathologic parameters. However, recognizing the variation in bone involvement by tumor is necessary to correlate histologic findings with preoperative radiographs. In cases with an expansive growth pattern, the radiographs will give a reliable picture of the extent of bone involvement, whereas in cases with an infiltrative pattern of bone involvement, the real tumor size will be underestimated as the tumor penetrates bone with an initially undisturbed architecture <sup>[41]</sup>.

SCC of the lower alveolar ridge is second to SCC of the tongue in its frequency of lymph node metastasis; an average of 30% is mentioned; the nodes mostly involved are the submandibular and upper jugular nodes. Owing to this high frequency of metastasis, elective treatment of the neck should be considered for patients with primary tumors that overlie the symphysis, are moderately or poorly differentiated, or display radiographic or histologic evidence of mandibular invasion. The 5-year survival rate varies from 70% to 30% depending on the T stage <sup>[41]</sup>.

### **Carcinoma of Retromolar trigone**

Squamous cell carcinoma of the retromolar trigone occurs primarily in men in the 55-70-year age range. Most present with a sore throat, referred otalgia, or trismus. At the time of diagnosis, approximately 50-75% of tumours are smaller than 4 cm, and 27-60% are associated with clinically positive cervical lymph nodes, especially the submandibular and jugulodigastric nodes <sup>[19]</sup>.

### **Carcinoma of floor of the mouth**

#### **Incidence & Prevalence**

It accounts for about 0.48-0.8% of all human cancers, 9% of all head and neck cancers and 15- 20% of all malignant lesions of the oral cavity. It is predominantly a disease of the elderly, with almost all cases occurring in the sixth and seventh decades of life. In general men are affected three to four times as often as women <sup>[19]</sup>.

## Clinical presentation

The tumors can develop *de novo* or from a preexisting focus of leukoplakia or erythroplakia. Although any segment can be affected, the most common site is the anterior compartment near lingual frenum <sup>[42]</sup>.

Typical clinical manifestation is that of an ulcer without any symptoms. As the tumor progresses, the patient may experience a feeling of discomfort, pain, excessive salivation, swelling or haemorrhage <sup>[43]</sup>. Proximity to, or actual invasion of tongue frequently produce some limitation of movement, resulting in slurring of speech <sup>[43]</sup>. Deep infiltration is suggested by the loss of sensation in the distribution of the lingual and mental nerves <sup>[44]</sup>.

Neoplasms occurring in anterior floor of the mouth commonly advance across the midline or extend into the overlying papilla or into the distal end of Wharton's duct itself. This particular phenomenon can eventuate in varying degrees of xerostomia and other symptoms indicative of salivary gland dysfunction secondary to obstruction <sup>[45]</sup>.

In general, nodes most commonly involved are of the submandibular triangle and upper jugular chain. Dissemination to the mid jugular, lower jugular and posterior cervical nodes occurs less often, and involvement of submental nodes is only rarely encountered.<sup>46</sup>

Feind and cole showed that patients who had midline lesions exhibited high incidence of contralateral nodal involvement, with most of them affecting the submandibular and upper jugular nodes. Anterolateral cancers demonstrated prevalence to homolateral or contralateral submandibular and upper jugular dissemination. Contralateral spread generally remains localized to the submandibular and upper jugular lymphnodes. Posterior lesions metastasize to the homolateral submandibular, upper AMD mid jugular and posterior groups <sup>[47]</sup>.

From histological stand point, the incidence of cervical lymphnode metastasis increases significantly when the tumor has penetrated more than 1.5-2.0 mm. It has also been observed that T1 and T2 tumors usually grow in a horizontal manner with only superficial involvement of the submucosa. Conversely, T3 and T4 tumors generally have extensive submucosal and deep soft-tissue invasion with corresponding high frequency of regional metastasis. These observations are explained on anatomical basis. Superficial lymphatic channels are of small caliber and tumor embolization is difficult and hence rare. However, when the underlying submucosa is penetrated, the caliber of the collecting lymphatic trunks is large enough to facilitate tumor dissemination <sup>[52]</sup>. Distant metastasis are unusual, occurring in only 10% of patients <sup>[48]</sup>.

Squamous cell carcinomas of floor of the mouth are among the most aggressive and potentially fatal neoplasms of the oral cavity. The difficulty in controlling the carcinomas locally and regionally can be attributed to their proximity to the mandible and also to the intrinsic poor mechanical barrier to spread [41].

## **Carcinoma of tongue**

### **Anterior two thirds of tongue**

It is the second most common malignancy of oral cavity. It is two times more common in men and at the time of diagnosis most patients fall between 40-80 years of age [19].

### **Clinical presentation**

Typically patients present with a painless, indurated ulcer on the lateral border of the tongue, several months of duration. Because often the ulcer is often only the tip of the iceberg it is imperative that the lesion be manually palpated to appreciate its third dimension. Exophytic growths and lesions that are painful, result in dysphagia or referred otalgia are less common [49]. May be preceded by leukoplakia or erythroplakia, or may arise denovo [19].

### **Posterior one third of tongue**

Of all lingual squamous cell carcinomas 23-30% arises in this site [50].  
Age & gender:

The tumor is two to five times more common in men and mean age of diagnosis is about 60 years [51].

### **Clinical presentation**

Because base of tongue is a silent area, not easily amendable to self-inspection, the tumors in this site are quite large at the time of diagnosis. The most common preceding symptom is a sore throat. Others include referred otalgia, dysphagia, hot potato voice, bleeding, weight loss, neck mass, sensation of foreign body in the throat, and trismus [19].

The tumor on physical examination presents as an ulcerative infiltrative growth, the extent of which can best be appreciated by palpation. Deep infiltration to the base of the tongue is manifested by limited ability to protrude tongue, dysphagia, induration of the suprahyoid tissue [50, 52].

In about 25% of cases, the tumor will extend into the adjacent structures, such as the floor of the mouth, gingiva, mandible or base of the tongue [53]. The median raphe of the tongue conveys no special resistance to tumor

invasion and when breached the incidence of contralateral or bilateral cervical lymphnode metastasis increases. Likewise the circumvallate papillae that separate the two major divisions of the tongue offer no anatomical barrier <sup>[54]</sup>.

## **Carcinoma of palate**

### **Incidence**

A retrospective review of 82 patients treated at the Massachusetts General Hospital from 1962 through 1976 for squamous cell carcinoma of the maxillary and mandibular alveolar ridge and soft and hard palates comprised only 9% and 5% of cases <sup>[19]</sup>.

### **Age & Gender**

Squamous cell carcinoma of the alveolar ridge and hard and soft palate remains a disease of the elderly.<sup>1</sup> Various studies reveal female predominance and this is attributed to increased alcohol and tobacco consumption by women. The majority of patients with squamous cell carcinoma of the alveolar ridge and hard palate presented with Early Stage (I and II) <sup>[19]</sup>.

### **Clinical presentation**

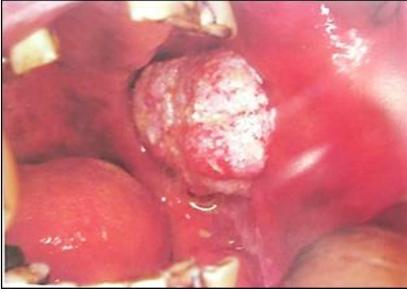
The first sign of the disease is usually a lump or ulcer that may or may not be painful, but occasionally bleeds. In reverse smokers, however, the cancer usually develops as an ulcer lateral to the midline in the glandular zone of hard palate <sup>[10]</sup>.

41% 5-year survival for squamous cell carcinoma of the soft palate and 54% for cancer of the hard palate is only slightly superior to that reported by other institutions since the 1940s <sup>[19]</sup>.

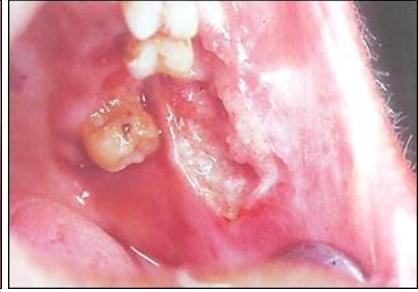
At the time of diagnosis, about half of the tumors are localized to the hard palate, 30% have been seemed to invade adjacent structures, 15-30% associated with positive cervical lymphnodes, 5% of which are bilateral <sup>[55]</sup>.

From the hard palate, the cancer may spread to invade the underlying bone, floor of the nasal cavity, maxillary sinus, gingiva, and soft palate. The lymphatics of the hard palate leave the maxillary area beyond the third molar tooth and empty into the submandibular and sub digastric lymphnodes. Systemic metastasis is rare.

## Colour plate-I



**Fig 1:** Exophytic squamous cell carcinoma



**Fig 2:** Endophytic squamous cell carcinoma



**Fig 3:** Leukoplakic clinical appearance



**Fig 4:** Erythroplakic clinical appearance

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## **Chapter - 4**

### **Concepts of Radiographic Justification**

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# Chapter - 4

## Concepts of Radiographic Justification

Dr. Rathi Rela and Dr. Daya Shankar

### Abstract

Justification of radiographic examinations is the practice of evaluating requested radiological examinations to assess for clinical merit and appropriateness based on clinical notes and patient information. This implies that justification in radiography requires the evaluation of requested examinations, the justification of exposures being applied and determining whether patients fit the recommended criteria for the procedure

**Keywords:** radiography, caries, dentition

### Introduction

Any X-ray exposure entails a risk to the patient. Under normal circumstances the risk from dental radiography is very low. Nonetheless, it is essential that any X-ray examination should show a net benefit to the patient, weighing the total potential diagnostic benefits it produces against the individual detriment that the exposure might cause. The efficacy, benefits and risk of available alternative techniques having the same objective but involving no or less exposure to X-rays should be taken into account.

In order that the justification process can be carried out, it is essential that selection of appropriate radiography is based on the individual patient's history and a clinical examination. The 'routine' use of radiography on patients based on a generalised approach rather than individual prescription is unacceptable. A 'routine' or 'screening' examination is defined as one in which a radiograph is taken regardless of the presence or absence of clinical signs and symptoms.

Choosing the appropriate radiographic examination should also be based upon consideration of the prevalence of diseases, their rates of progression and the diagnostic accuracy of the imaging techniques in question. Consulting guidelines facilitates the process of selecting radiographs. Such guidelines, called 'referral criteria' or 'selection criteria' exist for both medical and dental radiography. As with any guideline, these are not intended to be rigid

constraints on clinical practice, but a concept of good practice against which the needs of the individual patient can be considered. However, some dentists may refer patients for radiography to hospitals or dental colleagues where they do not have the necessary equipment in their own practices. When acting as a referrer, the dentist should ensure that adequate clinical information about the patient is provided to the person taking responsibility for the exposure.

### **Dental caries diagnosis**

Caries risk must be assessed for all new patients and then subsequently at recall appointment as risk factors may change in the intervening period. By identifying patients who are at the greatest risk of dental decay, clinicians can effectively implement prevention techniques to maintain low caries risk status. Caries is a multifactorial disease requiring a wide-ranging assessment of categories of risk. The important categories identified during the systematic.

Review were:

- Clinical evidence of previous disease
- Dietary habits
- Social history
- Use of fluoride
- Plaque control
- Saliva
- Medical history

When combined with the clinical judgement of the dentist, the use of these factors have been found to be an extremely efficient predictor of caries risk.

### **Children**

The early enamel lesion progresses at a relatively slow rate taking at least two years to progress into dentine, although progression is not inevitable. Early diagnosis of these enamel lesions is important, as with intervention lesion progression can be slowed or reversed.

Posterior bitewing radiographs are an essential adjunct to clinical examination. The initial clinical examination must include an assessment of caries risk (as high, medium or low). As outlined previously, the assessment of risk is relevant in determining when to take radiographs and therefore must be carried out at each subsequent recall examination ensuring that the time interval for radiography becomes patient-specific. It is feasible that adoption of the following recommendation may lead to more radiographs being taken.

However, this is justified as it will result in better patient care. In high caries risk children there is good evidence to support taking posterior bitewing radiographs at the initial examination, even in the absence of clinically detectable decay. The benefit is reported as being between 167% and 800% of the diagnostic yield from clinical diagnosis with or without fibre optic trans illumination assistance. Where a child is classified as high caries risk the subsequent bitewing examination should be after 6 months. Bitewing radiographs should not be taken more frequently than this and it is imperative to reassess caries risk in order to justify using this interval again. Evidence of no new or active lesions would be an indicator that the child had entered the moderate or low risk category.

In moderate caries risk children the evidence also supports the diagnostic use of bitewing radiographs. Many authors report significant addition to the diagnostic yield from the use of bitewing radiographs, varying from 150% to 270% of the yield from clinical examination alone. Where a child is classified as moderate caries risk the subsequent bitewing examination should be after 12 months. Evidence of no new or active lesions would be an indicator that the child had entered the low risk category.

In low caries risk children there is less good evidence to support the taking of posterior bitewing radiographs: diagnostic yield is lower than that with higher risk groups. Nevertheless, radiographs reveal 2-3 times more caries lesions than clinical examination alone. In low caries prevalence populations, it is suggested that selective radiography should be conducted of surfaces suspected clinically as being carious. Where caries population prevalence is not low, but a child is classified as low caries risk, the subsequent bitewing examination should be after 12-18 months in the deciduous dentition and 24 months in the permanent dentition. More extended recall intervals may be employed if there is explicit evidence of continuing low caries risk. Selective radiography of suspect surfaces may be appropriate as an alternative to bitewing radiography where caries prevalence is low. There is comparatively little evidence evaluating the diagnostic yield of radiographs for caries in adults. Therefore, in the absence of research data guidelines have been devised by extrapolation of studies in children and young adults.

### **Alternative methods to radiography for caries diagnosis**

Clinicians have recommended flossing teeth and the temporary separation of teeth, using orthodontic separators or wooden wedges, to assist in caries diagnosis during the clinical examination.

Alternative methods to ionising radiation with which to diagnose caries have also been developed. These include established techniques such as

fibreoptic transillumination (FOTI) and electrical conductance measurements (ECM). Other newer emerging technologies include Quantitative Light-induced Fluorescence (QLF), Infrared Laser Fluorescence (DIAGNOdent) and Digital Imaging Fiber Optic Transillumination (DIFOTI). Some of these techniques have limitations that affect their diagnostic or commercial availability and in some cases, their practicality within the dental, surgery. Others require further *in vivo* research and validation. However, several of these techniques have shown promise and may well become an accepted part of the routine diagnostic armamentarium of the practicing clinician in the future.

### **Radiographs in the management of the developing dentition**

Many children seek orthodontic treatment. When such treatment is clinically required, most children are appropriately treated at around 12-13 years of age and will require radiographs to confirm the presence and condition of all teeth.

Occasionally, there will be a need for a radiographic examination at an earlier age where there is a serious departure from normal dental development or when a child attends in pain or after trauma.

Children are subject to higher risks from X-ray exposure than are adults. Consequently the importance of justification for radiography is underlined. Usually the radiographic examination will consist of a panoramic radiograph (or right and left oblique lateral radiographs). Upper anterior occlusal radiographs are invariably required to supplement oblique lateral radiographs, but this is not the case for panoramic radiographs. Such films only provide additional information to the panoramic film in a minority of cases. Therefore they should be prescribed only after being justified by examining the panoramic radiograph.

### **Orthodontic radiographs**

Radiography is needed following clinical examination in a proportion of orthodontic patients. In addition, a patient in the mixed dentition stage may well require radiography to determine if interceptive treatment is appropriate. When previous radiographs are available, these may already contain all the information that the clinician needs for further management. A clinical examination is necessary to ensure that the radiographs requested will be appropriate for the patient's specific orthodontic problem. Similarly, the need for radiography to monitor treatment progress is dependent upon a careful clinical assessment. Furthermore research using algorithms and clinical indicators, has shown that a marked reduction in the numbers of orthodontic

films is possible without compromising patient treatment. From these studies, the effect of radiographs on changing orthodontic diagnosis and treatment plans is limited ranging from 16% to 37% and 4% to 20% respectively. Cephalometric radiography is often requested for selected patients undergoing orthodontic treatment. In addition, a cephalogram should be taken at:

- The end of functional appliance treatment to see the position to which the lowers anterior teeth have been proclined
- The end of presurgical treatment for orthognathic cases
- Just prior to the end of active fixed appliance treatment to assess the position of the lower incisors
- When assessing the position of the lower incisors, the lateral cephalogram is recommended only if the information is going to change the orthodontist's decision on their finishing mechanics or retention regime

### **Other views**

The poster anterior (PA) view of the face/head has been advocated in cases of patients who present with facial asymmetry. The value of hand or wrist radiography in clinical orthodontics has been questioned, as these views lack the reliability to predict growth spurts. Similarly, radiography for temporomandibular joint dysfunction cannot be justified and films taken for this reason have been shown to have no impact on treatment planning.

### **Radiography in periodontal assessment**

The diagnosis of periodontal diseases depends on a clinical examination. This may be supplemented by radiographs if they provide additional information, which could potentially change patient management and prognosis. However, there is no clear evidence to support any robust recommendations on selection of radiographs. The posterior bitewing projection offers both optimal geometry and the fine detail of intraoral radiography for patients with small amounts of uniform bone loss. Bitewings have the additional advantage in that they may have already been indicated for caries assessment, providing information about bone levels without the need for an additional radiation dose. More complex or extensive bone loss would require different imaging. Vertical bitewing, periapical and panoramic radiographs all have uses, either alone or in combination. Where periapical radiographs are used, the paralleling technique is indicated as this gives a better geometrical perspective on the periodontal bone than the bisecting angle technique.

## **Radiography in endodontics**

Radiographs are essential for many aspects of endodontic treatment. It is appropriate to consider their role at the different stages of treatment.

### **Pre-operative**

A periapical radiograph provides essential information about pulp and root canal anatomy that cannot be obtained in any other way. In addition it provides information about periradicular anatomy that may contribute to treatment planning or be essential if surgical endodontic treatment is being considered.

### **Working length estimation**

Some types of electronic apex locators are reliable at identifying the apical constriction and are useful for locating perforations. However, using these devices in certain clinical situations can result in a degree of inaccuracy. In view of this, periapical radiography is often still required during working length estimation. It may be necessary to take two (or more) radiographs in order to determine the length of all the root canals in multi-rooted teeth.

### **Pre-condensation**

If there is doubt about the integrity of the apical constriction, a check radiograph should be taken of the master gutta-percha cone before final condensation/obturation.

### **Post-operative**

A periapical radiograph should be taken immediately following obturation as this gives a basic assessment of the quality of the root filling and a reference image of the periapical condition for subsequent review.

### **New adult patients**

Many dentists follow a routine practice of examining new adult patients using panoramic or full-mouth intraoral radiography. As discussed above, such 'routine' practices are not acceptable.

Most evidence shows that conventional panoramic radiography has lower diagnostic accuracy for the common dental radiographic diagnostic tasks (caries diagnosis, periapical diagnosis) than intraoral (bitewing and periapical) radiography. Over and above these common tasks, routine panoramic radiography in search of asymptomatic bony lesions without clinical signs is not justified because of the low prevalence of such abnormalities. There is no justification for review panoramic radiography at arbitrary time intervals.

Full-mouth periapical radiography can be criticised in the same way as routine panoramic radiography. 'Routine' radiography will inevitably lead to unnecessary X-ray exposure. Selected periapical radiography of new adult patients will improve the relative risk/benefit for patients. Taking periapical radiographs of teeth with clinical symptoms, and of those with a history of endodontic therapy and deep caries as shown on bitewing radiographs, revealed 90% of periapical lesions in one research study. Others have also reported the effectiveness of selection criteria for identification of periapical pathosis.

### **The edentulous patient**

In the absence of any clinical signs or symptoms, there is no justification for any radiographic examination. The obvious exception is if implant treatment is planned, although if treatment is extensive other more advanced imaging (cross-sectional imaging) may well be appropriate. Where clinical examination identifies the possible presence of an abnormality, such as a possible retained root, then an intraoral radiograph of the site is the appropriate radiographic examination.

### **Radiography in implantology**

Imaging is essential in implantology. In treatment planning, radiographs provide information on the quantity and quality of bone in the proposed site of implant placement. Following treatment, imaging is used to assess implant osteointegration, bone healing and to periodically review the fixture. The review of the literature displays a paucity of evidence-based guidelines on radiography for implantology. Evidence has, in the main, been derived from expert opinion and review papers. An assessment of these papers revealed inconsistencies and little reliable information on the frequency of follow-up radiography. The imaging modality chosen is often a function of the treatment phase and a reflection of the number of proposed implants and their position in the oral cavity.

### **Pre-operative planning**

In evaluating a pre-operative site, the clinician requires information on:

- The quality and quantity of bone
- The buccolingual width and height of available bone
- The inclination of bony contours
- The presence of osseous undercuts
- Evidence of atypical anatomy such as enlarged marrow spaces

- Presence of pathology
- Exact location of certain anatomic structures (i.e. the maxillary antrum, inferior alveolar canal, the mental foramen etc)

With the exception of reformatted computed tomography (CT), all radiographic projections are magnified. The magnification factor must be derived and any assessments of available bone height must be calculated having taken this factor into consideration. Magnification factors can be derived by use of a reference object in the same plane as the alveolus. Periapical radiographs taken for single tooth replacement require the use of film holders and the paralleling technique for optimum geometry. Optimum geometry is often difficult to achieve in the edentulous jaw. The magnification factor in panoramic radiography is particularly variable and the consensus of one expert committee was to recommend that the panoramic film should be augmented by tomography, either conventional or computed, in order to provide the information necessary for optimum implant placement. When imaging using either conventional or computed tomography to generate cross-sectional images, proposed implants sites and/or tomographic Landmarks should be identified using surgical stents consisting of metal rods, balls or radiopaque markers. Conventional tomography is obtained either from dedicated software incorporated into panoramic equipment or from specifically designed X-ray machines for implantology. The latter comprises multimodal systems using narrow beam radiography and spiral tomography. In the past CT scanning has been restricted to general hospital facilities, however smaller dedicated head and neck CT imaging equipment is becoming more commonplace. Spiral CT techniques benefit from shorter scanning times and improved accuracy.

### **Choice of radiographic techniques**

The number of implants and their proposed position in the oral cavity are often the main factors dictating the choice of imaging technique. A proportion of patients need advanced imaging especially in cases involving bone grafts and in those in which there are multiple potential implant sites. In these cases CT has been recommended.

### **During surgery**

If any radiography is needed then periapical radiographs are readily available and use of digital imaging should be considered which offers the benefits of 'real-time' imaging.

## **Postoperative assessment**

Radiography has been recommended to evaluate the implant postoperatively. The frequency and timing of review radiographs appears to be purely subjective. During the healing phase, radiography would obviously be needed if the patient has clinical symptoms. If not, the next radiographic review should occur at 12 months and is considered essential to assess marginal bone levels. Subsequent review intervals range from annual reviews to once every three years. More frequent radiography is obviously needed if the patient is symptomatic.

A paralleling technique intraoral radiograph will provide a precise high-resolution image of bone height. The use of identical standardized intraoral radiographs enables the clinician to monitor longitudinally the fixture and adjacent bone levels. In screw-shaped implants, use can be made of the interthread distance to monitor mesial and distal bone loss. Digital radiography can be used to assess bone density, allow manipulation of the image and permit subtraction of two radiographs.

## **Radiography prior to oral surgery and tooth extraction**

In the case of third molars, if clinical guidelines for removal have been met, a panoramic radiograph (or alternatively oblique lateral views) is the most appropriate radiographic examination. The panoramic radiograph or oblique lateral views will provide information about the distance to the lower border of the mandible and the course and relationship of the mandibular canal.

In other surgical situations, such as apicectomy, root removal or enucleation of small cysts, an intraoral radiograph may be all that is required for treatment planning.

There is no convincing evidence to support the need for routine radiography prior to extraction of teeth. However, where a radiograph already exists, this should be referred to before commencing the procedure. The appropriate radiograph (with the exception of third molars) would normally be a periapical film.

## **Radiography of pregnant patients**

As the dose, and therefore the risk to the developing fetus is so low, there is no contraindication to radiography of women who are or may be pregnant providing that it is clinically justified. There is no need to use a lead protective apron. However, the use of a lead apron continues to be recommended (or advised) in some nation-states on the grounds it may reassure the patient.

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**Chapter - 5**  
**Equipment Factors in Reduction of Radiation**  
**Doses to Patients**

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# Chapter - 5

## Equipment Factors in Reduction of Radiation Doses to Patients

Dr. Rathi Rela and Dr. Daya Shankar

### Abstract

Despite the advent of non-fluoroscopic technology, fluoroscopy remains the cornerstone of imaging in most interventional electrophysiological procedures, from diagnostic studies over ablation intervention to device implantation. Moreover, many patients receive additional X ray imaging, such as cardiac computed tomography and others. More and more complex procedures have the risk to increase the radiation exposure, both for patients and the operators. There are many technological tools and new developments that may help to reduce patient and operator exposure. Different systems allow for non-fluoroscopic ('electro anatomical') localization of the catheters and the creation of 3D images. Magnetic resonance imaging is being used offline for 3D imaging, and being pioneered for online imaging during EP procedures as well. Indeed, by properly implementing these techniques, electrophysiologists can reduce the radiation dose dramatically. Radiation should always be reduced according to the ALARA principle, i.e. 'as low as reasonably achievable'.

**Keywords:** radiation, radiation protection, exposure, risk

### Introduction

Dental radiography is one of the most valuable tools used in modern dental health care. It makes possible the diagnosis of physical conditions that would otherwise be difficult to identify and its judicious use is of considerable benefit to the patient. However, the use of dental radiological procedures must be carefully managed, because X-radiation has the potential for damaging healthy cells and tissues. Although no known occurrence of cancer or genetic damage has been observed from radiation doses delivered in modern dentistry, and until more evidence is available, one should practice radiation hygiene with the same care as would be dictated if a hazard were known to exist.

The aim of radiation protection in dentistry is to obtain the desired clinical information with minimum radiation exposure to patients, dental personnel,

and the public. During an average radiological examination, the radiation dose received by an individual is generally low and relatively few cells are damaged. Though cellular repair is expected, it is not necessarily perfect. Thus, the effect of even low levels of exposure to ionizing radiation over periods of time may accumulate and could represent a potential hazard to health. Radiation effects are generally categorized as somatic and genetic. Somatic effects appear within a time frame of a few hours to years. Depending on the dose received and its duration, the consequence is greater for high doses incurred in short time periods.

Genetic effects are also a cause for concern at the lower doses used in dental radiology. The radiation doses may be small and appear to cause no observable damage, but the probability of chromosomal damage, with the consequence of mutations giving rise to genetic defects, can make such doses significant, when considered for a very large population.

### **X-ray generation and kilovoltage**

The kilovoltage of an X-ray machine is the potential difference that exists across the X-ray tube during use. Kilovoltage controls the mean and peak X-ray energies in the X-ray beam. Low kilovoltages, giving lower energy X-rays, leads to higher skin doses for patients. They also necessitate longer exposure times than would be needed for a higher kilovoltage X-ray set (milliamperage assumed to be equal). These factors have led to lower limits to be set for kilovoltage in legislation from various countries, usually in the 50 to 60 kV region. Higher kilovoltages reduce skin dose, but lead to higher 'depth' dose and more scatter of X-rays. In the case of dental (intraoral) X-ray sets, kilovoltage is usually either fixed or minimally variable. An important consideration with dental (intraoral) radiography is the X-ray spectral sensitivity of dental X-ray film and the image quality at different kilovoltages. Increasing the kilovoltage much beyond 70 kV would result in a spectrum ill-matched to the optimal sensitivity of dental film. 'Low' kilovoltages produce images of higher contrast than do higher kilovoltages. This reflects the different types of attenuation of low and high energy radiation. There is debate about the optimal kilovoltage for dental work, with some authorities recommending higher values, particularly in the USA. A kilovoltage of around 60-70 kV for intraoral radiography is considered to be a reasonable compromise choice in terms of limiting dose and all-round diagnostic efficacy. Unlike intraoral radiography, kilovoltage is used as the principle means of exposure control for panoramic radiography. Thus most panoramic X-ray machines offer a wide range of kilovoltages to the operator. Choice of kilovoltage is principally governed by the need to control X-ray intensity and

by the energy sensitivity of the film/screen combination. Constant potential ('direct current') X-ray generation is a modern alternative to traditional pulsating kilovoltage for both dental (intraoral) and panoramic /cephalometric equipment. Such a method of X-ray generation produces proportionately fewer low energy X-rays and hence gives reductions in skin dose for patients. The mean X-ray energy from a constant potential (DC) X-ray set is higher than that from an alternating potential (AC) X-ray set at the same operating kilovoltage. It has been demonstrated that for a constant potential set a kilovoltage setting of 5-8 kV lower is needed to maintain radiographic contrast. Thus 60 kV is recommended as the optimal operating potential for intraoral work. Constant potential equipment provides more predictable and accurate X-ray output and is therefore a better choice for use with digital receptor systems.

### **Filtration**

Filtration of the X-ray beam preferentially removes lower energy X-ray photons from the beam. Thus it is invaluable as a means of reducing skin doses to patients. Filtration using aluminium is an established component of dental X-ray equipment. Such filtration is fitted at manufacture and is therefore a factor that is not readily under the control of the dentist.

Additional filtration using materials (K-edge filters) other than aluminium, such as rare-earth materials, have been investigated as means of dose reduction in intraoral dental radiography by a number of researchers. The underlying reason for their use is that they 'shape' the X-ray spectrum and more closely match the spectral sensitivity of dental film. The evidence appears to be that all offer reductions in dose, but that this must be balanced against cost, effects on image quality and the likely increase in exposure times associated with their use. Dose reduction has also been demonstrated for panoramic radiography. Rare-earth filtration offers some dose reduction in intraoral radiography, but it should only be adopted after advice from a medical physics expert on setting new exposure factors.

### **Collimation, field-size trimming**

Reducing the size of the X-ray beam to the minimum size needed to image the object of interest is an obvious means of limiting dose to patients. Limiting beam area on the skin surface also limits the volume of the patient that is irradiated. As well as 'field size' on the patient's skin being important, the X-ray source to skin distance plays a role in limiting doses. Because of the divergence of the X-ray beam, increasing this distance reduces the divergence within the patient and therefore reduces the volume irradiated.

## **Intraoral radiography**

On dental X-ray sets for intraoral radiography field size is constrained by collimation of the beam. Visualisation of the field size is facilitated by the 'position indicating device' (PID).

Short pointed PIDs were once favored because the conical shape allowed a less obstructed view of film/teeth relationship and provided a visual indication of the central ray (9). However, in the last 20 years most dental intraoral sets have been manufactured with an open-ended PID of 60 mm diameter. A circular beam of this size is 135% larger in area than a conventional dental film (30 x 40 mm), indicating an obvious way of reducing patient dose. Various investigators have estimated that rectangular collimation can achieve

dose reductions exceeding 60% in dental radiography (9, 13, 18). Cederberg and associates (9) calculated and compared the effective dose and also estimated the risk from the use of short and long, round and rectangular openend PIDs and a short pointed closed-end PID. They reported that both long and short rectangular collimation resulted in the lowest effective doses, with values 3.5 to 5 times less than round collimation. They also demonstrated that

the use of pointed closed-end PIDs equates to a risk of 5.6 times that of a long rectangular PID. The adoption of rectangular collimation (30 x 40 mm beam) has been recommended in both UK (21, 36) and USA (2, 55). However, it is important to remember that use of rectangular collimation requires the use of film holding devices with a beam alignment guide to prevent cone cuts. Rectangular collimation can be achieved by replacing the round PID with a rectangular one, attaching a special rectangular collimating plate to the end of

the round PID or using a film holder that incorporates a metal shield to block radiation beyond the edges of the film (2). These possibilities mean that existing equipment can easily be adapted to allow rectangular collimation (36).

Where circular X-ray beams continue to be used, the beam diameter must not exceed 60 mm. Beam collimators/directors should be open ended and provide a minimum focus-to-skin distance (FSD) of 200 mm.

## **Panoramic radiography**

Panoramic radiography was designed originally as a means of examining the jaws and the teeth. However, the radiographed area is frequently far in excess of that of diagnostic interest. Dentists had no facility for reducing the

area irradiated. However, several machines now offer programmed field-size trimming as a means of reducing patient dose. Field limitation can significantly reduce patient exposure when specific diagnostic information is required. New equipment should be provided with automatic selection of beam limitation, although manual selection is acceptable (36). The beam height at the receiving slit or secondary collimator should be restricted to no greater than that required to expose the area of diagnostic interest and certainly no greater than the film (should normally be 120 or 150 mm). The beam width should normally be no greater than 5 mm (36). Some new panoramic machines have a 'child-imaging mode', which reduces the exposed area by 27 to 45% (22). Some also offer more sophisticated programmes to permit imaging of individual jaw segments and temporomandibular joints. In a study, Lecomber and Faulkner (27) reported that by using a field size programme on the Orthophos X-ray unit limited to the tooth bearing regions of the jaws, effective dose could be reduced by more than 50%. Such facilities offer a simple way of reducing dose and the purchase of machines with these facilities should be encouraged.

### **Cephalometric radiography**

Cephalometry (also known as teleradiography) traditionally produces images of the entire head and much of the cervical spine. However, the area of interest to orthodontists usually stops at the level of the base of the skull. A British Orthodontic Society working party supported the concept of reduction of lateral cephalogram dosage by the use of modified wedge collimation to remove part of the skull from diagnostic area (22, 32). This viewpoint is

supported in other publications (49, 55). Although such collimation should significantly reduce patient dose, manufacturers of cephalometric equipment have not yet included this form of collimation as standard. Further collimation of the lateral cephalogram to show the maxilla and mandible only is a viable alternative for measuring cephalometric values during treatment. Soft tissue profile using wedge filters is usual on lateral cephalometric radiographs. Some dose reduction can be included by placing the filter between the patient and the X-ray source rather than between the patient and the cassette (22, 55).

### **Choice of image receptor**

#### **Intraoral radiography**

Until 1980, the fastest intraoral film commercially available was film of group D. In 1981, E-speed films became available, capable of reducing the amount of radiation by approximately 50%. However, this fast film had a

lower inherent contrast, was very sensitive to aged and depleted solutions and lost its high speed at higher densities (48). This was probably the main reason that only a few dentists adopted this type of film (6, 8, 20, 38, 42, 45). Subsequent developments in film technology by various manufacturers have delivered improved E-speed emulsions (44, 56) and films that fall into the ISO speed group F. One brand of F-speed film that is widely available has been shown to offer dose reductions of 20-25% compared with the same manufacturer's E-speed film (14, 29, 43). In conclusion, for intraoral radiography the fastest available films consistent with satisfactory diagnostic results should be used. Intraoral films of ISO speed groups E or F are recommended because they reduce the radiation dose more than 50% compared with group D-speed films. The use of instant process film, which have slower speeds and limitations in image quality (10), should be limited to specific essential situations, as in endodontics or pre extraction cases during out-of-hours care.

### **Extraoral radiography**

For panoramic, cephalometric and other extraoral radiographs, the fastest available film-intensifying screen combination consistent with satisfactory diagnostic results should be used. The film screen combination should be at least 400 and the light sensitivity of the film should be correctly matched with the intensifying screens. The introduction of rare-earth intensifying screen/film combination has been shown to give dose reduction of around 50% for panoramic and cephalometric radiology (22). Manufacturers generally emphasize the use of matched combinations of orthochromatic film and rare-earth screens because such combinations more efficiently convert radiation energy to light in comparison with orthochromatic film combined with calcium tungstate screens (53). Since rare-earth phosphor screens were introduced in 1972, manufacturers have tried to develop such combinations in order to improve speed and to increase sharpness of the radiographic images.

A number of studies have been carried out to evaluate the sensitometric properties of these film-screen combinations (47, 51, 53). Wide latitude films perform better for panoramic radiography than higher contrast films.

### **Digital receptors**

Recently, several digital imaging systems have been introduced as alternatives to conventional radiographic techniques. The digital images are supposed to achieve images of high diagnostic quality, at least equal to that of for intraoral radiography, only the fastest available (Group E or faster) films should be used, as they significantly reduce patient dose.

For extraoral radiography the fastest available rare-earth intensifying screen/film combination consistent with satisfactory diagnostic results should be used. The speed of the system should be at least 400.

Two types of intraoral digital systems are currently available. The first type involves those systems that they are using imaging sensors based on charge coupled devices (CCD). The first system for direct digital intraoral radiography was introduced in 1989 and was based on a CCD sensor sensitive to visible light. CCD systems convert radiation into visible light by using a scintillation screen. The light is transferred to the CCD via fibre optic coupling or optical lenses. The pattern of light is detected and converted to an electronic signal that is passed to the computer for conversion into an image. The number of CCD systems available for intraoral radiography has increased rapidly. Today, most sensors use a scintillation layer to improve the quantum efficiency of the system. Improvements in pixel size, in the active area of the sensor, in spatial resolution, noise and image manipulation have been made by manufacturers in recent years. Recently some sensors have been developed with smaller pixel size and with the use of the so-called Active Pixel Sensor (APS) and Complementary Metal-Oxide Semiconductor (CMOS) technologies. Several studies have evaluated the physical and clinical performance of the majority of the intraoral digital systems (3, 4, 12, 17, 26, 35, 37).

The second type of digital intraoral system uses photostimulable storage phosphor (PSP) image plates. The plates consist of a polyester base coated with a crystalline halide composed of europium-activated barium fluorohalide compounds. When the image plate is irradiated, the absorbed X-ray energy is stored as a latent image within the phosphor crystals. In a scanner, a narrow laser beam causes the release of the stored energy as visible blue light that is turned into an analog electronic signal and thereafter digitized. Scanning is accomplished in about 25 seconds and the resulting image is displayed on the computer monitor. In contrast to CCD systems, storage phosphor systems are cordless.

Each of these two types of intraoral digital systems has advantages and disadvantages. Because image acquisition is more rapid with CCD systems than with PSP, the former may be more useful when 'instant' radiographs are desirable. In contrast, PSP systems are wireless and use a larger size image plate, approximately the size of a No.2 periapical film. One of the most important advantages of digital radiography is the reduction of radiation dose.

Various studies have shown that the amount of radiation needed to create an image for both types of intraoral system is lower than with film. One study

demonstrated that the optimal exposure time for all systems was approximately half that needed for conventional film and that digital images had to be modified by adjusting the contrast and brightness to optimize the visibility of the region of interest (37). Another study (39) reported that a CCD system provided reduction in average skin entrance dose of 31-34% when compared with E-speed film; with added niobium filtration the reduction was found to be 51-60%. PSP systems have a wide exposure latitude and Borg 48 and Grondahl found that reliable endodontic measurements could be obtained even at very low exposure settings. Although digital radiography offers a significant dose reduction, the number of retakes (essentially due to bad positioning of the bulky CCD with its' encumbering wire) may result in increased dose for the patient. Furthermore, due to smaller sensor sizes, more than one exposure may be required to cover the anatomical area imaged using a single conventional film. Problems with positioning sensors have been reported as leading to high reject rate. For panoramic and cephalometric radiography, the same two types of digital systems are also available. For CCD systems, conventional film is replaced by a long vertical CCD. The same sensor is used in cephalometric radiography, where the CCD is mounted on the cephalostat behind the patient's head. The patient's head is scanned in lines with a flat, fan shaped X-ray beam. During the scanning process, which takes about 15 seconds, the patient must stay motionless. The second type of digital panoramic and cephalometric system uses a PSP plate in place of the conventional film cassette. Panoramic and cephalometric digital radiography have the same clinical advantages as intraoral digital radiography, although dose reduction is not expected to be as effective as with intraoral systems. The exposure settings of CCD type panoramic units require exposures that are almost equal to those of machines using film/screen combinations. There will be no dose reduction. Some papers however, report that, depending on the diagnostic task, a lower exposure of the radiograph could be sufficient when density and contrast can be adjusted from the software features (11, 15, 16, 28, 50). This is one of the benefits of digital radiography where the density and contrast of an image can be optimized after the image has been taken. This is different to conventional radiography, where the contrast and density cannot be changed after the image is taken.

### **Leaded aprons**

Lead aprons do not protect against scattered radiation internally within the body and in the case of panoramic radiography, they may physically interfere with the procedure and degrade the final image (21). Despite the extremely low gonadal dose associated with dental radiography, the use of a lead apron has been recommended in the past in order to allay patient anxiety.

However, it has been shown that gonadal doses are not significantly different in dental radiography with and without a lead apron (22). UK Guidance Notes for dental practitioners on the safe use of X-ray equipment (36), clearly state that there is no justification for the routine use of lead aprons for patients in dental radiography. An official report of the American Academy of Oral and Maxillofacial Radiology (55), pointed out that the value of leaded aprons is minimal compared with the benefits of the use of E-speed films and rectangular collimation. It was concluded that their use could be considered optional except when required by law. See Section 3.8 for comments on radiography in pregnant patients.

### **Thyroid collar**

The thyroid gland is one of the more radiosensitive organs in the head and neck region. It is frequently exposed to scattered radiation and occasionally to primary beam during dental radiography. Because people under age 30 are at greater risk of radiation induced thyroid cancer than older individuals, some have argued that thyroid collars should be used when intraoral radiographic examinations are made on this population (55). However, it is probable that rectangular collimation for intraoral radiography offers similar level of thyroid protection to lead shielding, in addition to its other dose reducing effects (21, 22, 40). Thyroid shielding is inappropriate for panoramic radiography as it may interfere with the primary beam. In cephalometric radiography lead thyroid protection is necessary if the beam collimation does not exclude the thyroid gland. Thyroid shielding was found to reduce radiation doses of 45% during CT of the head and is strongly recommended, especially in younger age groups (5). Patient doses should be kept as low as reasonably achievable. In dental radiography, patient dose limitation involves consideration of the X-ray equipment, the beam size, the image receptor and, occasionally, the use of lead protection. Optimizations of each of these acts synergistically to substantially reduce doses. For intraoral radiography the effect of altering the various equipment factors is demonstrated in Table 4.1. It is possible to see that a shift from the baseline equipment to a constant potential set, rectangular collimation and F-speed film would lead to a dose reduction of about two thirds of the original level.

Similar modifications can be made for other types of dental radiography (panoramic, cephalometric). Some dose limitations can only be achieved by purchase of new equipment. However, some entail minimal (e.g. rectangular collimation) or no (e.g. FSpeed film) additional costs to the dentist. Such low cost options should be adopted as a priority.

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## **Chapter - 6**

### **Bruxism and Its Current Treatment Modalities**

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# Chapter - 6

## Bruxism and Its Current Treatment Modalities

Dr. Hema Kanathila, Dr. Ashwin Pangi and Dr. Bharathi Poojary

### Abstract

Bruxism is considered as the abnormal, forceful, non-functional contact of the occlusal surfaces of teeth. If this is left without proper treatment, it can lead to the breakdown of dentition and other orofacial problems. Bruxism can be due to many causes like local, systemic, mechanical or neurological factors, which have to be identified and managed by various treatment modalities. As bruxism events lead to tooth and restoration damage, it is of major concern for the dental practitioners. This chapter discusses in detail about the causes and management of bruxism.

**Keywords:** bruxism, clenching, teeth grinding

### Introduction

Masticatory system forms a complex and functional unit which includes teeth, supporting structures, the upper and lower jaws, the temporomandibular joints, muscles which help in mastication, nerves and blood vessels supplying these tissues. Masticatory system activities can be divided into

1. Functional
2. Parafunctional

Functional activities include chewing, speaking, and parafunctional activity includes clenching or grinding of the teeth. Bruxism is considered as the commonest of many parafunctional habits of dento facial system. It is the periodic repetitive clenching or rhythmic forceful grinding of the teeth, if ignored leads to the breakdown of dentition and oro facial pain. In other words, it is an oromotor disorder which is characterised by clenching and grinding of teeth when the individual is not chewing or swallowing. According to GPT 9, bruxism is defined as “the parafunctional grinding of the teeth; an oral habit consisting of involuntary rhythmic or spasmodic non-functional gnashing, grinding, or clenching of teeth, in other than chewing movements of the mandible, which may lead to occlusal trauma.

Bruxism activity leads to the wear and damage of teeth, fractures of restorations, temporal headache and other temporomandibular disorders. Bruxism has multiple etiology. The etiology can be systemic factors, local and mechanical factors, psychological factors, neurologic factors and genetics related. Hence these causes have to be identified and managed by various treatment modalities.

## **Prevalence**

In the general population, the prevalence range is from 8-31% and 14-20% in children. In children it is related to family history with either father or mother having the same history, distressing events in life, hyperactivity, parasomnias and depression. Elderly individuals above the age of 60 years are less likely to be affected showing a prevalence decreasing to around 3%. Bruxism affects males and females equally with females showing awake bruxism more than males. Males and Females show equal prevalence of sleep bruxism. Individuals with severe conditions of bruxism show more complications like damage of teeth and restorations, tension type headaches, facial or jaw pain and temporomandibular disorders. Early diagnosis and management of bruxism by various therapeutic approaches is important, in order to prevent complications.

## **History**

Early in the beginning of 20<sup>th</sup> century, a Viennese dentist explained bruxism as “traumatic neuralgia”, which was stated as the cause of periodontitis. The term “bruxamine” was put forward by Marie and Pletkiewicz <sup>[2]</sup> in the year 1907. In 1931, Frohman created the term bruxism, from the greek word “brychein odontas”, meaning to grind or gnash the teeth. In 1960’s, Sigur Peder Ramfjord stated that occlusal factors were responsible for bruxism and he defined bruxism as the habitual habit of grinding teeth when the individual is not chewing or swallowing. Researches were focused on occlusal adjustments and splints during the period between 1966-2007.

Miller stated a difference between grinding of the teeth at night which was referred as bruxism and the daytime habitual grinding of teeth as bruxomania <sup>[3]</sup>. In 1983 a difference was made between clenching and grinding. Clenching was mentioned as centric bruxism and grinding as eccentric bruxism. In 1995, bruxism was defined by Vanderas as the nonfunctional movement of the mandible with or without an audible sound occurring during the day or night <sup>[4]</sup>. And bruxism at night time was classified as sleep related movement disorder according to recent

classification of sleep disorders <sup>[5]</sup>. Lobbezoo and Naeije in 2001, suggested that various neurotransmitters in the central nervous system appeared to modulate bruxism <sup>[6]</sup>.

## **Classification**

Bruxism can be classified based on several criteria.

### **1. Based on the occurrence**

#### **Awake Bruxism or Diurnal bruxism**

Bruxism which happens during day hours is known as diurnal bruxism or awake bruxism. Awake bruxism usually shows a close relation to the stress caused due to familial responsibility or work pressure, anxiety, anger or frustration. Awake bruxism is more commonly seen in females compared to males. Diurnal bruxism prevalence rate is noted to be 20%.

#### **Sleep bruxism**

Bruxism during sleep at day time or night time is known as sleep bruxism. Sleep bruxism is regarded as an oro mandibular movement disorder which is sleep related. Individuals who brux during sleep are more likely to have other sleep disorders, snoring and pauses in breathing (sleep apnea). Sleep bruxism occurs with no gender difference. This is seen more frequently in the younger population, especially children showing a prevalence rate of 14-20%.

### **2. Based on the etiology**

- Primary bruxism or idiopathic bruxism

Cause is not known.

- Secondary bruxism

This occurs secondary to diseases like coma icterus, cerebral palsy. Can be due to medications (antipsychotic, cardioactive) and drugs (cocaine, amphetamines)

### **3. Based on period of occurrence**

- Past bruxism
- Present bruxism

### **4. Based on the type of motor activity**

- **Tonic:** Masticatory muscle contractions sustained for more than 2s
- **Phasic:** Repeated brief muscle contractions which lasts between 0.25-2s

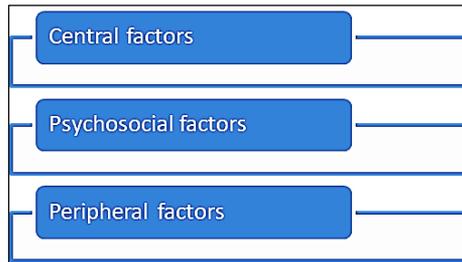
- **Combined:** In this alternating tonic and phasic events appear.

## 5. Based on the severity

- **Mild:** No damage to teeth or psychological impairment
- **Moderate:** Mild psychological impairment
- **Severe:** With damage to teeth, psychological impairment and temporomandibular disorders

## Causes of bruxism

Bruxism is multifactorial, which includes central factors, psychological factors and peripheral factors.



### Central factors

Researches have shown bruxism episodes associated with arousal response along with involuntary leg movements, suggesting a close association of arousal response with bruxism events.

It is hypothesized that the direct and indirect pathways of the basal ganglion, a group of five subcortical nuclei involved in the coordination of movements gets disturbed in patients with bruxism<sup>[5]</sup>. There may be an imbalance in both the pathways in bruxism.

### Psychosocial factors

**A major etiology of bruxism is stress:** Stress can be due to many external sources as well as internal sources.

- External sources of stress-social, work place load, major life changes or any unpredictable events
- Internal sources of stress-psychological, illness, any medical condition

Inability to express various emotions like anger, hate, aggression etc can also cause bruxism. Hence minimizing exposure to different stressful situations should be considered.

## Peripheral factors

Bruxism is related to deviations in dental occlusion and articulation. Establishment of harmony between maximum intercuspation and centric relation is required for an effective management of bruxism [6]. Recent literatures on this point state that there is hardly any relationship between bruxism and occlusal factors.

## Risk factors of bruxism

Various risk factors of bruxism are listed below-

- **Age:** Bruxism is more common in children and less in adulthood
- **Stress:** Increased stress and anxiety leads to bruxism
- **Hereditary:** Nocturnal bruxism tends to show a family history
- **Habits:** Smoking, tobacco chewing, drinking caffeinated beverages may increase the risk of bruxism
- **Personality:** Hyperactive and competitive type of personality can increase the risk of bruxism
- **Medications:** Antidepressants can result in bruxism as a less common side effect

Bruxism can be related to medical disorders such as epilepsy, sleep related disorders, parkinson's disease, gastroesophageal reflux disorder and dementia.

## Signs and Symptoms

1. Pain and sensitivity of teeth to heat and cold
2. Facial pain with tension headaches
3. Uneven tooth wear
4. Microfractures of the enamel of tooth
5. Chipped teeth
6. Mobile teeth
7. Pain in the jaw joint (temporomandibular joint or 'TMJ') that cause restricted mouth opening and difficulty in chewing
8. Ear pain

## Assessment of bruxism

If bruxism activity is left untreated, it can affect the quality of life by causing tooth and restoration fracture, disharmony of occlusion and TMJ

disorders. So assessment methods are to be followed for accurate interpretation of the condition and apt management. Assessment methods include questionnaires, clinical evaluation, intraoral appliances and electromyographic recording.

### By questionnaires

The questions asked are-[8]

1. Has anyone heard you grinding teeth at night or while sleeping?
2. Do you have teeth or gum soreness on awakening in the morning?
3. Do you feel jaw fatigueness or soreness in the morning?
4. Are you aware of your clenching or grinding of teeth during the day?
5. Have you experienced headache on awakening in the morning?

Eventhough Questionnaires present an easiest and simplest way of assessment, it has a main disadvantage that it is subjective in nature.

### By clinical evaluation [9,10]

A good case history forms the basis of a proper diagnosis and evaluating the tooth mobility, tooth wear and TMJ clinically also adds to the accuracy of diagnosis.

Indications of Bruxism activity		
Presence of tooth wear in normal and eccentric jaw movements. Tooth hypersensitivity to cold air or liquids consumed.	Complain of masticatory muscles fatigue, stiffness or discomfort in the morning	Clicking or locking of temporomandibular joint

Evaluation of tooth wear is controversial as tooth wear can be because functional and parafunctional activities.

### Using intra oral appliance

By assessing the wear facets and by assessing the bite load on the intra oral appliance, bruxism activity can be evaluated.

Bruxcore Bruxism Monitoring Device (BBMD) helps to assess the bruxism events. It is evaluated by counting the number of abraded microdots

on the surface of Bruxcore plate and by scoring the volumetric magnitude of abrasion. This device uses 0.51-mm-thick polyvinyl chloride plate consisting of four layers with two alternating colors and a halftone dot screen on the topmost surface. And count of microdots missing, helps to evaluate the abraded area and the number of layers uncovered depicts the depth parameter. These parameters are combined in order to obtain an index for the amount of bruxism activity.

Disadvantage-It is difficult to count the number of missing dots with good accuracy.

Intra-splint force detector (ISFD), uses an intra-oral appliance to record the force that is produced by tooth contact on the appliance. This recording device helps in detecting the force by using a deformation-sensitive piezoelectric film, which is thin and embedded 1-2 mm below the occlusal surface of the appliance<sup>[11]</sup>.

Disadvantage-It is not suitable for detecting the magnitude of force while steady-state clenching behaviour.

### **Using masticatory muscle electromyographic recording**

By using Masticatory muscle electromyographic recording we can assess bruxism by measuring the actual sleep bruxism activity.

Advantage-Occurrence of bruxism can be evaluated without intra-oral appliances which has the possibility of changing the natural bruxism activity

A miniature self-contained EMG detector-analyser (bite-strip) can be used for moderate to high level bruxers. It is attached to the skin over the masseter muscle and thereby recording the bruxism events. A detector and biofeedback device (grindcare, medotech, denmark) for sleep bruxism was developed recently which recorded the EMG activity of the anterior temporalis muscle. Thus it helps to detect clenching and grinding of teeth and signals biofeedback stimulation for reducing sleep bruxism activities<sup>[12]</sup>.

In case of nocturnal bruxism, Polysomnographic (sleep laboratory) recordings signals with simultaneous audio-video recordings. It provides a controlled recording environment, hence other sleep disorders like sleep apnoea and insomnia can be ruled out. As well, sleep bruxism can be differentiated from other orofacial activities like coughing and swallowing which can occur during sleep<sup>[13-15]</sup>.

Limitation-Any change in the environment of sleep can influence the actual nature of bruxism activity.

**Why is bruxism of major concern to dental professionals?**

It becomes a major concern for the dental professionals because of bruxism causes tooth and restorative damage leading to other problems affecting the social and psychological life of an individual.

Effect on prosthetic restorations	<ul style="list-style-type: none"> <li>• Loss of retention of prosthetic restorations, fracture or chipping of ceramic veneers in metal ceramic restorations.</li> </ul>
Effect on implant restorations	<ul style="list-style-type: none"> <li>• Complications of the superstructures in case of both fixed and removable implant-supported restoration</li> </ul>
Effect on Dentures	<ul style="list-style-type: none"> <li>• Soreness of the denture-bearing mucosa</li> <li>• Deleterious effects on the residual dentition and the denture-bearing tissues (Removable Partial denture wearers)</li> </ul>

**Applied treatments in bruxism**

Treatment aspect of bruxism aims at-

- Finding and removing the cause
- Changing the behaviour that causes bruxism
- Repairing the damage that bruxism often causes

Treatments of Bruxism			
Occlusal therapy	Pharmacological therapy	Behavioural therapy	Biofeedback

**A. Occlusal therapy**

The first-line of managing the teeth grinding and wear in case of nocturnal bruxism is Occlusal Splints/Night guard/Bite plate/Bite Guard. Hard splints are effective in reducing the bruxism activity. Soft splints are difficult to adjust than hard splints. Hence, hard splints are mainly chosen over soft splints <sup>[16]</sup>.

**B. Behavioural modification**

Along with relaxation techniques and self- monitoring, psychoanalysis, hypnosis, meditation have been considered for the management of bruxism. The management of sleep bruxism commences with counselling of the

patient. The patient is instructed in regard to the sleep hygiene. Bruxer is instructed to quit smoking and drinking alcohol, caffeinated drinks at night, to limit the physical or mental activity before sleeping, and to maintain quiet and dark bedroom conditions <sup>[17]</sup>.

### **C. Biofeedback**

Biofeedback mainly works on the principle that “bruxers can unlearn their behaviour when a stimulus makes them aware of their adverse jaw muscle activities”. An auditory feedback from patient’s muscle activity helps him know the degree of muscle activity <sup>[18]</sup>. Another way to reduce the sleep bruxism is by the use of taste stimulus to awaken the sleeping patient <sup>[19]</sup>.

Contingent electrical stimulation (CES) has taken attention in these recent years, due to its attempt in reducing the masticatory muscle activity which is associated to nocturnal bruxism. CES inhibits the masticatory muscles which are responsible for bruxism by applying a low-level electrical stimulation on the muscles when they become active <sup>[20]</sup>.

### **Pharmacological management**

Some drugs are said to have paralytic action on the muscles. They act by inhibiting acetylcholine release at the neuromuscular junction (NMJ). Thus it helps in decreasing bruxism activity in conditions like brain injury, coma etc. Studies have shown usage of botox injections over a period of 20 weeks to decrease in bruxism activity <sup>[21]</sup>.

### **Conclusion**

Bruxism is a distinct condition which presents as a key challenge for the dentists. As long-term effects of bruxism increases the risk of other problems and affects one’s quality of life, it needs early diagnosis and management.

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**Chapter - 7**  
**2D and 3D Planning in Orthognathic Surgery**

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# Chapter - 7

## 2D and 3D Planning in Orthognathic Surgery

Dr. Abhishek Kumar

### Abstract

Conventional treatment planning for orthognathic surgery uses two dimensional (2D) cephalometric analysis, dental casts mounted in the articulator with face bow transfer, and model surgery to predict the direction and extent of jaw movement. The presentation and analysis of a complex three dimensional (3D) maxillofacial structure in two dimensions have limitations, such as landmark identification and overlapping of anatomic structures, especially for patients with facial asymmetry. Cone-beam computed tomography (CBCT) allows reconstruction of a 3D craniofacial skeletal model for accurate presentation of the complex 3D shape and position, and has been applied widely in the field of orthognathic surgery. With the advancement of software, the 3D Computer Assisted Orthognathic Surgery accurately transfers the virtual surgical plan to actual surgery, achieves superior predictable aesthetic outcome & occlusion, reduces operative time, is more readily available and user friendly.

**Keywords:** orthognathic surgery, 2D, 3D, planning, CBCT

### Introduction

#### What is orthognathic surgery?

Orthos means straight and gnathos means jaw and hence Orthognathic Surgery means straightening of the jaw by surgery. An Oral & Maxillofacial Surgeon carries this out. It is a cosmetic surgery and the surgeon envisages changing the face of a person from distortion to proportion. Orthognathic Surgery is sometimes called “Surgical Orthodontics” because just as an orthodontist repositions the teeth with the help of braces within the oral cavity, the Oral & Maxillofacial Surgeon repositions one or more jaws through surgical procedures to produce a much more pleasing appearance and also improved ability to chew, speak and breathe. The main objective of Orthognathic Surgery is the correction of a wide range of minor and major facial and skeletal (jaw) irregularities. The shape of the face depends on the

architectural framework of the facial skeleton. Through Orthognathic Surgery the surgeon could reposition the bones of the face and the jaw to a more aesthetically acceptable position.

### **Who needs orthognathic surgery?**

Jaw growth is a slow and gradual process and in some instances the upper and lower jaw or one side of the jaw to the other may grow at different rates. This may cause many functional and psychological problems. Injuries to the jaws at a young age or during birth (delivery) or birth defects may also affect the normal growth and positioning of the jaws. While Orthodontic treatment (braces) can correct many problems if only the teeth are involved Orthognathic Surgery may be required if the jaws (bone) also need repositioning. The results of orthognathic surgery can have a dramatic and positive affect on many aspects of your life.

The common Maxillofacial deformities and their clinical appearances are the following-

#### **1. Protruded maxilla**

The upper jaw is protruded beyond the normal limits along with the teeth. The person cannot close his lips (lip incompetence) without effort. The teeth are always visible and in most cases the whole of the gums are visible on smiling (gummy smile). A gummy smile is mainly due to the vertical excess of the maxilla.

#### **2. Retruded maxilla**

This deformity is due to under development of the upper jaw mainly seen in people who have cleft lip or palate. After the surgical correction of the cleft lip or palate at a young age the growth of the maxilla is retarded along with displacement or destruction of the tooth bud. This results in a dish shaped face with a hooked or flaring nose and irregularly aligned, rotated or missing teeth.

#### **3. Protruded mandible**

In some people there will be extra growth of the lower jaw resulting in long jaw.

#### **4. Retruded mandible**

In some people due to developmental deformity or due to hereditary factors the lower jaw is very small resulting in a “bird face”. There is no proper development of the chin.

## **5. Facial asymmetry**

Sometimes a part of the face maybe overdeveloped or underdeveloped causing one part of the face to be small or large. One side of the face is not in symmetry with the other side giving an unaesthetic appearance.

## **6. Ankylosis of Temporomandibular Joint (TMJ)**

Injury during birth or trauma or infection at a young age to the temporomandibular joint will result in restricted mouth opening and reduced growth of the mandible.

## **7. Nasal deformity**

Nasal deformities are often seen along with deformities of the jaw. Some common deformities of the nose are: deviated nasal septum, flared or constricted ala of the nose, saddle nose, hooked nose and asymmetrical nose.

### **At what age can Orthognathic Surgery be done?**

The ideal age for Orthognathic Surgery is after the growth period has been completed, after 18 years for girls and 20 years for boys. Ankylosis of TMJ is an exception. For this the surgery should be done as early as possible to rehabilitate function and growth of the mandible. If the patient has got psychological problems due to the deformity of the face then other orthognathic surgeries may be taken up at an earlier age.

### **What are the steps in orthognathic surgery?**

After the initial checkup a detailed examination with facial measurements, photographs, x-rays and dental impressions are made. A complete medical examination is done to rule out any health problems that would interfere with the surgery or the administration of General Anesthesia.

Oral & Maxillofacial Surgeons and Orthodontists work closely together. The teeth are moved and repositioned into proper alignment before surgery if necessary. Common surgical procedures are Lefort I Osteotomy, Anterior Maxillary Osteotomy, Sagittal Split Osteotomy, Genioplasty and Rhinoplasty. The surgical procedures require meticulous planning and apt application necessitating the mandatory need for 2D and 3D planning in orthognathic surgery. With the advancement of software, the 3D Computer Assisted Orthognathic Surgery accurately transfers the virtual surgical plan to actual surgery, achieves superior predictable aesthetic outcome & occlusion, reduces operative time, is more readily available and user friendly. Conventional treatment planning for orthognathic surgery uses two

dimensional (2D) cephalometric analysis, dental casts mounted in the articulator with face bow transfer and model surgery to predict the direction and extent of jaw movement.

## **Pre-surgical planning and analysis**

### **1. Facial proportions**

The human face can be divided into three almost equal parts from the front.

- **Upper part or the forehead:** From hairline to glabella
- **Middle part or the midface:** From glabella to subnasale
- **Lower part or the lower face:** From subnasale to menton

### **2. Cephalometric analysis**

Lateral Cephalogram is traced to analyze the proportion of the various parts of the face. It helps to find out the areas of disproportion by marking out the various points, but should be correlated with clinical observations. Innumerable analyses have been proposed but great variations are seen in the "normal values" between different human races. More importance should be given for soft tissue measurements than skeletal analysis. The points, lines and angles marked are very arbitrary and different values can be obtained from different analysis of the same person. COGS analysis is the most commonly used and it describes the horizontal and vertical position of the facial bones by use of a constant coordinate system. Both the skeletal and soft tissue evaluation can be done by this analysis.

### **3. Prediction tracing**

This is a tracing on the facial profile to find out the outcome of surgery and gives a two-dimensional assessment of the profile. A cut and paste technique on the tracing paper is used for predicting the outcome. Computer prediction is now available due to the development of various software programs. This helps in visualizing the postoperative results better, but chances are, expectations become higher and the surgeon may have difficulty in producing the same results clinically.

### **4. Model surgery**

The plaster models are articulated on an anatomical articulator with face bow transfer. The area of the bone to be cut (site of osteotomy) is measured and marked on the plaster models and a mock surgery is done. This will help to

- Get an idea about the extent of bone reduction required in the surgery
- Understand the post-operative relations of the jaws
- Understand the post-operative occlusion
- Helps in the fabrication of splints
- Decide about the post-surgical orthodontic treatment

Wafer, thin occlusal splint should be fabricated to prevent the condyle from being unseated vertically, which can cause "condylar sag" post-surgically. The splint should allow the teeth to occlude properly in the preplanned occlusion.

## **5. Presurgical orthodontics**

A good teamwork is necessary between the Orthodontist and the Maxillofacial Surgeon. The goal of pre-surgical orthodontia is to position the teeth in the arches to facilitate a good and stable occlusion post-surgically. Extraction of teeth for pre-surgical orthodontia is to be reviewed with cephalometric analysis, prediction tracing and model surgery. Commonly pre-surgical orthodontia is done to close any interdental space, derotation and proper alignment of all teeth.

### **Need of 2D and 3D planning**

As the demand for improved facial esthetics increases, more patients complain of the development or the progression of facial asymmetry, particularly mandibular asymmetry, during or after orthodontic treatment. Patients who undergo orthognathic surgery for sagittal relationship problems, such as maxillary protrusion or mandibular prognathism, also tend to become aware of facial asymmetry after the surgical procedure. Because a misdiagnosis of facial asymmetry can result in the wrong treatment for a patient, accurate evaluations of facial asymmetry are crucial in orthodontic practice.

In most cases, the presence and degree of facial asymmetry can be diagnosed by using posteroanterior (PA) cephalometry. However, a PA cephalometric radiograph does not provide sufficient information for identifying the causes of asymmetry or determining a suitable treatment plan. Chin deviation is a common form of facial asymmetry. It usually develops from a right and left side difference in ramus length, but there are also other possible causes, such as a difference of body length in the mandible. Distinguishing a problem causing structure is extremely important

in treatment planning, but PA cephalometry does not always provide accurate information, even with the aid of lateral and submentovertex projections. Conventional radiographic images can be misleading in interpreting the cause of the deviation because complex 3-dimensional (3D) structures are projected onto flat 2-dimensional (2D) surfaces, creating possible distortion of the images and subsequent magnification errors.

The development of computed tomography (CT), however, has greatly reduced the possibility of these errors and improved our ability to understand the 3D nature of facial structures. In addition, recently introduced 3D CT software enables 3D reconstruction and accurate measurement of the maxillofacial complex. Exact measurement is the key element in evaluating asymmetry: 3D images can provide accurate and detailed information for the diagnosis and treatment planning of facial asymmetry by means of quantitative measurement and comparison between the right and left sides of the structures. These 3D images are easily rotated and viewed from any angle. This rotating function enables us to precisely analyze asymmetrical facial structures and to clearly visualize structures that cannot be well described with PA cephalometry.

### **Computer-assisted simulation system for orthognathic surgery (CASSOS Software)**

All of the data were analysed by one operator. Five key stages to the data analysis-

- i) Landmark identification
- ii) Creation of CASSOS (Computer-Assisted Simulation System for Orthognathic Surgery)
- iii) Superimposition of the computer prediction
- iv) Soft-tissue profile analysis
- v) Assessment of skeletal change

#### **I) Landmark identification**

Landmarks chosen in the study consisted of the pre-defined landmarks utilised by CASSOS using Adobe Photoshop (Adobe Photoshop v7.0, Adobe Systems Inc., USA), 45 hard-tissue and 26 soft-tissue landmarks were identified on the pre and postoperative radiographs.

#### **II) Creation of computer prediction**

A composite image composed of the superimposed landmarked pre- and postoperative lateral cephalometric radiographs was created using Adobe

Photoshop. The radiographs were superimposed on the best fit of the anterior cranial base anatomy. A horizontal reference line with 7 degree of angular divergence from the line sella-nasion was constructed with origin at sella. A vertical reference plane was then constructed perpendicular to the horizontal reference plane with its origin at sella.

The composite image was then imported into CASSOS. The CASSOS soft-tissue profile cephalometric simulation was produced using the hard-tissue movements shown on the postoperative radiograph as a guide. It was decided to use only the cephalometric simulation option and not the photocephalometric simulation in this study.

### **III) Superimposition of computer prediction**

Using Adobe Photoshop CASSOS cephalometric simulation was superimposed on to the actual postoperative radiograph using the reference lines and the previously identified reference hard-tissue landmarks that were distant from the surgical site.

### **IV) Soft-tissue analysis**

The following 12 soft-tissue landmarks: glabella (G), nasion (Ns), pronasale (Pn), columella (Cm), subnasale (Sn), superior labial sulcus (SLs), labrale superius (Ls), labrale inferius (Li), labiamental fold (Lf), soft-tissue pogonion (Pogs), soft-tissue gnathion (Gns) and soft-tissue menton (Mes) were identified on the computer prediction and the postoperative lateral cephalometric radiograph using Adobe Photoshop. The measurement tool within Adobe Photoshop, calibrated using the scale included in the mid-sagittal plane of the preoperative lateral cephalometric radiograph, was used to make linear measurements between the CASSOS prediction and the actual surgical result. All measurements were made using the horizontal and vertical reference planes as previously described. This technique eliminated orthodontic, surgical and growth errors, and resulted in an evaluation methodology of the computer program itself.

### **V) Assessment of skeletal change**

The skeletal changes between the preoperative and postoperative lateral cephalometric radiographs were assessed using the same method as for the soft-tissue analysis. The following maxillary landmarks were used: A point, posterior nasal spine and anterior nasal spine. B point was used for assessment of mandibular skeletal changes.

## **3D Planning**

### **Image acquisition for 3D virtual orthognathic surgery**

The introduction of cone beam computed tomography (CBCT) scanners with the potential to vertically scan the patient with a low radiation dose and a scanned volume large enough to capture the entire face (triad of hard & soft tissues and teeth) will revolutionize how orthognathic surgery will be planned in the future.

The ideal CBCT apparatus for 3D virtual treatment planning of orthognathic surgery, however, is not yet available. A number of problems will be encountered in the routine clinical situation. First, the scanned volume of CBCT scanners is currently too small to capture all types of maxillofacial deformities. Second, because of the limits in the scanned volume, accurate positioning of the patient in natural head position in the CBCT apparatus is sometimes difficult or not feasible. Third, the gray value of the same tissue changes between scans and with the position of that tissue in the field of view of the scanner. Fourth, a single scanning procedure of the patient's head does not allow for accurate occlusal and intercuspatation data. Finally, the fast evolution in acquisition software of CBCT scanners inherently necessitates frequent software updates for the purchased CBCT apparatus.

### **Processing of acquired image data for 3d virtual augmented model of patient's head**

The aim of 3D virtual imaging for orthognathic surgery is to create one virtual anatomic model of the patient, including the triad of the facial soft mask, underlying bony structures, and teeth. To enable 3D virtual treatment planning of orthognathic surgery, the acquired volumetric CBCT image data are segmented by semiautomated thresholding. The resulting surface representations of the patient's anatomy are then drawn on the computer screen, called "surface rendering". A tetrahedral soft-tissue mesh can subsequently be built to enable fast soft-tissue simulation using a biomechanical model. Although surface representations of the hard & soft tissues and teeth can be rendered and visualized in the 3D viewer of the software, some problems are still present.

Probably the most important obstacle was the inaccurate visualization of the interocclusal relationship; however, this issue has been resolved. Gateno *et al.* should be credited for developing the first method applicable to the clinical routine of orthognathic surgery to integrate accurate dental information into the patient's skull.

The next challenge is to further augment the patient's CBCT model of the head with detailed visualization of the dental roots. "Surface rendering" is based on thresholding and currently leads to improper visualization of certain anatomic structures (e.g., sella turcica, condyles, orbital walls) owing to the inherent inhomogeneity of the CBCT gray value data. However, a volume of voxels can be rendered with "volume rendering". For each voxel, a color and opacity can be assigned, and a projection image according to the viewing direction of the virtual camera can be computed and presented on the computer screen. "Volume rendering" of the acquired image data provides beautiful anatomic images and is useful for 3D virtual diagnosis of the patient's anatomy. Because "volume rendering" is still complex and it is expensive to manipulate the image data, it is not yet suitable for 3D virtual treatment planning of orthognathic surgery. Therefore, mixing "surface" and "volume" rendering probably will allow one to combine the benefits of both. It is expected that this "mixed" visualization approach will become possible in the near future.

### **3D Virtual diagnosis of patient**

The combination of a good clinical examination and 3D inspection of the virtual model of the patient's head has an unprecedented potential toward the diagnosis of the patient with a maxillofacial deformity.

Both "volume rendering" and "surface rendering" offer a thorough in-depth 3D virtual inspection of the patient's anatomy in the 3D virtual scene. Both viewing methods also incorporate the original axial CBCT slices and coronal and sagittal reconstructions, which allow 2-dimensional inspection of the patient's anatomy in the 3 standard planes (axial, sagittal, coronal) and multiplanar planes. A large amount of relevant clinical information with regard to the patient with a maxillofacial deformity can be gained from these slices (e.g., condylar anatomy, maxillofacial bony and dental pathologic features, maxillary sinus pathologic features, nasal septum deviation, hypertrophic inferior turbinates, a restricted airway, dentoalveolar bone support to the teeth, and the pathway of the inferior alveolar nerve).

### **3D Virtual treatment planning of orthognathic surgery**

One of the important advantages of 3D virtual planning compared with conventional treatment planning of orthognathic surgery is that the clinician inherently has more information on the patient's anatomy during planning. Moreover, 3D virtual treatment planning allows one to focus more on 3D facial harmonization, rather than on the facial profile. A standard approach towards 3D virtual treatment planning of orthognathic surgery includes four consecutive virtual planning steps (VPSs) in clinical practice:

**VPS1:** 3D cephalometric analysis for the ideal facial soft-tissue mask

**VPS2:** 3D soft-tissue analysis

**VPS3:** 3D virtual osteotomies

**VPS4:** 3D virtual surgery toward the ideal facial soft-tissue mask

VPS1 consists of 3D cephalometric analysis (11 angles, 7 linear distances, and 2 facial proportions) of the hard and soft tissues and teeth using conventional cephalometric analysis. Moreover, 4 additional vertical orthogonal measurements were included to verify the vertical position of the repositioned maxilla at 4 levels, both canines and both mesiobuccal cusps of the first molars, during surgery.

VPS2 consists of additional 3D soft tissue cephalometric analysis (2 angles, 10 linear distances and 4 facial proportions) using direct anthropometric analysis.

In VPS3, the most performed facial osteotomies (Le Fort I, bilateral sagittal split osteotomy, and genioplasty) are routinely done virtually, which creates the potential to virtually conduct different surgical treatment plans.

Finally, VPS4 consists of virtual surgery toward the ideal facial soft tissue mask, including virtual occlusal definition. The latter consists of a best fit between the dental arches guided by virtual elastics and subsequently visualized by a color scale.

Some major advantages using 3D virtual treatment planning in the clinical routine compared with conventional orthognathic surgery treatment planning are that first the occlusal plane cant in the frontal plane can be recorded more accurately and subsequently transferred to the patient using a 3D surgical splint in 3 dimensions just as done conventionally (e.g., wooden spatula, face bow transfer). The correction of the frontal occlusal plane cant has an important effect on the paranasal area, gonial angles, lower mandibular borders, and chin. Second, the upper dental midline is often clinically misjudged, because it is often determined in a clinical setting for the esthetic columella-philtrum unit, which can be deviated. The upper dental midline can be assessed more accurately here and corrected by rotation, translation, or combined rotation and translation of maxilla toward the skull base. This will have an important effect on the symmetry of the lower face and facial harmony. Third, the chin position anatomy can be assessed much more accurately in the frontal and basal planes. Fourth, because the proximal virtual fragments of the mandible remain stable and thus the condyles remain seated during virtual surgery, the amount of

mandibular movement (advancement or setback, clockwise or counterclockwise, and medial or lateral deviation) can accurately be measured on both sides. Finally, different virtual surgical treatment plans (e.g., bimaxillary rotation clockwise vs counterclockwise) can be evaluated.

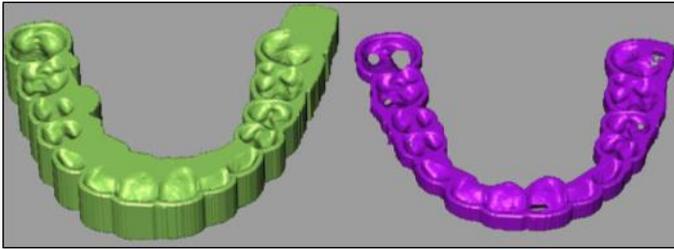
### **3D Surgical splint manufacturing**

Once the final 3D virtual treatment plan has been set up, the necessary 3D virtual surgical splints can be made. Subsequently, the 3D virtual surgical splints are processed using computer-aided design and computer-aided manufacturing techniques into surgical splints that can be used during the actual surgery.

Gateno *et al.* have shown that stereolithographic surgical splints fit the same as conventional surgical splints. Compared with conventional surgical splints, 3D virtually made surgical splints seem to have the following advantages:

- 1) The surgical splints are directly made using the 3D virtual augmented model of the patient without the intermediate plaster dental models
- 2) The intermediate 3D virtually made surgical splint can incorporate more accurately the surgical treatment plan, especially in complex cases with combined leveling, rotation, and translation movements of the jaw

To use 3D virtual made surgical splints in orthognathic surgery some important problems still exist. First, the base material for 3D surgical splint production must be medically approved. Second, 3D surgical splints are still too bulky and need to be trimmed manually by the surgeon, which is time consuming. It is expected that this will be solved by virtual trimming before processing and refinement of the computer-aided design and computer-aided manufacturing techniques. Finally, the manufacturing of 3D surgical splints is still a time-consuming process. The clinician must upload the virtual treatment planning data to be processed out of office, and the surgical wafer or wafers need to be shipped back to the clinician. Decreasing the time for out-of-office processing or in-office manufacturing could solve this problem. Finally, 3D surgical splints for segmental surgery are still very demanding in the presented 3D virtual approach, because virtual occlusal definition of the segmented jaws is still very difficult. Once again, improvements in software will solve this problem.



**3D virtual intermediate and final surgical splint  
(Maxilim, version 2.2.2, Medicim NV, Mechelen, Belgium)**

### **3D Virtual treatment planning transfer to operating room**

3D virtual surgical treatment plan can be easily transferred to the operating room in a viewer format. To transfer the individualized 3D virtual treatment to the patient, 3D surgical wafers and calipers are used.

### **3D Virtual treatment outcome evaluation**

Probably the most powerful aspect of 3D treatment planning of orthognathic surgery in the era of virtual imaging is the unprecedented potential for the evaluation of the treatment outcome. The techniques of voxel-based rigid registration and superimposition on a 3D cephalometric reference system have been extensively described. Evaluation of treatment outcome using CBCT imaging is in 3 stages. First, CBCT should be performed at 3 to 6 weeks postoperatively to evaluate the accuracy of the transfer of repositioning the bony parts. Because postoperative swelling of buccal mucosa can interfere with occlusion, it is not recommended to perform CBCT in the first 2 postoperative weeks. In contrast, bony consolidation appears at 6 weeks postoperatively and will no longer allow for proper virtual identification of the osteotomy lines. Second, CBCT should be performed at 6 months to 1 year postoperatively once the orthodontic brackets have been removed to evaluate the soft tissue response and the accuracy of the soft-tissue simulation. Finally, CBCT should be performed at 2 years postoperatively to evaluate the long-term treatment outcome. Meticulous 3D evaluation of the pretreatment status, the 3D virtual treatment goal, and the actual treatment outcome will bring new insights and substantial information on long-term stability, airway stability, condylar resorption, facial harmony, aesthetics and concepts in orthognathic surgery that will lead to better care of the patient with a maxillofacial deformity.

A large amount of basic laboratory and clinical research has been done by different research groups worldwide in the field of 3D virtual treatment planning of orthognathic surgery. The translation of this research into

clinical practice (translational research) has already shown an unprecedented potential toward the diagnosis, treatment planning, and evaluation of the treatment outcomes of maxillofacial deformity. However, to make the paradigm shift from conventional planning to 3D virtual planning, 3 basic requirements must be fulfilled:

- 1) The quality of care needs to improve
- 2) The workflow process should become more efficient
- 3) The cost should decrease

No doubt exists any longer that 3D virtual planning definitely improves the care of the patient with a maxillofacial deformity. Efficiency difficulties still exist, however, in both computer hardware and software in the daily clinical routine. Moreover, both the CBCT apparatus and the virtual 3D software packages are too expensive. Hence, the challenge and common goal is to develop 3D virtual treatment planning of orthognathic surgery as an efficient and cost-effective clinical tool that improves the care of the patient with a maxillofacial deformity.

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**Chapter - 8**  
**Efficacy of Conchal Auricular Cartilage Graft in  
the Treatment of Orbital Floor Blow out  
Fractures**

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# Chapter - 8

## Efficacy of Conchal Auricular Cartilage Graft in the Treatment of Orbital Floor Blow out Fractures

Dr. Ritesh Vatsa and Dr. Priyanka Priyadarshni

### Abstract

The aim of this study was to assess the efficacy of conchal auricular cartilage graft for the reconstruction of orbital floor in the treatment of orbital floor blowout fractures.

Eight patients with fractures of orbital floor were included the study. All the patients in the study were men and the age range was between 20 years to 53 years. The main cause of fractures was road traffic accidents. Out of eight patients enophthalmos (n=7), diplopia (n=4), infraorbital nerve involvement (n=5), restriction of eyeball movement (n=4). All patients were treated within one month of trauma. All the fractures were reconstructed with conchal auricular cartilage graft.

The follow up assessments were performed between three to six months post-operatively, calculated from the date of treatment. The symptoms were treated in 6 patients with enophthalmos, 4 patients with diplopia, 4 patients with limited ocular motility, 5 patients with impairment of the infraorbital nerve. Postoperative infections in 2 patients with systemic antibiotics.

Conchal auricular cartilage grafts are reliable, safe and effective implants and may be used for reconstruction of the orbital floor fractures with minimal donor site morbidity.

**Keywords:** conchal auricular cartilage, orbital floor fracture, orbital floor reconstruction

### Introduction

Fracture of the floor of the orbit which may be accompanied by displacement of the orbital contents into the maxillary sinus <sup>[1]</sup>. Based on the involvement of the orbital rim fracture along with floor fracture, Converse and Smith introduced the concept of *pure blow out* and *impure blow out* fractures <sup>[2]</sup>.

The treatment of orbital floor fractures is still controversial with regard to indications, surgical timing <sup>[3]</sup> access and reconstruction techniques. The eyes should be bright and reflect light; they are the windows to the soul <sup>[4]</sup>.

Over the years different authoritative opinions have alternated in the literature. Wide ranges of choices are available regarding the materials used for orbital floor reconstruction. They can be classified as autografts, allografts or alloplasts <sup>[5]</sup>. Alloplasts can be classified as non-resorbable and resorbable materials. Titanium mesh, Teflon, Medpore, silicone come under the non-resorbable category. Resorbable materials include poly-L-Lactide, polydioxanone, polycaprolactone, polyglactin-910 and polyglycolic acid<sup>6</sup>. Allograft materials include lyophilized dura and lyophilized cartilage <sup>[6]</sup>.

Autografts include periosteum, rib grafts, nasoseptal cartilage, auricular cartilage, iliac bone graft, mandibular bone graft, calvarial graft.

Though autogenous bone grafts provide framework for orbital walls, they carry the main disadvantage of donor site morbidity including nerve and blood vessel injuries, gait disturbance, cosmetic disturbance and donor site pain <sup>7</sup>. Non resorbable alloplasts become as permanent foreign bodies and can cause late complication such as infection, migration of implants, extrusion of implant and also residual diplopia <sup>[5]</sup>.

The reconstructive surgeon must always be aware that any nonresorbable material has the potential to cause infection even after an interval of many years. For this reason, autogenous grafts are still widely used, in full awareness of their limits: risk of resorption and morbidity at the donor site.

Of autografts, auricular cartilage <sup>[7, 8]</sup> is indicated for the reconstruction of gaps in the orbital floor, due to a shape that is very similar to that of the floor, the simplicity and speed with which it can be removed, its malleability, its good support function and the limited morbidity at the donor site.

## **Materials and Methods**

Eight patients with orbital floor blowout fractures were included in the study; in 5 cases, there was associated fracture of the inferior orbital rim. All had reconstruction of the orbital floor with auricular cartilage. Medically compromised patients, patients with optic neuropathy or post traumatic blindness, previous history of ophthalmic surgery, only eye with vision and whom the orbital floor fracture was associated with other facial fractures (nasoethmoidal, zygomatic or maxillary fractures) were excluded from the study.

The procedures to be performed were explained, followed by written informed consent. A detailed history was taken followed by clinical examination. PNS view and CT in all the three planes was taken and findings were recorded in a specially prepared case history proforma. Pre-operative surgical defect was measured in the CT and volume was measured using Volume share II, an installed application. ophthalmologic examination done to check visual acuity, diplopia, ocular motility using the Hess-Lancaster screen and measurement of enophthalmos with the Hertel exophthalmometer and detection of any damage to the infraorbital nerve with consequent paresthesia, through a subjective evaluation of the patient. The same clinical tests were repeated at 3 and 6 months from the operation.

The decision to proceed surgically to explore and reconstruct the orbital floor was based on the presence of at least one of the following conditions:

- 1) Diplopia
- 2) Enophthalmos
- 3) Herniation of orbital tissues through gaps in the orbital floor bone
- 4) Concomitant displacement of bone fragments of the inferior orbital rim. fig 2.

Post-operative, all the patients were followed for 6 months to evaluate enophthalmos, diplopia, any limitations of extraocular movements, patients with impairment of the infraorbital nerve. The surgical sites were examined for evidence of infection, or extrusion of the graft. Post-operative volume measurements were done for comparison.

Access to the Orbital floor was approached via a subciliary incision in 6 patients and transconjunctival incision in 2 patients. fig 1, 2 & 3.



**Fig 1:** Traction sutures placed



**Fig 2:** Transconjunctival incision placed



**Fig 3:** Exposure of orbital floor and rim



**Fig 4:** Fixation of rim 1

**Table 1**

Patient	Gender	Preop findings	Postop 3 Months	Postop 6 months	Complications
1.	M	E+D+O+N	E		Ectropion
2.	M	E			
3.	M	E+N			
4.	M	E+D+O+N	E	E	
5.	F	E+D+O			
6.	M	E+N			Ectropion
7.	M	N			
8.	M	E+D+O	D	D	

**Results:** Postoperative results shown in Table: 1.

### Abbreviations

M: Male, F: Female, E: Enophthalmos, D: Diplopia, O: Ocular Motility, N: Infraorbital Nerve Paresthesia

Auricular cartilage was used to reconstruct the orbital floor in all cases. The graft was taken beneath the perichondrium to ensure earlier fibrosis and thus greater stability over time <sup>[9]</sup>. fig 5 Inferior orbital rim was fixed using miniplate. fig 4.

The shape and size of the cartilage graft required can easily be determined using an intraoperative template <sup>[10]</sup>.



**Fig 5:** Graft harvesting



**Fig 6:** Placement of graft



**Fig 7:** Preop CT



**Fig 8:** Postop CT

## Discussion

Management of orbital fracture is a challenging problem for the oral and maxillofacial surgeon.

Their reconstruction requires

- 1) Release of entrapped orbital floor muscle
- 2) Reduction of the fractured floor
- 3) Reduction of the floor defect
- 4) Prevention of infection from the antrum
- 5) Return of physiologic function of the extraocular muscles
- 6) Elevation of the depressed zygoma
- 7) Correction of volume discrepancy between the orbits<sup>[11]</sup>

Various factors influence the choice of material for use in orbital floor reconstruction. The choice depends on the size of the defect, involvement of multiple walls, adaptation to internal contours, restoration of proper volume,

presence of adjacent sinus cavity, prevention of displacement, risk of further trauma, adhesions or restriction of ocular motility, and early versus late repair <sup>[12]</sup>.

There is general consent that the ideal floor inlay material should be inexpensive, readily available in sufficient quantities, adaptable to regional anatomy (i.e. easy to contour and sharpen), easy to position, suitable to all types of defects, able to provide support to orbital contents, biocompatible, nontoxic, non-carcinogenic, free of any potential for disease transmission, inert, or biodegradable to zero remnant <sup>[13]</sup>.

Alloplasts are available as either resorbable or non-resorbable materials. Non-resorbable materials are titanium mesh, porous polyethylene sheet, BAG plate, hydroxyapatite sheet. Resorbable materials used are PLLA and PLLA/PGA sheet, polyglycolic acid membrane, PDS sheet, polyglactin 910 mesh, periosteum polymer complex <sup>[13]</sup>. Unfortunately resorbable materials have not always performed well for orbital reconstruction. Two major problems have been encountered that limit their potential. First is the ability of these materials to maintain support to, in the orbital soft tissues sufficiently long until replaced by fibrous or bony tissue to prevent enophthalmus. Second is the progress of degradation that is not always benign <sup>[14]</sup>.

The other choice for orbital floor reconstruction is the use of allogeneic materials. WAITE AND CLANTONS (1988) have reported that these grafts give successful results as reconstruction materials <sup>[15]</sup>. The main concern with regard to the use of allogeneic materials is the antigenicity of the material and transmission of infectious diseases. Delayed hypersensitivity reactions have also been reported with the use of xenografts. Despite being careful on the sterilization techniques, risk of infectious disease transmission is the main disadvantage of using allogeneic materials <sup>[13]</sup>.

Because of the various shortcomings associated with alloplastic materials and allogeneic materials, autogenous grafts still widely used for orbital reconstruction. Disadvantages associated with autogenous bone grafts are donor site morbidity, variable rates of resorption with subsequent development of enophthalmus and or ocular dystopia, difficulty in contouring and shaping, intracranial complications such as cerebrospinal fluid leakage, subdural hematoma, and intracerebral hemorrhage. Additionally there are other donor site problems such as scarring, alopecia, and injury to the temporal branch of facial nerve. A further disadvantage of using bone is the separate surgical field and time taken to harvest the graft <sup>[14]</sup>.

The idea behind using auricular cartilage is that an ideal implant for orbital floor reconstruction for orbital defects because of its natural curve that fits into the orbital defects.

Auricular cartilage seems to provide an excellent source of autogenous tissue for the repair of orbital floor defects. The thickness of the cartilage and its concave shape are ideal qualities that enable a precise fitting to the concave floor, especially at the junction of the floor with the medial wall, the most common location of disruptions caused by trauma. The intrinsic strength characteristics of this cartilage make it highly suitable in the repair of large gap defects. Less resorption if the perichondrium is left intact, the perichondrium becomes vascularized soon after transplantation. With attention to surgical technique, the cartilage can be harvested without creating auricular deformities and objectional scarring. Other advantage auricular concha include a donor area that is located in the proximity of the recipient site that can be prepared and draped within the same surgical field [16].

Bayat *et al.* (2010) [17] and Dharindra *et al.* (2013) [18] stated auricular cartilage seems to provide an excellent source of autogenous tissue for the repair of orbital floor defects because of

- 1) Its thickness and concave shape
- 2) Ease and less time to harvest
- 3) Minimal donor site morbidity

Castellani *et al.* (2002) [19] stated that cartilage is only slightly vascularized and thus requires little blood perfusion, which means that it undergoes less resorption.

Considering all the observations in our study, conchal auricular cartilage graft can be used as a suitable implant for orbital floor reconstruction. The clinical outcome is comparable or even better, to other materials for orbital defects.

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# Contents

Chapters	Page No.
1. Articulator and Facebow <i>(Dr. Priyanka Priyadarshni)</i>	01-14
2. Centric Relation <i>(Dr. Priyanka Priyadarshni)</i>	15-41
3. Neural Crest Cells <i>(Dr. Priyanka Priyadarshni)</i>	43-54
4. Biomaterials for Orbital Floor Reconstruction <i>(Dr. Ritesh Vatsa)</i>	55-67
5. Warm Vertical Condensation Technique and Its Implications <i>(Dr. Seema Yadav)</i>	69-90
6. Implant Maintenance <i>(Dr. Karishma Mohanani, Dr. Hema K, Dr. Abhilash A, Dr. Giridhar Kamath, Dr. Srinidhi and Dr. Bharthi)</i>	91-106
7. Growth Factors <i>(Dr. Shubham Kumar)</i>	107-132
8. Endoscopic Surgery in Oral and Maxillofacial Surgery <i>(Dr. Abhishek Kumar)</i>	133-152



**Chapter - 1**  
**Articulator and Facebow**

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# Chapter - 1

## Articulator and Facebow

Dr. Priyanka Priyadarshni

### Abstract

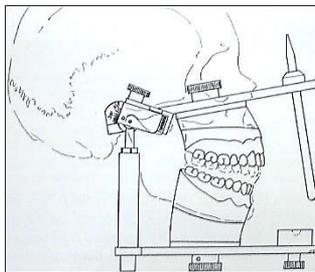
A dental facebow includes a U-shaped frame which carries on its cross-piece a rearwardly projecting bite fork for angular, lateral and longitudinal adjustments. A fixed stylus is resettable located on one frame arm and an axially adjustable second stylus is carried by the other frame arm. The facebow is used with an articulator having opposite inter condylar adjustments provided with intercondylar setting indicia, and the second stylus carries spacing indica of twice the scale of intercondylar setting indicia. In adapting facebow to a particular articulator the facebow and the articulator are adjusted to the same setting indicia and the facebow is brought into engagement with the articulator and the first stylus is reset to effect mating engagement between the articulator and the facebow.

**Keywords:** face bow, articulator, intercondylar setting

### Introduction

Full Mouth Rehabilitation a challenging procedure for Prosthodontist requires knowledge & skills. It requires meticulous use of instrument like Articulator and face bows. Articulators accept facebow record, Centric Jaw Relation Record, protrusion record, lateral record and inter condylar distance record.

### Articulators



**Fig 1**

## **An articulator is used to simulate the movements of the mandible**

Awni Rihani <sup>[11]</sup> has classified articulators as-

- 1) Fully adjustable articulator
- 2) Semi adjustable articulator
- 3) Non-adjustable articulator

Fully adjustable articulators can accept-

- 1) Face bow record
- 2) Centric jaw relation record
- 3) Protrusive record
- 4) Lateral record
- 5) Inter condylar distance record

**Examples:** Hanau Kinoscope, McCollum Gnathoscope, Stuart articulator Hanau 130-21, Denar D4-A.

Semi adjustable articulators can accept-

- 1) Face bow record
- 2) Centric jaw relation record
- 3) Protrusive record

**Examples:** Hanau H, Wadsworth, Dentatus, Hanau 130-28, Whipmix.

Non-adjustable articulators can accept one or two of the following three records-

- 1) Face bow record
- 2) Centric jaw relation record
- 3) Protrusive record

**Examples:** Snow, Gysi simplex, Monson, Stransberry, Transgraph, Pankey Mann.

The two basic types if semi adjustable articulators are <sup>[17, 18, 19, 20, 21]</sup>.

- 1) Arcon type
- 2) Non-arcon type

Semi-adjustable articulator cannot record the full range of protrusive and lateral condylar movement but mechanical equivalent of tooth movement can be recorded with much accuracy if instrument's shortcomings are compensated.

The instrument's shortcomings are compensated with-

- 1) Customized anterior guidance
- 2) Simplified fossae contour technique to relate lower fossae form to anterior guidance
- 3) Functionally generated path procedures to capture the precise border movements of posterior teeth at correct vertical dimension

The two basic methods for recording condylar paths are <sup>[11]</sup>-

- 1) Pantographic tracings
- 2) Stereographic tracings

### **Pantographic instruments**

McCollum and Stuart (1955) developed a mechanical type pantograph which required complex clinical handling procedures.

Hobo and Takayama (1983) developed the Cyberhoby pantograph which is an electronic pantograph and has an opto-electronic sensor fixed to the maxilla. Since the condylar path data is computed in electronic pantograph, transferring the measurement apparatus is not necessary.

All occlusal interferences are disengaged using the centre bearing point at an opened vertical.

### **Stereographic instruments**

All border movements can be accurately recorded in three dimensions by means of simple intraoral clutches that are stabilized by a central bearing point <sup>[11, 29, 30, 31]</sup>.

The recordings are made by indenting three to four points into doughy self-cure acrylic resin on opposite clutch surface and then moving the mandible through all border movements. Since three dimensional recordings are made in the mouth by paths of the condyles the procedure can be reversed and the path in the clutch can dictate the mechanical equivalent of condylar movement on the articulator.

This can be used in combination with customized anterior guidance procedure. The procedure is simple and practical. Intra-oral clutches are very stable since they have no extra-oral appendages.

The conditions which require fully adjustable articulator are-

- Disclusion of posterior teeth during protrusion when posterior teeth do not need restoration

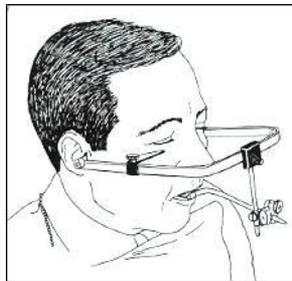
- Extensive restorative cases which require severe changes to establish an ideal occlusal plane
- Severe worn dentitions especially when upper functional cusps have worn flat

### **Non-articulator instruments**

All border movements of the teeth can be accurately recorded and duplicated even without using an articulator. An instrument which accomplishes this is called a Gnathic Relator. It records the 'effect' of condyle movement at the site of teeth. It is accurate and adaptable to all techniques and is used to best advantage in combination with some type of semi adjustable articulator. After the posterior teeth are prepared, stereographic recording is made at the correct vertical dimension with anterior teeth contact during the recording. Since both anterior and condylar guidance influence the border movements, no interpolation is required <sup>[11]</sup>.

### **Facebow**

A facebow is a caliper-like device that is used to record the relationship of the jaws to the TMJ and to orient the same relationship to the opening axis of the articulator.



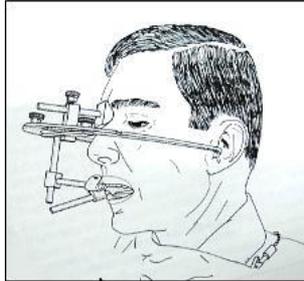
**Fig 2:** Hanau spring bow facebow

The two types of facebows are-

- 1) Kinematic facebow or Hinge-axis facebow
- 2) Arbitrary facebow
  - a) Earpiece facebow
  - b) Fascia facebow

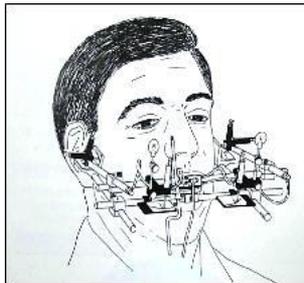
Arbitrary facebows are less accurate than kinematic type but they suffice for most dental procedures. Kinematic facebows are indicated when it is critical to record precisely and if the centric bite record is made at an

extreme open vertical. For full mouth rehabilitation kinematic facebow should be used.



**Fig 3:** Quick-mount facebow

### **Kinematic facebow**



**Fig 4:** An air activated pantograph

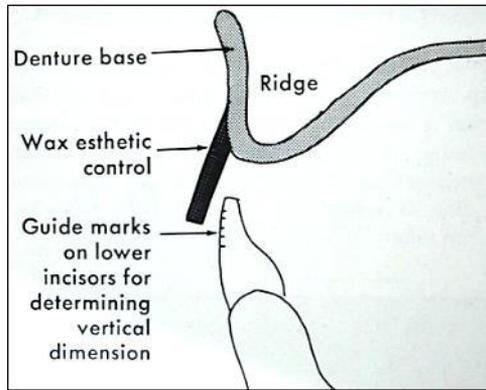
When fixed prosthodontic treatment is indicated for all teeth in one or both arches, the dentist must evaluate the existing vertical dimension of occlusion.

There has never been a scientific, practical and accurate method by which vertical dimension of the patient could be recorded. Classic techniques have been used to determine the vertical dimension of occlusion like phonetics, interocclusal distance, facial soft tissue contour, cephalometrics, electromyography and patient's neuromuscular perception [19].

### **Methods for determining vertical relation**

#### **Phonetic method**

Silverman determined vertical dimension by using speaking method [42, 43, 44, 45].



**Fig 6**

The patient was made to sit erect and close into maximum intercuspation. When the patient is edentulous, wax esthetic control rim is added to the labial region. Then a line was drawn on lower anterior teeth at horizontal level of incisal edge of opposing upper anterior teeth. Patient was then asked to pronounce 's' as in 'yes' and closest speaking line was drawn on lower anterior teeth. Distance between centric occlusion line and closest speaking line are called 'closest speaking space'. Normally this places the lower incisal edges 1mm lingual and posterior to upper incisal edges. The closest speaking space can range from 0 to 10mm in different patients and this indicates that there is no average speaking space <sup>[444]</sup>

### **Interocclusal distance**

Patient is encouraged to relax his jaws so that it goes into physiologic rest position. Swallowing and pronunciation of 'M' sounds have been used. Then the interocclusal distance should be measured.

Niswonger <sup>[46]</sup> had used vertical relation of rest to determine vertical relation of occlusion by subtracting 2 to 3mm from it.

Tallgren reported that interocclusal distance remains constant relative to occlusal dimension regardless of changes in occlusal vertical dimension.

Landa <sup>[47]</sup> said chances are 95% that the freeway space is between 3.07-3.67mm.

### **Facial appearance**

Diminished facial contours, thin lips with narrow vermilion borders and drooping of commissure are associated with over closure where as increased vertical dimension gives a stretched-out appearance.

## **Cephalometrics**

Atwood <sup>[48]</sup> used Cephalometrics to study the rest position of mandible and found a great variability between different readings in a single sitting, in different sittings, before extraction and after extraction, with or without dentures.

## **Neuromuscular perception**

Robert Lytle <sup>[49]</sup> used centre bearing device to permit the patient to experience different comfort levels during use of different vertical relations for comparison. The proprioceptive nerve endings in these ligaments which are a part of the neuromuscular mechanism permit the patient to recognize undesirable occlusal vertical relation if he is permitted to experience a more desirable relationship.

## **Can vertical dimension be altered?**

Out of the experience gained in occlusion of natural teeth has come awareness that there are certain underlying treatment principles. These principles are so important that they cannot be overemphasized. The origin and the crystallization of these observations can be appreciated best, perhaps by showing how the practice of oral rehabilitation has grown up while being applied.

Sicher <sup>[50]</sup> (1949) and Silverman <sup>[42]</sup> (1952). They concluded that as the teeth wear or become abraded, the teeth and alveolar bone elongate through growth to maintain the original vertical dimension with the maintenance of the same closest speaking space. However, occlusal wear may occur more rapidly than continuous eruption depending upon the etiology of the wear <sup>[4]</sup>.

Harry Kazis and Albert Kazis <sup>[51]</sup> stated that treatment of reduced vertical dimension is not designed to increase the vertical dimension beyond the normal, but is intended to restore the amount of vertical dimension that has been lost. A young person will tolerate a greater correction of vertical dimension and become adjusted more easily to a reduction in the interocclusal distance as necessitated by the changes.

Silverman (1956) <sup>[43, 44]</sup> said that closest speaking space can range from 0 to 10mm in different patients and that there is no average closest speaking space. But it is constant in an individual. Vertical dimension must not be increased beyond the normal for each patient. Increasing the vertical dimension only 1mm will cause discomfort to the patient. It is better to use a vertical dimension that is too small than to use one that is too great.

Landa (1955) <sup>[3]</sup> stated that increasing the vertical dimension places the muscles of mastication and temporomandibular joint under strain. The crown to root ratio is also affected and hence 'bite rising' is contraindicated.

Dawson (1974) <sup>[53]</sup> even when the teeth have grown down to the gum line the vertical dimension is not lost because of the eruption of the teeth along with the alveolar bone. Increase in vertical dimension interferes with the optimum length of the resting muscles which serve as a stimulus to produce hypertonicity. Closing the vertical dimension does not interfere with muscle lengths. When it is not practical to restore severely worn dentition without restoring the vertical dimension to obtain space for the restorative material, the dimension can be increased to 1-1.5 mm.

The potential problems of restoring the vertical dimension are clenching, muscle fatigue, soreness of teeth, muscles and joints, headache, intrusion of teeth, fracture of porcelain, occlusal instability due to shifting of restored teeth and continual wear. In such cases, checking and periodic occlusal adjustment must be done up to a year before normal stability returns <sup>[53]</sup>.

Carlsson *et al.* (1979) <sup>[52]</sup> increased the vertical dimension in natural dentition by cementing acrylic resin splints in lower canines, premolars and molars for 7 days. He found that subjects experienced moderate symptoms of discomfort initially but symptoms decreased later and no clinically demonstrable symptoms were found. He concluded that moderate increase in vertical dimension of occlusion does not create problem provided that occlusal stability is provided.

Rivera-Morales (1991) <sup>[54]</sup> Experiments in animals proved that moderate changes in occlusal vertical dimension do not cause hyperactivity of masticatory muscles and symptoms of temporomandibular dysfunction. Occlusal vertical dimension is a variable range like other quantifiable aspects of a body.

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## **Chapter - 2**

### **Centric Relation**

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# Chapter - 2

## Centric Relation

Dr. Priyanka Priyadarshni

### Abstract

Centric relation is the terminal hinge position of the mandible which establishes the relation of the axis of the condyles to the teeth as they will close with muscular force against the resistance of a bolus of food in every contacting position. It is the core topic of dentistry and Prosthodontics in particular. Centric relation is clinically significant since the only clinically repeatable jaw relation and logical position to fabricate the prostheses.

**Keywords:** centric relation, jaw relation

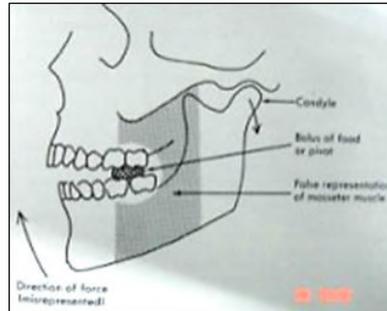
### Introduction

Centric relation defined as “the maxillo-mandibular relationship in which the condyles articulate with the thinnest avascular portion of their respective discs with the complex in the anterior-superior position against the slopes of articular eminences. This position is independent of tooth contact”.

Significance and Advantage of Centric Relation position <sup>[1, 2, 3, 4, 5, 6]</sup>

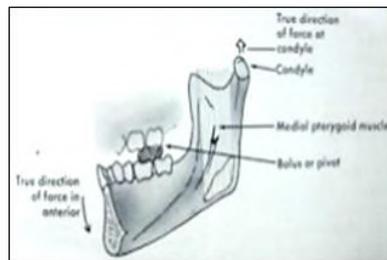
Centric relation is a fixed anatomic position. It can be relocated repeatedly by mechanical methods with acceptable accuracy.

- Ramjford and Ash <sup>[7]</sup> by EMG recordings state that muscle functions more harmoniously with less intensity when condyles are at centric relation at the time the teeth are in maximum intercuspation
- Major muscles that stabilize the TMJ act in anterior-superior direction to position the condyles in centric relation



**Fig 1:** Misinterpretation of muscle pull direction

- When the condyles are retruded the mandible is capable of repeatedly making a pure rotational movement through an incisal separation of 10-25mm, permitting location and transfer of the hinge axis to the articulator
- When patient chews or brings teeth together, condyles are seated in the anterior-superior direction



**Fig 2**

- All normal swallowing occurs in centric relation
- According to Lucia <sup>[8]</sup>, unless centric occlusion occurs when mandible is in centric relation, there will be strain on periodontal tissues of the teeth. Teeth that have lost their supporting structures can least afford to be the fulcrums of masticatory mechanism. Upper teeth get rocked distally and mesially while lower teeth can be rocked only mesially when mandible is out of centric relation
- Patient appears to function comfortably in centric relation after occlusal equilibration, full mouth rehabilitation and during occlusal splint therapy
- Patients with pain in temporomandibular joints frequently report surprisingly quick relief of pain and other symptoms after equilibrating to centric relation

- Histologically the anterior-superior area of disc is avascular whereas posterior area has nerve fibres which can lead to pain upon impingement by the condyle

There are two aspects of taking centric relation

- 1) Proper manipulation of mandible as in equilibration position when no bite record is taken
- 2) Manner of taking bite record for correct articulation of mounted models

There are many methods available to guide the mandible into centric relation-

### 1. Chainpoint guidance method

Guichet described this method. It places the condyles in most posterior and superior position which can result in trauma to TMJ. Hence use of this method is not advocated <sup>[5]</sup>.

### 2. Bilateral manipulation method

Dawson introduced this method that guides the condyles into most superior position in the glenoid fossa. Condyle is within 0.02 mm accuracy in three dimensions with this method. This small area supports the concept of point centric in which the centric relation position and maximum intercuspation are coincident.

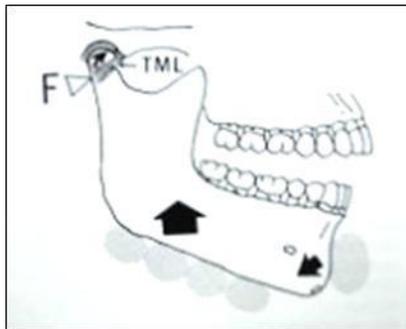
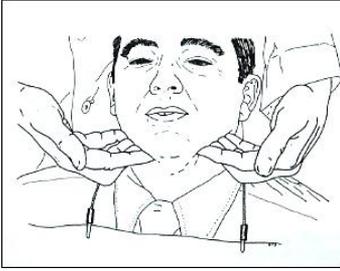


Fig 3

### 3. Unguided method

Brill <sup>[9]</sup> introduced a muscular position which allows patient's natural muscle functions to position the mandible into centric relation position.

## Manipulation for centric relation



**Fig 4**



**Fig 5**

Patient is made to lie back flat in supine position, chin pointed up. Dentist should be seated behind the patient. All four fingers of both hands are placed on the lower border of mandible on the bone and pressure is exerted in an upward direction. Thumbs are placed in the midline over symphysis exerting downward and outward pressure. Gentle arcing of the jaw of 2-3 mm is done without allowing teeth to contact. The terminal hinge area is thus located by free rotation of the condyles. Pressure towards the condyles will not cause any pain when the condyles are in centric relation.

### Method for taking centric bite records

Most patients have a reflex closure, an engram determined and guided by the teeth. Proprioceptive mechanism determines path of mandibular closure and is responsible for awareness of position of mandible in space.

To enable the condyles to be placed in an unstrained position, the musculature must first be deprogrammed from its habitual closing pattern.

### Mandibular deprogramming

Mandibular deprogramming can be done by-

Ask the patient to bite on these with anterior teeth for 5-10 minutes. The memory position of teeth intercuspation is lost.

- 1) Cotton role
- 2) Anterior Jig
- 3) Leaf gauge

### Techniques for taking centric bite records

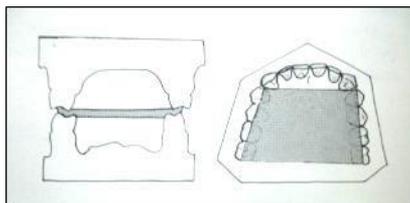
The four basic techniques for making a centric bite record are-

- 1) Wax bite procedures
- 2) Anterior stop technique

- 3) Use of pre-adapted bases
- 4) Central bearing point technique

Each technique has advantages and disadvantages and it would be unreliable to single out any one of these techniques as being practical for all cases.

### 1) Wax bite procedure



**Fig 6:** Wax wafer for recording centric relation

It is the most popular procedure because of its simplicity. Hard wax is used which becomes brittle when cooled and is soft when warm. Extra hard baseplate wax is an excellent bite material. When it is warm it becomes soft enough not to cause movement of teeth. It should be brittle and not bend to mould itself to fit the models as it will mask the errors if not rigid.

Modification of wax bite can be used with additional wash of zinc oxide eugenol paste to reline for greater accuracy.

Lucia <sup>[9, 10]</sup> explained a two-stage procedure in which tenax wax is used for indentation of upper teeth and soft wax is then added to indent the lower teeth.

This method is not suitable for patients having extremely mobile teeth or large edentulous area.

### 2) Anterior stop technique

Anterior stop techniques are the easiest to learn and offer greatest flexibility. Accuracy can be achieved even with loose teeth, posterior edentulous areas and patients with temporomandibular joint discomfort. This technique allows the condyles to seat up without any possible deviation from posterior teeth.

The term 'anterior stop' refers here to contact in the incisor area only. It may be made from acrylic or hard compound, on mounted models or intraorally. Bite record for posterior teeth can be made with a variety of materials. Plaster, zinc oxide eugenol paste, self-cure acrylic or wax and heavy bodied silicone can be used as the posterior bite record material.

### 3) Readapted bases

It is indicated whenever there is a danger that teeth will move or soft tissues be compressed by the bite record. Preformed bases can stabilize hypermobile teeth in correct position while the bite record is being made. It is made with triple layer of extra hard baseplate wax adapted on an accurate model, usually of the upper arch to avoid dislodgement by the tongue. Heated strip of dead soft wax should be added over it in edentulous region to indent the lower teeth in centric occlusion without tooth to tooth contact.

### 4) Central bearing point technique

It enables free movement of the mandible without influence of teeth proprioceptive. Drawback is that vertical dimension must be increased considerably to accommodate the clutches and bearing point apparatus. If the terminal axis is not recorded precisely it will result in mounting error.

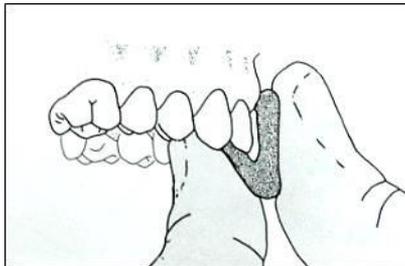
#### Anterior jig

##### Principle

Anterior jig prevents posterior teeth from occluding and thus disrupts the proprioceptive memory. As the anterior stop is rigid on contact with lower incisor teeth, anterior resistance is created and a mandibular leverage is created with naturally braced tripod effect along with two condyles.

Jig breaks the patient's habitual closure pattern and acts as the third leg of the tripod by creating resistance while stopping the closure.

##### Fabrication of anterior jig

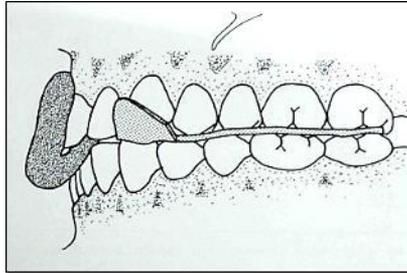


**Fig 7:** Fabrication of anterior jig

##### Procedure

A ball of red compound is softened and added to upper incisors so that their lingual surfaces are completely covered. The patient closes into the compound until the posterior teeth barely miss the contact while in supine position the lower central incisors contact the smooth lingual incline of the

jig at only one point. The jig incline must stop the mandible before posterior tooth contact and should be angled 45-60 degrees posteriorly and superiorly from the occlusal plane.



**Fig 8:** Centric relation record using anterior jig

The jig can also be made of autopolymerizing acrylic resin on mounted casts and then adjusted intraorally.

### **After the jig is made posterior bite record is taken**

Leaf gauge was first introduced by Dr. James. H. Long in 1973 <sup>[11]</sup>

### **It is the most useful and practical alternative to anterior jig**

Leaf gauge can be used for-

- 1) Centric relation interocclusal records
- 2) Occlusal equilibration
- 3) Relieve painful spasms of lateral pterygoid muscle.

Previously they were made of unexposed X-ray films after developing to remove the emulsion coating. Clear film was then cut into 1cm X 5cm sections.

Recently, leaf gauges of uniform 0.1mm thickness which are sequentially numbered are described. They are convenient and measure the exact vertical opening between the incisors.

Woelfel <sup>[12]</sup> described a disposable leaf gauge made of firm paper.

Williamson <sup>[13]</sup> used leaf gauge to deprogram the proprioceptive impulses from the periodontal membrane.

Golsen and Shaw <sup>[14]</sup> recommended leaf gauge in occlusal adjustment and for centric relation records.

McHarris advocated leaf gauge for centric interocclusal records and relieving painful spasm of lateral pterygoid muscles.

Rosenbulm <sup>[15]</sup> in 1985 found that when leaf gauge was placed between the anterior teeth and subjected to patient's own biting force, it permitted the condyles to seat them to the muscle dictated centric relation position.

Alber's *et al.* <sup>[16]</sup> stated in 1997 that the use of cotton roles for initial joint compression and retrusion followed by recording with leaf gauge appears to be the best method for obtaining accuracy.

Huffman <sup>[17]</sup> (1987) advocated use of leaf Gauge for occlusal equilibration.

Woelfel <sup>[18]</sup> (1991) used leaf gauge wafer technique to record jaw relation.

Solomen and Shetty (1996) found obtaining centric relation with the use of leaf gauge to be accurate compared to unguided technique and operator guided closure.

## **Procedure**

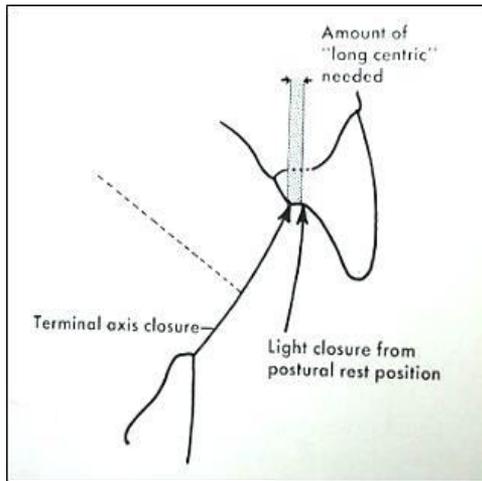
Arbitrary numbers of leaves are placed at the maxillary anterior midline parallel to the lingual plane of central incisors. Patient is instructed to close on back teeth until lower incisors touch on back side of leaf gauge. Leaves are added or subtracted until patient can barely feel a posterior tooth touch while closing firmly on leaf gauge. Often the patient can often feel a posterior tooth contact in 15-52 seconds after the jaw is closed with a 'half hard' closing force. This procedure is repeated after adding a leaf gauge until the patient can close for 2-5 minutes without feeling a posterior tooth contact.

## **Long centric**

The fit of the condyle into the disc is not like the fit of machine ball in bearing. Some front-back play is permitted by the disc that allows the condyles to hinge freely. So there will be a slight difference between the firm terminal hinge closure of centric relation and a light closure from rest position.

The term 'Long Centric' could be defined as 'freedom to close the mandible either into centric relation or slightly anterior to it without varying the vertical dimension of occlusion.

This term is now referred to as "Freedom in Centric".



**Fig 9:** Long centric

Posseltin 1952 studied the difference between retruded contact position and intercuspal position and found  $1.25 \pm 1$  mm difference between them.

Schuyler <sup>[19]</sup> in 1959 found the initial contact from rest position to be 1 mm anterior to the border path produced along the transverse horizontal axis.

Ramfjord and Ash <sup>[20]</sup> advocated 0.5 to 0.8 mm space between retruded contact position and maximum intercuspation.

Dawson in 1974 advocated freedom in centric relation of occlusion of 0.2 mm which allows space between condyle and fossa.

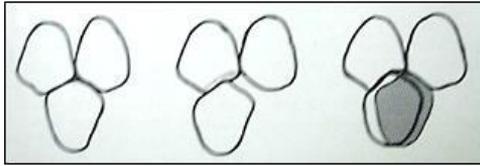
Freedom of movement in centric occlusion provides patient comfort and reduces the tendency to bruxism and other traumatogenic influence on the supporting structures.

All interference to terminal closure should be eliminated. If centric relation interference is present, path of closure will be dictated by the proprioceptors instead of the muscles. When interference in centric relation is eliminated by equilibration 'long centric' will usually be provided automatically.

The most important aspect is that the vertical dimension of occlusion must be the same from back to front of each long centric contact area.

There is no relationship between the length of a 'slide' and length of a 'long centric'. Length of a slide is the result of interference of the teeth whereas long centric is dependant on anatomy of the condyle disc relationship and varying patterns of muscle activity in different individuals.

## Procedure

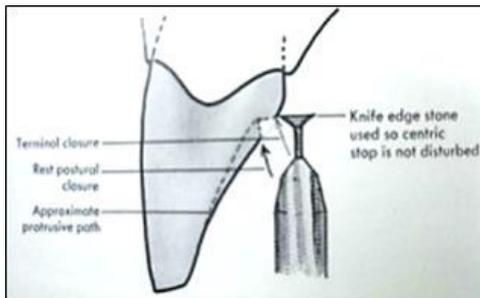


**Fig 10**

- Centric occlusion centric relation freedom in centric
- Before adjustment before adjustment after adjustment

To determine the patient's long centric two different colors of marking ribbon are used. Red ribbon is used first to mark slight closure from postural rest position without head rest. Then green or blue ribbon is used for marking centric relation points. When both points are identical, 'long centric' is not essential.

When red mark is forward of green, each centric stop should be extended forward at the same vertical. Green marks should not be ground. A knife edge inverted cone carborundum stone is used for accurate grinding.



**Fig 11**

Not all patients require long centric. Their centric closure and closure from rest are identical. If such patients are given a long centric, they will not use it but it will not hurt them either. There are no contraindications for providing the freedom.

## Occlusal equilibration in natural dentition

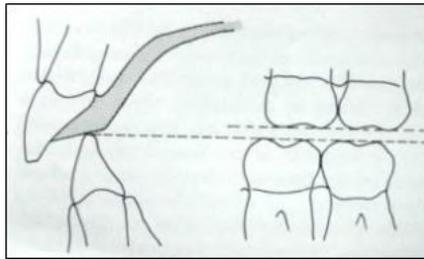
The term 'Occlusal equilibration' refers to the correction of stressful occlusal contacts through selective grinding.

Occlusal equilibration is a phase of treatment that eliminates only that part of tooth structure that is in the way of harmonious jaw function.

## Objectives

- Centric relation occlusion
- Coupling of anterior teeth
- Acceptable disclusion of anterior teeth in harmony with condylar movement
- Stability of occlusion
- Resolution of temporomandibular joint symptoms

Bite plane appliances can be given in patients with trismus prior to occlusal equilibration to relax the musculature in case of pain. They act by contacting on anterior teeth thus eliminating any chance of deviating contact from a posterior tooth incline <sup>[78]</sup>.



**Fig 12:** Anterior bite plane

## Equilibration procedures

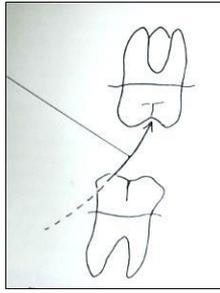
They can be divided into four parts-

- 1) Eliminating interference to terminal hinge axis closure
- 2) Eliminating interference to lateral excursions
- 3) Eliminating posterior tooth interferences with protrusive excursions
- 4) Harmonization of anterior guidance

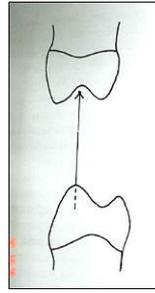
## Interference to centric relation

Centric interference can be differentiated into two types-

- 1) Interference to arc of closure
- 2) Interference to line of closure



**Fig 13: Arc of closure**



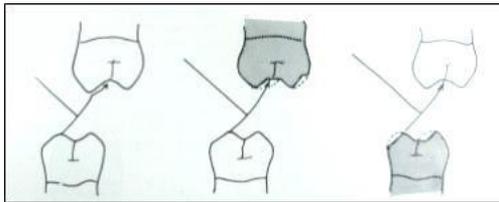
**Fig 14: Line of closure**

### **Interference to arc of closure**

As the condyles rotate on the terminal hinge axis, each lower tooth follows an arc of closure. Any tooth structure that interferes with this closing arc has the effect of forcing the lower teeth forward of the interference to reach the most closed occlusal position. The primary interferences that deviate the condyle forward produce 'anterior slide'.

Rule to correct anterior slide-MUDL.

### **Grind mesial inclines of upper or distal inclines of lower**



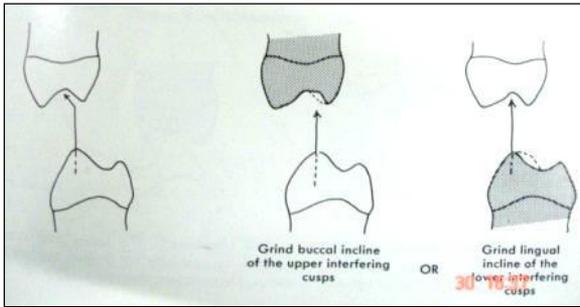
**Fig 15: Grind mesial inclines or Grind distal of upper cusps of lower cusps**

### **Interference to line of closure**

It refers to those primary interferences that cause the mandible to deviate to left or right from the first point of contact to the most closed position.

- 1) When mandible deviates from the line of closure towards the cheek, grind the buccal incline of upper or lingual incline of lower.

The selection of which incline to use depends upon which adjustment will most nearly place the cusp tip in line with center of its fossa contact or that which will direct the forces most favourably to the long axis of both upper and lower teeth.



**Fig 16**

- 2) When the mandible deviates off the line of closure towards the tongue, grind the lingual inclines of upper or buccal incline of lower.

Both these rules can apply to any cusp and they are valid even in crossbite relationship.

### **Moving cusp tip by selective grinding**

Tilted teeth or wide cusp teeth can be adjusted to improve stability while removing interferences. The lower tooth is shaped by grinding without shortening the cusp out of centric contact. To grind only the upper tooth may mutilate the upper cusps unnecessarily without improving the direction of forces.

### **Interference in lateral excursion**

Lateral interference should be located by gentle manipulation of the mandible into terminal axis and then firmly manipulating all the way out to its outer limit.

Lateral interferences can be divided into-

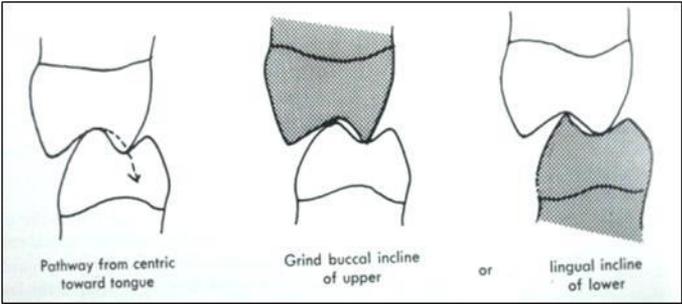
- 1) Interferences on balancing side
- 2) Interferences on working side

### **Balancing side interferences**

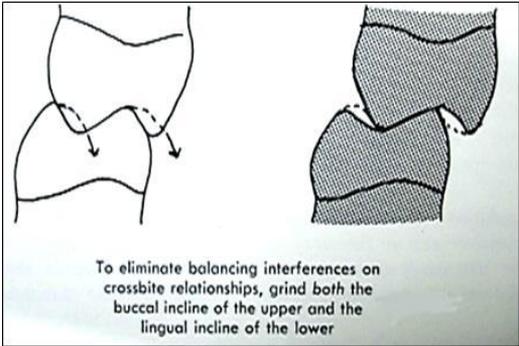
Balancing side interferences are adjusted first and are least complicated. The goal here is to eliminate all contact on inclines as soon as the lower teeth move out of centric relation and start toward the tongue.

Grinding rule-BULL.

**Grind buccal inclines of upper or lingual inclines of lower teeth**



**Fig 17**



**Fig 18**

**Working side interferences**

Before adjusting the excursion on the working side, it is necessary to determine the type of occlusion that will best suit that particular patient.

**Group function**

The lower posterior cusp tip and lower working side incisal edges maintain continuous contact from centric relation out toward cheek.

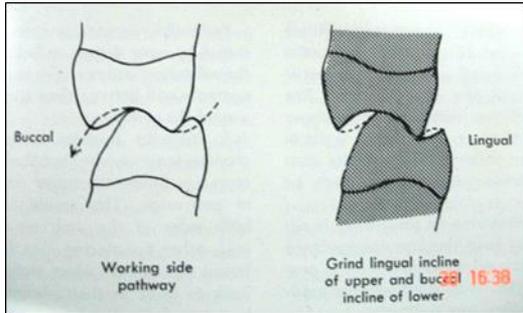
**Posterior disclusion**

In mouths with strong anterior teeth but periodontally weakened posterior teeth, it is usually wise to disclude the posterior teeth in all excursions except centric.

**Grinding rule-LUBL.**

Since cusp tips are used for centric holding stops, all adjusting is done on fossa inclines. Since condyles dictate a concave lateral pathway to the posterior teeth (because of the immediate side shift during rotation),

adjustments on fossa usually take the form of ‘hollow grinding’ or opening up of fossae.



**Fig 19:** Working side pathway grind lingual incline of upper and buccal incline of lower

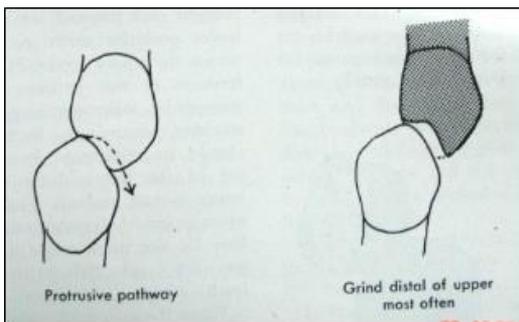
### **Protrusive interference**

Posterior Disclusion in protrusive is accomplished by both the anterior guidance and downward movement of the condyles. With steep anterior guidance, correction of protrusive interferences is usually minimal. Flat anterior guidance requires extensive corrections.

During protrusion only anterior teeth should touch and all posterior contact should be eliminated.

Grinding rule-DUML.

### **Distal incline of upper or mesial incline of lower**



**Fig 20**

As the stressed teeth return to normal equilibrium after occlusal adjustment, readjustment of occlusion must be done until maximum stability has been achieved.

## **Materials for marking interferences**

### **Ribbons**

The most efficient method of marking is to use thin silk marking ribbons. Two colors, red and green should be used.

### **Marking paper**

The ink rubs off soon and paper is easily penetrated or torn. Since it is not soft like ribbons it has the tendency to smudge and give false marking.

### **Joffe marker**

It is an excellent marking device. It utilizes an ink coated rubber dam material stretched on a special holder.

### **Waxes**

It is an extremely accurate material that requires much more chair side time than marking devices.

## **Determining the plane of occlusion**

Plane of occlusion refers to an imaginary surface that theoretically touches the incisal edges of the incisors and tip of occluding surface of the posterior teeth.

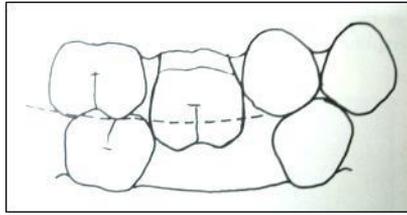
The two basic requirements of plane of occlusion are-

- 1) It must permit the anterior guidance to do its job of discluding the posterior teeth when the mandible is protruded
- 2) It must permit the disclusion of all teeth on the balancing side when the mandible is moved laterally

Curvature of anterior teeth is determined by establishing an esthetically correct smile line, proper phonetics and anterior guidance.

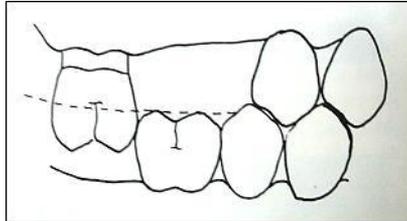
Curvature of posterior plane is divided into Curve of Spee and Curve of Wilson.

Posterior interference in protrusion must be due to faulty occlusal plane and not an improper incisal guidance. Any supraerupted tooth which causes interference in protrusion must be shortened even if it requires devitalization of the elongated tooth.



**Fig 21**

Curve of Spee too low posteriorly presents no major problem because it can't interfere with protrusion, except producing some esthetic problems.



**Fig 22**

### **Curve of wilson**

It is an imaginary line drawn mediolaterally to touch cusp tips of similar teeth on each side of lower arch. It places the lower buccal cusp higher than lingual cusps and upper palatal cusps lower than lower buccal cusps.

There are two ways of effectively changing the curve of Wilson-

- 1) Change the lateral anterior guidance angle
- 2) Change the length of upper lingual cusps

If the curve of Wilson is made too steep, it may eliminate the use of upper lingual cusps as holding contacts since they would interfere with the lateral movement of the mandible.

### **Establishing the plane of occlusion**

There are three practical methods of establishing the plane of occlusion

- 1) Analysis on natural teeth through selective grinding

If it is not possible to eliminate excursive interferences without losing stable centric holding contacts, the plane of occlusion is acceptable as it is.

- 2) Analysis of models with fully adjustable instrumentation
- 3) Use of Pankey-Mann-Schuyler methods of occlusal plane analysis

It is a technique for determining the occlusal plane when all or most of the posterior teeth need restorations.

Pankey-Mann-Schuyler method accomplishes the following-

- 1) Determine plane of occlusion
- 2) Determine the amount of tooth reduction
- 3) Simple transfer to mouth
- 4) Help in laboratory wax-up to determine cusp height
- 5) Determine cusp height in restoration
- 6) Select the type of occlusal scheme

It utilizes the concept of Monson's curve that occlusal curvature has the radius of 4 inches. Two arcs, one from the tip of lower canine, called 'anterior survey' line and one from condyle called 'condylar survey' line are made to intersect at a point called 'survey centre'. Another arc with the same radius is marked on cast from the point of intersection i.e. the survey centre. This arc determines the occlusal plane.

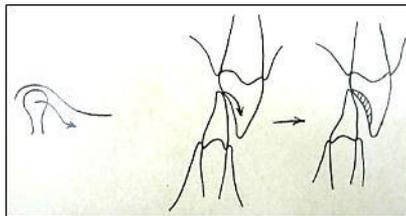
The survey centre may be moved up and down upto 1 cm to favour either the upper or lower posterior tooth as long as it remains on the anterior survey line.

### **Anterior guidance**

The correct relationship of the upper and lower teeth is so critical that differences of a millimeter in the incisal edge position can feel grotesque to the patient.

Along with esthetics and function of mastication, anterior teeth have a very important job of protecting the back teeth.

The dynamic relationship of the lower anterior teeth against the upper anterior teeth through all the ranges of function is called 'anterior guidance'.



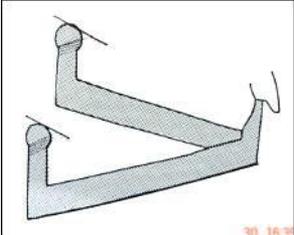
**Fig 23:** Anterior guidance

Pankey Mann <sup>[22]</sup> & Schuyler <sup>[23]</sup> reported that both condylar guidance and anterior guidance control condylar movement.

McCollum & Stuart <sup>[24]</sup> stated that both anterior guidance and condylar guidance are independent factors.

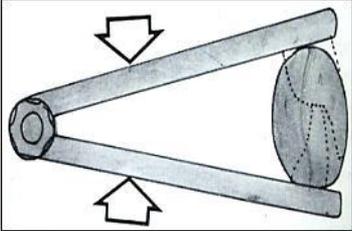
Dawson stated that condylar path is not a determinant of anterior guidance.

Iwata *et al.* described the relationship of anterior guidance and immediate mandibular lateral translation (immediate lateral shift). During side shift the incisal edge also shifts laterally in equal amount.



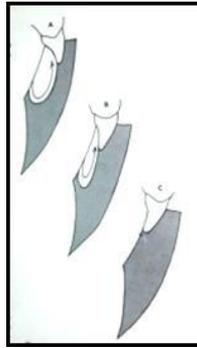
**Fig 24:** Mandible as inverted tripod

Mandible works on class III lever principle and can be compared with an inverted tripod. Two legs are the condyles and anterior teeth form the front leg. The mandible should be closed into a stable tripod relationship with the anterior contact as the front leg. Since anterior teeth are far from the fulcrum of the condyles and ahead of the closing muscular force, the resistance decreases as the distance from fulcrum increases.



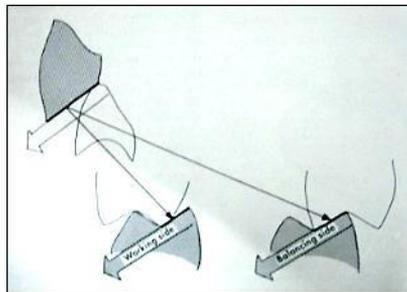
**Fig 25:** Nut cracker illustration

The outer limit of the mandibular movement dictated by the condyle is called “envelope of motion”. The path that the front end of the mandible follows is dictated by the functional movements of the muscles as it relates the lower anterior teeth to the upper anterior teeth.



**Fig 26:** Lateral anterior guidance [8, 25, 26]

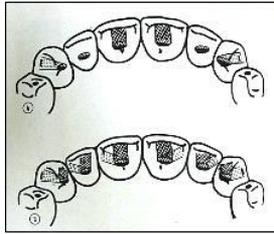
Cuspids play a major role in determining the lateral stress bearing capabilities of all anterior teeth. The lateral pathways established on anterior teeth have greater influence on posterior tooth form. It affects the buccal incline of each lower lingual cusp on the same side and lingual incline of each lower buccal cusp on the opposite side.



**Fig 27:** Lingual inclines of upper canines dictating lower posterior inclines

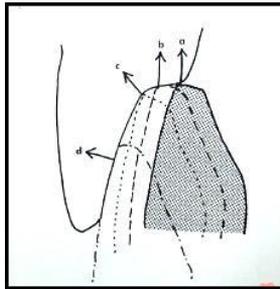
When anterior teeth are strong enough to function on its own, posterior contact in centric relation is sufficient. If anterior teeth are weak in resisting lateral stresses, posterior teeth may be brought into group function to help share the load of lateral forces. If anterior teeth are too weak, splinting may be necessary.

The main vector force is at right angles to the surface contacted. Vector of force against a steep incline is directed almost horizontally and on a flat incline would redirect force more nearly up the long axis. Forces are redirected by changing the shape of the contacting surfaces. Correction of upper lingual contours is patterned to accomplish two effects, redirection of forces and improved distribution of forces. Improved distribution of forces is accomplished by bringing more teeth into simultaneous contact during excursions.



**Fig 28:** Protrusive and lateral movement [25]

- A) Minimal excursive contacts desirable for both protrusive and lateral excursive movements
- B) Group function of all anterior incisors in all protrusive and lateral mandibular movements



**Fig 29:** Vector force is at right angles to the surface

**Steps in harmonizing anterior guidance [28]**

First the esthetic and phonetic requirements should be fulfilled. For that, the lower anterior teeth are restored first. Then the only portions of anterior teeth remaining are areas on the lingual surfaces of maxillary incisors.

The following six steps aid in establishing a harmonious anterior guidance-

**1) Establish coordinated centric relation stops**

If an anterior tooth had a centric stop in acquired position, it may be necessary to replace that contact. If a tooth did not have a stop in the acquired position (maximum intercuspation), It should not be necessary to establish such a contact in centric relation.

**2) Centric stops in a postural position must have the same vertical dimension as those for centric relation**

**3) Refine protrusive excursions**

Contact should be established on both maxillary central incisors throughout protrusive movement, from centric occlusion to edge-to-edge position. Simultaneous contact on lateral incisors and canines is acceptable but not necessary unless there are overriding periodontal considerations.

**4) Establish ideal anterior stress distribution in lateral excursions**

Give a canine guidance in lateral border movements. The distal slope of mandibular canine should function on the lingual surface of maxillary canine. When there is minimal periodontal support, group function should be given.

**5) Check lateral-protrusive movements**

As the patient moves from border lateral movement toward the midline, there should be a smooth transition from contact on canine to central incisors. Lateral incisors may come in contact at any point throughout the change but they may never contact alone.

**6) Smooth transition to a crossover position**

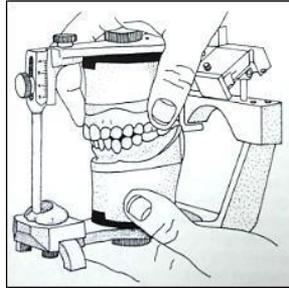
Patients will not usually masticate beyond the edge to edge position, mandible can move in nonfunctional situations. It is important to maintain contact in this crossover position thus protecting the posterior teeth.

Once the anterior guidance is accepted on the provisional restorations, we must duplicate it carefully. Making the customized anterior guide table is a most effective method of transferring the guidance <sup>[53]</sup>.

Condylar guidance must be set prior to making a custom guide table if both anterior and posterior teeth are to be fabricated. If functionally generated technique is used there is no need to precisely duplicate condylar pathway. Condylar settings cannot be changed after customized anterior guide table is fabricated.

Customized anterior guide table <sup>[53, 86, 87]</sup>

## Method of fabrication



**Fig 30:** Fabricating customized anterior guide table

- After the anterior guidance has been finalized in the mouth, upper and lower impressions along with the temporaries are made
- Centric bite record is taken. If posterior teeth have been prepared, centric record can be taken at correct vertical dimension with front teeth only
- After mounting the models the anterior guide table is flattened and guide pin is raised by 1 mm
- Specialized acrylic with filler is added and placed on guide table. On centric contact, the guide pin should indent 3 mm into the dough
- Upper model is guided to all excursions from protrusive to lateral
- After acrylic is hardened, the customized acrylic table should be checked for accuracy by pin maintaining contact with guide table

Richard. L. Alpert <sup>[31]</sup> (1996) used a stone core made intraorally over the lingual surface of provisional restorations after marking the centric contacts and functional disocclusion pathway using felt tip pens. This anterior functional core becomes the blue print for transferring the anterior guidance to the articulator.

Martin, Gross and Cardash <sup>[32]</sup> used alginate impressions with temporary restorations in mouth and after removing temporary's poured molten wax into impression. These wax temporaries were fitted onto the articulator and custom anterior guidance table made.

Alexander <sup>[33]</sup> used elastomeric impression material and wax technique in a similar manner for duplicating the anterior guidance.

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## **Chapter - 3**

### **Neural Crest Cells**

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# Chapter - 3

## Neural Crest Cells

Dr. Priyanka Priyadarshni

### Abstract

The neural crest is a highly migratory multipotent cell population that forms at the interface between the neuroepithelium and the prospective epidermis of a developing embryo. Following extensive migration throughout the embryo, neural crest cells eventually settle to differentiate into multiple cell types, ranging from neurons and glial cells of the peripheral nervous system to pigment cells, fibroblasts to smooth muscles cells, and odontoblasts to adipocytes. They migrate in large numbers and their migration is regulated by multiple mechanisms, including chemotaxis, contact inhibition of locomotion, and cell sorting.

**Keywords:** neural crest cells, multipotent, contact inhibition

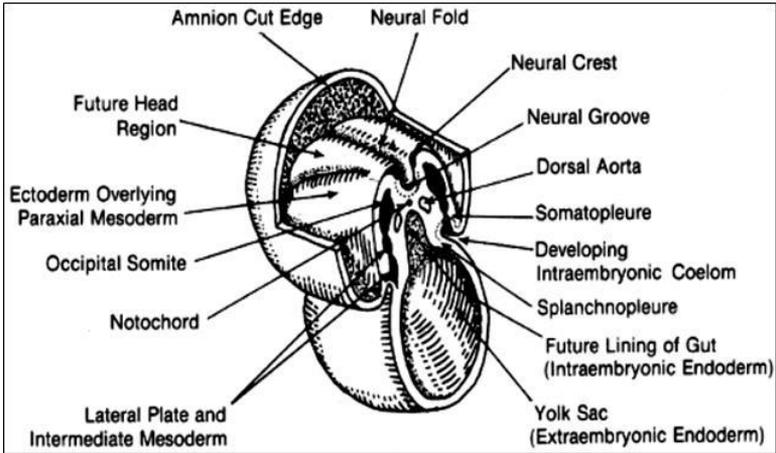
### Introduction

The amazing neural crest is a multipotent population of cells that originates at the border of the neural epithelium during early development in vertebrates. Later on, NCCs undergo an epithelial to mesenchymal transition (EMT) and delaminate from either

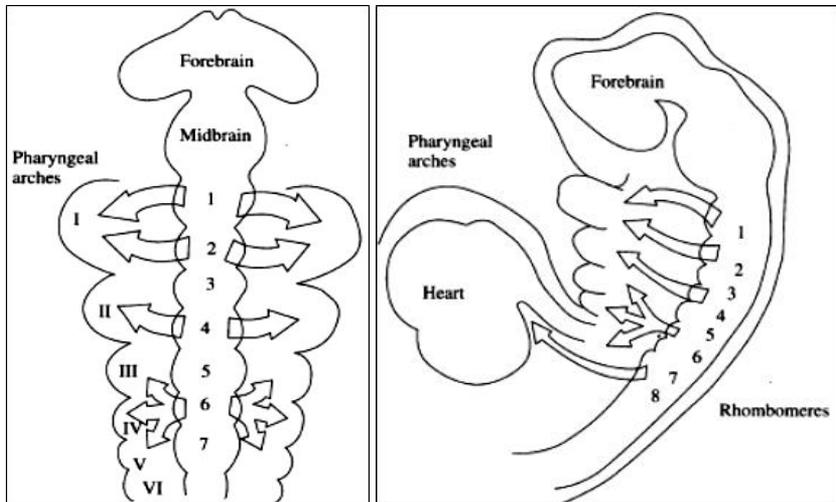
- 1) The open neural folds (amphibians and mammals)
- 2) An ectodermal thickening at the neural plate-epidermis boundary (fish)
- 3) The closed neural tube (birds)

From this departure point, NCCs follow stereotypic migratory pathways permeating throughout (essentially) the entire vertebrate body. The formation of neural crest cells, and their EMT and migration, are carefully orchestrated and proceed sequentially in a rostral-caudal wave closely linked to the rostral-caudal development of the neural epithelia. Due to largely unknown signals, NCCs stop migrating at their final destinations, and in several cases they condense and differentiate; however, some evidence indicates that these cells might initiate differentiation prior to the cessation of migration.

During development, critical events endow daughter cells with different potentials, which are modulated by specific environmental signals. In order to understand how NCCs are able to execute their remarkable migration and differentiation potentials, it seems critical to unveil their cellular origin, and the possible environmental effectors, which clearly depend on the time and regions where NCC precursors appear.



**Fig 1:** Neural Crest Cells



**Fig 2:** Direction of Neural Crest Cells

### Discovery and early history of the neural crest

The story of the neural crest begins in the hands of the talented Swiss scientist, Wilhelm His (1831-1904). He provided some of the earliest

embryological tools by developing methods to hold, move and cut thin sections of samples with precision (innovations that have been cited as the origin of the microtome). In a landmark study, His collected chick embryos during the first 2 days of development and generated accurate serial sections that allowed for an analysis of whole embryos for the first time in a systematic way.

In this initial study by His of chick embryo sections, neural crest cells are identified for the first time. However, His does not refer to them as neural crest cells. Rather, he identifies a specific set of cells as a middle furrow or groove (“zwischenrinne”) surrounding the neural plate in early stages, and as a middle cord or thread (“zwischenstrang”) of tissue in between the neural tube and the epidermis in more advanced stages of development. His suggested that these zwischenrinne and zwischenstrang cells are the same, and that they migrate from their original position to generate the cranial and spinal cord ganglia. This proposal endured many years of dedicated research and controversy to yield our current understanding of the origin, formation and extent of the contributions of the neural crest. His’ proposal that the neural crest generated the cranial and spinal cord ganglia was eventually rectified (cranial ganglia actually have a dual origin, made of placodal and neural crest derivatives), and extended to incorporate NCCs as the source of mesenchymal tissues of the head all cited in and the melanocytes of the skin.

Although neural crest cells initially fell under the umbrella of zwischenrinne and zwischenstrang, the actual term “neural crest” was first coined by Marshall in 1879 and adopted soon after by the rest of the community. Marshall referred to the borders of the neural plate as “neural ridges” (on either side of the neural plate at its rostro-caudal axis). As the neural plate closes to form a neural tube, the neural ridges on either side fuse with each other, generating a mass of cells separate from the neural plate and the overlying ectoderm. Initially, Marshall called this mass a neural ridge, but in a 1879 paper he opted for a term to differentiate between the two neural ridges lateral to the neural plate and the neural ridge above the neural tube, baptizing the latter as “neural crest”. Both the neural ridge and the neural crest correspond closely to the zwischenrinne and zwischenstrang identified by His. Thus, the developmental biology community has embraced the term Neural Crest (NC) to refer to the transient cell population found at the edge of the neural plate and dorsal neural tube, which then migrates to contribute to varied derivatives throughout the vertebrate body.

## Relevance of neural crest development

Neural Crest cells (NCCs) constitute a fascinating population of multipotent migratory cells that contributes to a wide range of derivatives of the vertebrate embryo. NCC derivatives include the neurons and supportive cells of the peripheral nervous system, melanocytes, and endocrine cells. In addition, NCCs also generate a set of derivatives collectively known as mesectoderm, which includes a large portion of the head skeleton (both bone and cartilage). The astonishing capacity of neural crest cells to generate such a broad spectrum of derivatives, specifically those traditionally seen as mesodermally derived, collides with our preconceptions of the potential of the three germ lines. Perhaps the early ectoderm has an extended capacity which is lost in epidermal and neural tissues, but not in the neural crest. An alternative proposal is that a fourth germ layer -constituted by NCCs generates both ectodermal and mesodermal derivatives.

The diverse differentiation capacity of neural crest cells is suggestive of stem cell like properties. Furthermore, true stem cells derived from this cell population have been isolated from regions colonized by differentiated NCCs (in embryos, newborns and even adults). The isolation of neural crest stem cells was initially achieved from embryonic dorsal root ganglia, a tissue derived from the neural crest. More recently, neural crest stem cells have been identified from varied sources in both infants and adults, including the carotid body, the dental papillae, the skin, and the hair follicles. These cells can be propagated *in vitro*, retaining cell renewal capacities, and are able to differentiate into various neural crest derivatives upon proper stimulation.

As a consequence of the robust contribution of NCCs to many specific cells, organs and systems during development, this cell population is implicated in a large number of human pathologies. Birth defects resulting from aberrations in NCC development include craniofacial malformations (cleft lip/cleft palate, fetal alcohol syndrome), congenital malformations of the cardiac outflow tract, and Hirschsprung's disease, amongst other disorders. Additionally, neural crest related tumors include melanoma, neuroblastoma, neurofibromatosis, and pheochromocytoma. Thus, studying the basic developmental biology of NCCs is a critical step to improve our understanding of these conditions, and to generate diagnostic and therapeutic strategies.

### Neural crest differentiation potential

Connective tissues	<b>Ectomesenchyme of facial prominences and pharyngeal arches</b>
	Bones and cartilages of facial and visceral skeleton (basicranial and pharyngeal-arch cartilages)

	Dermis of face and ventral aspect of neck
	Stroma of salivary, thymus, thyroid, parathyroid, and pituitary glands
	Corneal mesenchyme
	Sclera and choroid optic coats
	Blood-vessel walls (excepting endothelium); aortic arch arteries
	Dental papilla (dentine); portion of periodontal ligament; cementum
Muscle Tissues	Ciliary Muscles
	Covering connective tissues of pharyngeal-arch muscles (Masticatory, facial, faucial, laryngeal) combined with mesodermal components
Nervous Tissues	Supporting tissues
	Leptomeninges of prosencephalon and part of mesencephalon
	Glia
	Schwann's sheath cells
	Sensory ganglia
	Autonomic ganglia
	Sensory ganglia (in part) of trigeminal, facial(geniculate), glossopharyngeal (otic and superior), and vagal (jugular) nerves
	Autonomic nervous system
	Sympathetic ganglia and plexuses
Parasympathetic ganglia (ciliary, ethmoid, sphenopalatine, submandibular, and enteric system)	
Endocrine Tissues	Adrenomedullary cell and adrenergic paraganglia
	Calcitonin parafollicular cells-thyroid (ultimopharyngeal body)
	Carotid body
Pigment cells	Melanocytes in all tissues
	Melanophores of iris

## 1. Variety

The derivatives generated by NCCs are astonishing due to their variety and number. NCCs generate most of the neurons (sensory, cholinergic and adrenergic) and glia of the peripheral nervous system, all the pigmented cells in the skin (melanocytes), and endocrine cells of the thyroid and adrenal gland. Perhaps the most striking derivative of the NCCs is the mesectoderm, a special mesenchyme from ectodermal origin capable of generating derivatives once thought to be made exclusively by mesoderm. NCC-derived mesectoderm is capable of forming cartilage, endochondral bones, dermal or intramembranous bones, teeth, dermis, smooth muscle, and other connective tissues.

## **2. Number**

The NCC derivatives referred to above, are only subtypes which represent many different cell types, and which contribute to several tissues and organs throughout the vertebrate body. For example, more than 20 different cranial bones are made by neural crest cells. Furthermore, many different sensory neurons expressing a different array of molecules and employing characteristic neurotransmitters are made by neural crest cells in specific locations of the embryo. The same is true for the other neuronal subtypes (parasympathetic, sympathetic, and enteric).

## **3. Regional contributions of NCCs *in vivo***

Fate map studies generated via ablation or grafting strategies have provided a very detailed picture of the specific contribution of neural crest cells from different regions of the avian embryo. Neural crest cells from the cranial region, which are subdivided into prosencephalon, mesencephalon and rhombencephalon groups, generate mesectoderm and pigmented cells. The prosencephalon makes no other crest contributions, while NCCs from a slightly more caudal location (the mesencephalon) generate, in addition to neurons and glia of the parasympathetic and sensory ganglia, mesectoderm and pigmented cells. Yet, in the caudal portion of the rhombencephalon, sensory ganglia, enteric ganglia and endocrine cells accompany the mesectoderm and pigmented cells as NCC derivatives. In the rest of the embryo (caudal to the head), a similar display of specific derivatives has been described. The cervical spinal cord, thoracic spinal cord, and lumbosacral spinal cord regions generate a variety of derivatives according to specific locations within each territory. However, no mesectoderm or parasympathetic ganglia are generated in these more posterior locations; instead, posterior NCCs contribute to sympathetic and sensory ganglia, and pigmented cells. In addition, the anterior cervical spinal cord and the lumbosacral region (but not the interceding territories) also to the enteric ganglia. Similarly, only the caudal portion of the cervical, and the anterior half of the thoracic spinal cord generate endocrine cells.

## **Cellular and molecular events responsible for neural crest formation**

The neural folds (where prospective neural crest cells reside) are surrounded by the neural plate medially and by non-neural ectoderm (prospective epidermis) laterally. Additionally, the ectoderm of the embryo is underlined by mesoderm. Specifically, axial mesoderm lays under the central most region of the embryo, and paraxial mesoderm under the more lateral sides of the embryo (beneath the neural folds). The location of these

tissues has prompted investigators to suggest their involvement in the formation of the neural crest, and a considerable body of evidence based on juxtaposition experiments performed *in vivo* and *in vitro* supports a role of these tissues in NCC development. Juxtaposition of “naïve” intermediate neural tissue (ventral to the neural folds and dorsal to the ventral midline or prospective floor plate) against prospective epidermis (lateral non-neural ectoderm) triggers crest induction. Interestingly, these experiments have shown that epidermal and neural tissues signal to each other, and both tissues generate neural crest cells. Most attention has focused on the possible signal(s) from the epidermis that trigger neural crest induction in the neural tissue. However, a similarly large body of experiments demonstrates that mesoderm is the source of induction activity, and it is this germ layer that directs the overlaying ectoderm to form the neural crest.

At the molecular level, several signals have been identified as neural crest inducers. The most prominent of these are BMP, FGF and Wnt. Studies from the Jessell laboratory were the first to identify, at the molecular level, a neural crest inducer. Members of the TGF- $\beta$  family (Dorsalin-1, Activin, BMP2, 4, & 7) effectively induce neural crest formation from the naïve neural plate. Together with studies in *Xenopus* and zebrafish, this research suggested that BMP signals operate at intermediate concentrations during neural crest formation.

### **Genes required and/or sufficient for NCC development**

Our understanding of the regulation, function, and interactions between the NCC molecular markers is limited. Most of our knowledge is based on the study of a few transcription factors expressed by early NCC precursors, or by both premigratory and migratory NCCs. The function of these transcription factors has been investigated through over expression and inhibition approaches in whole embryos, or in explanted tissues. These studies have identified transcription factors that are required for neural crest development (Ap2, FoxD3, Msx1, Pax3, Pax7, Snail1, Snail2, Sox9, Sox10, Zic2, etc.), some of which are able to promote an expansion of NCCs in relatively endogenous territories (FoxD3, Pax3, Snail1, Snail2, Sox9, Sox10, Zic1, Zic3, Zic5).

A more stringent test has been to challenge the inductive capacity of certain factors to trigger the formation of neural crest cells in naïve ectoderm. To date, only FoxD3 and Snail1 have been identified as having this capability. However, Snail and/or Snail2, Sox9 and FoxD3 are all vital to neural crest formation, and are considered by the neural crest community

to be *bona fide* neural crest markers. Therefore, the current understanding of the participation of these three factors in NCC development is addressed below:

### **Snail**

Amongst the most prominent markers of neural crest development are the zinc finger transcription factors of the Snail family, Snail1 and Snail2 (formerly known as Slug. These genes are expressed in neural crest cells, as well as in early mesodermal tissues and are associated with morphological changes and movements including those necessary for the epithelial to mesenchymal transition that neural crest cells undergo prior to their migration.

### **FoxD3**

The fork-head or winged-helix transcription factor FoxD3, is expressed in prospective and migrating NCCs in mice, frog, fish and chick embryos. Its earliest expression is concomitant with the expression of Snail genes. Over expression experiments offer controversial results, in some contexts leading to an expansion of the neural crest territory. Furthermore, combinatorial experiments suggest that Snail genes and FoxD3 genes may act in parallel pathways leading to NCC development.

### **SoxE**

SoxE genes (Sox8, Sox9 and Sox10) are a subgroup of transcription factors containing a high mobility group (HMG) DNA binding box. SoxE genes are also expressed by precursors and migratory NCCs, and their functions are required for different aspects of NCC development. Sox9 appears to be critical for early NCC development, and downregulation experiments demonstrate this requirement. In contrast, overexpression experiments suggest that Sox9 can trigger the formation of neural crest cells.

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**Chapter - 4**  
**Biomaterials for Orbital Floor Reconstruction**

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# Chapter - 4

## Biomaterials for Orbital Floor Reconstruction

Dr. Ritesh Vatsa

### Abstract

Fractures of the floor of orbit commonly known as blow out fracture. It may be classified into pure and impure fractures. Isolated fractures of orbit are known as pure. Many biomaterials have been used over the years to reconstruct the floor. This review discusses the role of different biomaterials for orbital floor reconstruction.

**Keywords:** blowout fractures, biomaterials

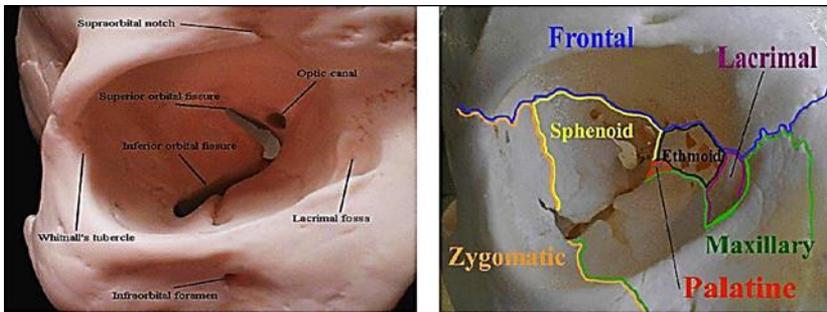
### Introduction

Fracture of the floor of the orbit which may be accompanied by displacement of the orbital contents into the maxillary sinus <sup>[1]</sup>. Based on the orbital rim fracture along with floor fracture, Converse and Smith introduced the concept of pure blow out and impure blow out fractures <sup>[2]</sup>. The treatment of orbital floor fractures is still controversial with regard to indications, surgical timing <sup>[3]</sup> access and reconstruction techniques. The eyes should be bright and reflect light, they are the windows to the soul <sup>[4]</sup> Over the years different authoritative opinions have alternated in the literature. Wide ranges of choices are available regarding the materials used for orbital floor reconstruction. They can be classified as autografts, allografts, or alloplasts <sup>[5]</sup>. Alloplasts can be classified as non-resorbable and resorbable materials. Titanium mesh, Teflon, Medpore, Silicone come under the non-resorbable category. Resorbable materials include poly-L-Lactide, polydioxanone, polycaprolactone, polyglactine-910 and polyglycolic acid <sup>[6]</sup>. Allograft materials include lyophilized dura and lyophilized cartilage <sup>[6]</sup> Autografts include periosteum, rib grafts, auricular cartilage, iliac bone graft, mandibular bone graft, calvarial graft. Though autogenous bone graft provide framework for orbital walls, they carry the main disadvantage of donor site morbidity including nerve and blood vessel injury, gait disturbances, cosmetic disturbance, and donor site pain <sup>[7]</sup>. Non resorbable alloplasts become as permanent foreign bodies and can cause late

complication such as infection migration of implants, extrusion of implant and residual diplopia [5]. The reconstructive surgeon must always be aware that any non-resorbable material has the potential to cause infection even after an interval of years. For this reason, autogenous grafts are still widely used. Of autografts, auricular cartilage [7, 8] is indicated for the reconstruction of gaps in the orbital floor due to a shape that is very similar to that of floor [9, 10].

## Surgical anatomy

It is very important to know and appreciate the anatomy of the orbit to understand the injuries sustained by the orbit and to postulate how to reconstruct it. The orbit can be anatomically classified into many ways. It has been described in relation to its bony components, the periocular soft tissues, the globe and the protective soft tissue apparatus consisting of the upper and lower eyelids and the lacrimal apparatus.



### The bony orbit comprises of seven bones

1. Zygoma
2. Maxilla
3. Frontal bone
4. Lacrimal bone
5. Ethmoid bone
6. Sphenoid bone
7. Palatine bone

The orbit contains the eye and its accessory structures. The globe of the eye takes up one quarter of the volume of the orbit. The orbit is a quadrangular pyramid with its base on the facial surface. Its apex is the optic foramen and the medial end of the superior orbital fissure. The medial wall made of ethmoid bone is almost paper thin of about 0.2 to 0.4mm.

The orbital rim is composed of cortical bone. Its strength comes from its circumorbital continuity.

The floor is almost triangular with rounded corners, being narrower posteriorly and merging medially with the almost quadrilateral plate of the ethmoid bone. The floor is not horizontal but slopes upwards and medially at 45 degree and ascends posteriorly at about 30 degree. The floor is very thin being almost 0.5mm in most areas and is further weakened by the presence of infra orbital groove and canal. It is concave anteriorly and convex posteriorly. Medially there is no distinct border. The orbital floor behind the orbital rim is initially concave until a point just behind the equator of the globe. Posteriorly, it becomes convex upwards inclining to about 30 degrees creating the retrobulbar constriction of the orbit. The inferior orbital fissure separates the lateral wall and the floor of the orbit. It is roughly 2cm long and runs posteromedially.

There is a 45 degree inclination from the lateral to the medial wall and antero-medially and posteromedially to it there is a bulge called Hammer's key area, which is a very important area for graft placement to efficiently correct enophthalmos. The inferior and the lateral wall can be safely dissected for about 35mm to reach the area.



**Fig 1:** showing Hammer's key area

The inferior orbital margin is clearly defined on its outer aspect and is readily palpated but the inner third is more rounded. It is not able to withstand direct force in the central and medial areas because of the proximity of the underlying maxillary antrum and the closely related infra orbital canal. Just within the rim at the junction of the outer two thirds and the inner one third, there is a small depression which marks the origin of the inferior oblique muscle, the only extra ocular muscle which does not arise from the back of the orbit. This part of the inferior oblique rim is often fractured producing associated disruption of the muscle and subsequent diplopia.

Rontal *et al.* (1979) studied 48 orbits in 24 skulls to determine the relationship of important structures to determine the relationship of important structures of the orbit to well defined landmarks in the wall. By summarizing the useful measurements given by them, it may be stated that a subperiosteal dissection may be safely extended for a distance of 25mm posterior to the inferior and lateral rim and for a distance of 30mm from the superior rim and the anterior lacrimal crest. Distance from the infra orbital foramen to the midpoint of inferior orbital fissure is around 24mm.

### **Methods of collection of data**

patients with orbital floor fractures were included. The procedures to be performed were explained, followed by written informed consent. A detailed history was taken followed by clinical examination. PNS view and CT in all the three planes was taken and findings were recorded in a specially prepared case history proforma. Pre-operative surgical defect was measured in the CT and volume was measured using Volume share II, an installed application.

Post-operative, all the patients were followed for 2 months to evaluate enophthalmos, diplopia and any limitations of extraocular movements. The surgical sites were examined for evidence of infection, or extrusion of the graft. Post-operative volume measurements were done for comparison.

### **Inclusion criteria**

Patients who have sustained orbital floor fractures:

- Diplopia
- Herniation of orbital tissues through gaps in the orbital floor
- Enophthalmos
- Concomitant displacement of bone fragments of inferior orbital rim

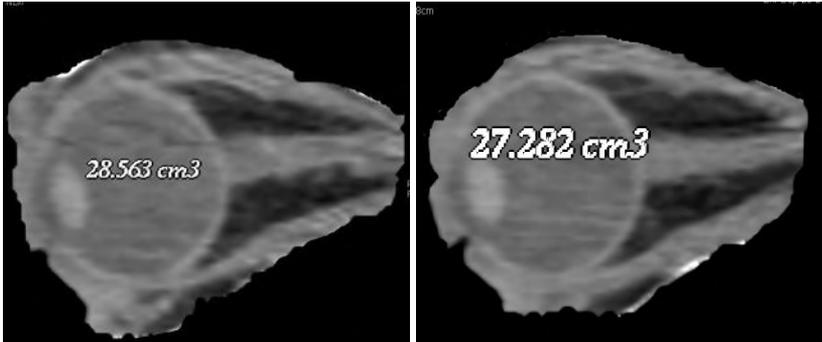
### **Exclusion criteria**

- Medically compromised patients
- Optic neuropathy or post traumatic blindness
- Previous history of ophthalmic surgery
- Only eye with vision

Ethical approval was obtained for the study from the institutional ethical committee and informed consent obtained from each patient in the regional language (Tamil) explaining nature of the surgical procedures and the study.

## Pre-operative assessment

A detailed history, clinical examination, including general examination and ophthalmologic examination, radiograph, CT scan and facial photographs CT scan using GE Discovery Workstation. Volumes of the orbits using Volume share II, an installed application.



## Clinical examination

Both extra oral and intraoral examinations.

## Ophthalmologic examination

Parameters	Right Eye	Left Eye
Ocular movement		
Conjunctiva		
Cornea		
Pupil		
Lens		
Fundus examination		
Visual acuity		
Diplopia		
Forced duction test		
Infraorbital sensation		

## Hess charting

### Armamentarium



### Micromotor and handpiece



### Surgical procedure



**Fig 1:** Traction sutures



**Fig 2:** Corneal Protection



**Fig 3:** Transconjunctival incision



**Fig 4:** Dissection



**Fig 5:** Exposure of Rim & Retrieval of herniated Soft tissue



**Fig 6:** Fixation of rim



**Fig 7:** Placement of graft



**Fig 8:** Closure

## Discussion

Management of orbital fracture is a challenging problem for the oral and maxillofacial surgeon.

Their reconstruction requires

- 1) Release of entrapped orbital floor muscle
- 2) Reduction of the fractured floor
- 3) Reduction of the floor defect
- 4) Prevention of infection from antrum
- 5) Return of physiologic function the extraocular muscles
- 6) Elevation of the depressed zygoma
- 7) Correction of the volume discrepancy between the orbits <sup>[11]</sup>

Various factors influence the choice of material for use in orbital floor reconstruction. The choice depends on the size of the defect, involvement of multiple walls, adaption to the internal contours, restoration of proper volume, presence of adjacent sinus cavity, prevention of displacement, risk of further trauma, adhesions or restriction of ocular motility, early vs.

Late repair <sup>[12]</sup>. There is general consent that the ideal floor inlay material should be inexpensive, readily available in sufficient quantities, adaptable to regional anatomy (easy to contour and sharpen), easy to position, suitable to all types of defects, able to provide support to orbital contents, biocompatible, non-toxic, non-carcinogenic, free of potential for disease transmission, inert or biodegradable to zero remnant. <sup>[13]</sup> Alloplasts are available as either resorbable or non-resorbable materials. Non resorbable materials are titanium mesh, porous polyethylene sheet, BAG plate, hydroxyapatite sheet. These non-resorbable materials remain as permanent foreign body, potential for disease transmission, expensive, not readily adaptable to walls <sup>[13]</sup> Resorbable materials used are PLLA and PLLA/PGA sheet, polyglycolic acid membrane, PDS sheet, polyglactin-910 mesh, periosteum polymer complex. <sup>[13]</sup> Unfortunately resorbable materials have not always performed well. Two major problems have been encountered that limit their potential. First is the ability of these materials to maintain support to the orbital tissues sufficiently long until replaced by fibrous or bony tissue to prevent enophthalmus. Second is the progress of degradation that is not benign. <sup>[14]</sup> advantages of alloplasts are that they can be applied in wider defects, good support to orbital contents.

The other choice for orbital reconstruction is the use of allogenic materials. WAITE AND CLANTONS (1988) have reported these grafts as reconstruction material <sup>[15]</sup>. The main concern with regard to the use of these materials is the antigenicity of the material and transmission of infectious diseases. Delayed hypersensitivity reactions have also been reported with the use of xenografts. Despite being careful on the sterilization techniques, risk of infectious disease transmission is the main disadvantage of using allogenic materials. <sup>[13]</sup> Because of various shortcomings associated with use of alloplastic and allogenic materials, autogenous grafts still widely used for orbital reconstructions.

Disadvantages associated with autogenous bone grafts are donor site morbidity. variable rates of resorption with subsequent development of enophthalmus and or ocular dystopia. Difficulty in contouring and shaping. Intracranial complications such as scarring. Alopecia and injury to the temporal branch of facial nerve. A further disadvantage of using bone is the separate surgical field and time taken to harvest the gift. <sup>[14]</sup> The idea behind using auricular cartilage is that an ideal implant for orbital floor reconstruction for orbital defects because of its natural curve that fits into the orbital defects. Auricular cartilage seems to provide an excellent source of cartilage seems to provide an excellent source of autogenous tissue for the

repair of orbital floor defects. The thickness of the cartilage and its concave shape are ideal qualities that enable a precise fitting to the concave floor, especially at the junction of the floor with the medial wall, the most common location of disruptions caused by trauma. The intrinsic strength characteristics of this cartilage make it highly suitable in the repair of large gap defects. Less resorption if the perichondrium is left intact. The perichondrium becomes vascularized soon after transplantation. With attention to surgical technique, the cartilage can be harvested without creating auricular deformities and objectional scarring. Other advantage auricular concha include a donor area that is located in the proximity of the recipient site that can be prepared and draped within the same surgical field. [16] Bayat *et al.*, [17] and Dharmindra *et al.*, [18] stated auricular cartilage seems to provide an excellent source of autogenous tissues for the repair of orbital floor defects because of-

- 1) Its thickness and concave shape
- 2) Ease and less time to harvest
- 3) Minimal donor site morbidity

Castellani *et al.*, [19] Stated that cartilage is only slightly vascularized and thus requires little blood perfusion. Which means that it undergoes less resorption.

## **Conclusion**

Considering all the observations in our studies, conchal auricular cartilage graft can be used as a suitable implant for orbital floor reconstruction. The clinical outcome is comparable or even better to other materials for orbital defects.

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**Chapter - 5**  
**Warm Vertical Condensation Technique and Its  
Implications**

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# Chapter - 5

## Warm Vertical Condensation Technique and Its Implications

Dr. Seema Yadav

### Abstract

The obturation of thoroughly cleaned and disinfected root canal system is necessary for the success of the endodontic treatment. The traditional obturation method requires the use of cold gutta percha and sealer. The secondary or accessory cones were inserted laterally to occupy the unfilled space of the canal. The laterally compacted cold gutta percha against the wall of the canal represents the cold lateral compaction procedure. This is the oldest method of obturation and very popular amongst the clinicians. It has fast learning curve and requires no special instruments. There are certain stumbling block with these approach such as large number of voids, more amount of sealer and difficulty in filling the canal irregularities. The large volume of sealer may disintegrate on exposure to the tissue fluids and along with voids present within the obturating material may jeopardize the impermeable seal of the root canal.

In order to have densely compacted gutta percha core material with minimal volume of sealer and less gaps or empty spaces within the obturation, newer obturation approach was developed. The use of heat to soften and compact the gutta percha provided a densely packed obturation with minimal voids and conforms to the asymmetry of the canal. The contemporary warm vertical compaction technique is based on this concept. This technique provides complete seal to the canal and is now frequently used by the clinician. This chapter will discuss the warm vertical condensation technique, various different ways of using this technique and several important clinical factors associated with the procedure during its use in obturating the root canals.

**Keywords:** warm vertical compaction technique, downpack & backfill, heated pluggers; endodontic heating devices

## **Introduction**

The “obturate” word has its Latin origin which means to block or to obstruct. The obturation in dentistry means to seal all the pathways in thoroughly disinfected and shaped root canal by a biocompatible material so as to prevent its invasion from microorganisms and to provide conditions favourable for healing. The goals of endodontic treatment is to eliminate pulpal or periapical pathosis and provide long lasting survival of the tooth to maintain its function in the oral cavity. These objectives can be achieved by meticulous debridement, shaping and three dimensional obturation of the entire root canal system.

Gutta percha is most commonly used obturating material. The material is radiopaque, semi-solid and can be molded within the canal by means of compaction. It is an inert material and is easily introduced within the canal and can be easily removed if needed. It can be readily disinfected. The issue with gutta percha obturating material is lack of adhesiveness to the tooth structure and thus needs root canal sealer. The high quality obturation requires dense core material with less sealer. The obturation techniques resulted in varied levels of obturation. The cold lateral compaction of gutta percha resulted in more sealer and less dense obturation while the heated gutta percha which can be molded and compacted produce well condensed obturation with less sealer and less gaps within the obturating material.

The timing of obturation is also of paramount importance for the success of any obturation technique. The obturation should essentially be performed when the canals are scrupulously cleaned and prepared without any clinical manifestation. The canal should be diligently instrumented to an optimum size to receive the obturating material. The canal should be dry without any purulent or serous exudates. These considerations should be followed before filling the canals for proper endodontic prognosis.

Root canal filling can be performed with various obturating materials and techniques. The preexisting conditions of root canal should be considered before the selection of obturation technique. The canal anatomy such as oval canals, branched canals; canal defects such as internal resorption, open apex; procedural errors such as perforation, ledges or roots in proximity to vital structures such as mandibular canal or maxillary sinus should be appraised.

The obturation techniques require certain basic necessary needs to dispense the quality obturation. The traditional cold obturating methods require specific spreaders for each canals and the contemporary warm

obturation procedure needs specific pluggers along with specialized heating devices. The warm gutta percha strategies has given more stable and consistently good quality obturation in endodontics. This chapter will address on warm vertical condensation technique for obturating root canal and their various issues pertinent within the clinical framework.

### **Warm vertical condensation technique**

The warm vertical condensation technique requires use of heat to soften the gutta percha (GP) followed by vertically compacting it into the smooth flared root canal preparation. Herbert Schilder in 1967 first develop this technique where the gutta percha is plasticized within the root canal and offers downpack and backfill obturation <sup>[1]</sup>. The downback is the vertical condensation of heat softened GP from coronal to apical in the apical part of the canal while the backfill is the filling of the residual space of the canal from apical to coronal.

The procedure provides three dimensional seal at the terminus of the canal (4 to 5mm of the apical canal). It fills the canal irregularities with the help of apical and lateral hydraulic forces by pressing the sealer and gutta percha along its path. It delivers the densely compacted obturation of the root canal system than the traditional obturation techniques <sup>[2]</sup>.

The technique given by Schilder was very painstaking, labour intensive, required numerous instruments and had the risk of Lip injury as the instruments were heated outside the oral cavity to soften the gutta percha within the canal. Since its introduction various remarkable transformations have been made in the technique to simplify the procedure and to ensure more easier application. The instruments used in the Schilders technique of vertical condensation were heat carrier and cold plugger of appropriate sizes. The heat carrier instruments were heated in Bunsen burner and were used to soften gutta percha within the canal while cold pluggers were used to vertically compact the softened gutta percha.

The electric heat carriers (Touch and heat) were later introduced and provided more control over heat application. Subsequently, the other systems were introduced such as System B which thermostatically controlled heat carrier and has simplified technique <sup>[3]</sup>.

The warm vertical condensation techniques of gutta percha are

- Interrupted technique
- Continuous wave technique

The procedure for placing master cone is similar in both interrupted and continuous wave technique. A non-standardized accessory cone can be used as master cone as it is more wider than the standardized cone. The sealer is coated to the wall of the canal. The GP of about 1-2mm is removed from the tip of the master cone and is inserted short of working length. The excess GP at the canal orifice is then discarded with the help of heated plastic instrument.

### **Interrupted technique**

This technique is also known as multiple wave technique. The increments of GP of 3-4mm is being heated by heat carrier for 2-3sec and bits of GP with heat carrier is removed followed by the vertical compaction of plasticized GP using cold pluggers of appropriate size. The plasticization of 3-4mm of GP by heat carrier and its vertical compaction by cold plugger produces an individual wave of compaction. Such multiple compactions were performed so as to achieve seal of the GP in the remaining 5mm from the canal terminus <sup>[3]</sup>.

### **Continuous wave technique**

This technique requires one individual wave of compaction rather than several multiple compaction. A single appropriate plugger is selected which fits the taper of the canal from 5-6mm of the canal terminus. The selected plugger is heat activated for 2-3 seconds and is moved apically in the canal so as to reach to its determined location. Once reached, the heat is inactivated and a vertical pressure for 10 seconds is applied by the same plugger. The heat is again activated for 1second and ceased for 1 second. This activation and inactivation of 1 second will help the plugger to be removed easily from the canal along with excess GP <sup>[4]</sup>.

The empty unfilled space of coronal two thirds of the canal is obturated by backfill. Backfilling of the canal is achieved by the injection molded thermoplasticized gutta percha technique.

### **Injection molded thermoplasticized gutta percha technique**

Injection molded GP exhibits excellent flow properties. This technique involves placing increments of thermoplasticized GP and condensing it until the coronal extent of the canal is filled. The increments of thermoplasticized GP is deposited using the obtura Gun. Small increments of 2-3mm are placed and condensed to minimize shrinkage. The downpack of the GP ensure adequate apical resistance form to prevent extrusion of GP during backfilling <sup>[2]</sup>.

## **Canal preparation for warm vertical compaction technique**

1. The canal should have a continuous gradual taper
2. The apical constriction should be maintained as small as practical
3. The prefit GP cone must have a snug fit in the apical third within 0.5mm of radiographic terminus
4. The canal should allow the prefit plugger within 3-5mm from the working length <sup>[5]</sup>

## **Heating devices**

Variety of systems are available for heating the cold GP to render it thermoplasticized for obturation.

### **System used to heat the gutta percha inside the canal**

1. Touch and Heat
2. System B

### **System used to heat the gutta percha outside the canal**

1. Obtura (High Heat) System
2. Ultrafil (Low heat) System

## **Touch and Heat source**

The Touch and Heat is a thermosoftening device introduced by Johan Masreleiz in 1982. It can be used with interrupted wave of obturation. It requires various sizes of vertical pluggers which fits the coronal, middle and apical third of the canal.

The Touch and Heat system consist of an electrical unit with a front panel, a probe handle and a cord to connect the two.

The front panel of Touch and Heat system consist of-

- Power control dial
- Heat light (green)
- Charge light (Yellow)
- Low battery light
- Selector push button

The power control dial regulates the amount of heat to the tip of the plugger. The heat increases linearly from the setting of 0 (low power) to 10 (maximum power) such that the setting of 5 is 50% of the maximum power

output. The maximum power at setting of 10 can reach 1200-1400F (640-760C) in air within 8seconds and the lowest setting of 0 has power output of 100F (37C) <sup>[6]</sup>.

The manufacturer recommends vertical condensation should be performed at the power setting of between 6-8 and the heat applied for 1-2 seconds.

The green heat light on the front panel indicates the tip of the plugger is in heating mode. The unit operates from rechargeable battery. The battery charged or low is also shown by lights on the front panel. The push button switch can be selected for the use or the store mode. The store mode will deactivate the unit and prevents the battery from discharging and should also be used when changing tips of the plugger. It also prevents the tip from heating in case the touch switch is activated accidentally <sup>[6]</sup>.

The probe handle consists of pin vise nut which provides casing/housing for the different tips for its application while the contact spring on the pin vise nut turns on or start up the Touch 'n Heat device. Depressing the spring will heat the tip of the plugger.

### **System B heat source**

The System B heat source was introduced by Stephen Buchanan in 1987 provides precise amount of heat and regulates the tip temperature of the heat carrier plugger. It is used with continuous wave of obturation. Similar to Touch and heat device, System B heat source consist of a electronic unit with a front panel, a probe handle and a cord to connect the two.

The front panel of System B consist of more buttons to provide more temperature settings. It consists of selector button for use or store mode, power control dial for power settings from 1 to 10, temperature dial for precise temperature which is displayed on LCD, the temperature selector button for touch or continuous mode and the heat light and the two battery lights (charged or low) The probe handle is similar to touch and heat.

### **Next generation of system B devices**

The newer version of System B devices are-

- Cordless System B devices consisting of exclusive probes with the electronic unit placed within.
- Electronic Unit (Element obturation unit) consisting of two probes. One is System-B Heat Source and the other is for injecting thermoplasticized GP

Newer feature incorporated were

1. The handpiece/Probe diameter has been enlarged to have more snug grip. The contact spring button is raised 2 mm for easy location and has an indicator light and sound prompts whenever the heat source is activated.
2. Selection buttons were provided for different heating functions such as downpacking, backfilling, pulp testing with heat, and heat cautery as each requires different power and heat settings (temperature setting, touch/continuous mode).
3. The downpacking mode has an automatic shutoff after four seconds to prevent damage associated with heat. The downpacking mode also has a sound prompts at five seconds and another at ten seconds indicating the termination of the heating cycle [7].

### **Obtura system**

The obtura system consists of a control unit and a syringe with a pistol grip handle for heating of GP (beta phase). The syringe contains GP which is heated to 160-200C. The silver needle attached to the syringe will release the thermoplasticized GP when required. The silver needles are available in 18, 20, 23 & 25G sizes. The temperature of the released GP from the tip of the needle is 62-65C. The heating syringe does not require preheating of GP and takes about less than 2mins to establish the required operating temperature [8].

### **Ultrafil system**

The cannules containing GP were heated to 70C in a heating unit for a minimum of 15mins. These GP are available as: regular set, endoset and firm set. The cannules must be discarded after 4hrs heating [8].

### **Implications of warm vertical gutta percha compaction techniques**

#### **1. Effect of heat**

Use of heating devices for thermosoftening the gutta-percha has become increasingly popular in endodontics. A better understanding of these systems may help to provide good quality fillings and to prevent irreversible molecular modifications of the root filling material and damage to the vital tissues around the root. The actual temperature at the plugger tip, plugger penetration depth, accuracy of the set temperature used with warm vertical compaction devices may have influence on the quality of the obturation. The heat applied during warm vertical compaction technique exerts effects on the

obturator material, external root surface and the supporting structures. There is a need to discuss these factors individually in order to understand the implications.

### **Heat carrier/Pluggers**

The higher pluggers temperature may overheat the gutta percha leading to shrinkage while the lower temperature may underheat the gutta percha leading to increase pressure and inadequate molding <sup>[9]</sup>. The temperature should be such that it allows the penetration of GP into the small lateral canals or isthmuses without altering the properties of gutta percha. Buchanan <sup>[4]</sup> recommended the warm vertical compaction technique should be used at 200C for a duration of no more than 4s.

The quality of the vertically compacted filling depends on the penetration depth of the pluggers. The pluggers penetration depth of 5mm from the working length is sufficient or adequate and produced least apical leakage <sup>[9]</sup>.

The penetration depth of the pluggers is also directly related to the apical width of the shaped canal at 5mm. The apical flaring using larger taper instruments facilitates the penetration of pluggers provided the width of the apical portion is kept to a minimum <sup>[10]</sup>. However it is not always possible in clinical situations.

The set temperature of the heat source do not match the actual temperature at the tip of the heated pluggers <sup>[11, 12]</sup>. The temperatures recorded at the tip of the pluggers has shown varied readings between the different tapered pluggers. The actual temperature at the tip of the pluggers was shown to be lower than the set temperature on the System B LCD display <sup>[12]</sup>. This may be explained due to loss of the heat during conduction of heat from the heating source to the tip of the pluggers.

Warm vertical compaction technique can exerts influence on

- a. Root canal sealers
- b. Obturator material (Gutta Percha)
- c. External root surface and supporting structures

### **Root canal sealers**

The temperature effect on the root canal sealers during warm condensation technique has not been well reported. The laboratory studies are reported largely than the clinical studies on warm vertical compaction techniques.

The root canal sealers behaved as thermal insulators during warm gutta percha technique and due to their varied compositions have shown different heat-conductive properties <sup>[13]</sup>. The heat application with smaller heating time and lower temperature will not affect the relevant physical or chemical changes to sealers <sup>[14]</sup>. It was seen in an experimental model that there was no substantial physical or chemical changes within the root canal sealer when subjected to thermal treatment similar to the clinically accepted temperature levels not exceeding 60 seconds <sup>[14]</sup>.

The higher temperature may however affect the physical and chemical properties of the root canal sealers. The overheating or inappropriate implementation of warm condensation technique will result in deleterious effects on the physical and chemical properties of the sealer as is shown in the literature <sup>[15-18]</sup>.

### **Gutta percha**

Gutta-percha is the most acceptably used obturating material for its stable physical and chemical properties and its thermoplasticizing quality. Gutta percha is available in alpha and beta forms. Both forms can be used with warm vertical compaction technique.

The quality of obturation by warm vertical compaction technique depends on the thermal plasticization property of the gutta percha. The gutta percha is not an excellent heat conductor but the temperature of the apical gutta percha has an effect on the length control and dimensional stability <sup>[19]</sup>.

Gutta percha, when heated, changes the physical characteristics of not more than 4 to 5mm <sup>[19]</sup>. The gutta percha molding temperature without affecting its molecular transformation for compaction was found to be in the range of 40-60C <sup>[20-22]</sup>. It has been shown that heating and compacting gutta percha two times at 3mm from the apex can mold the gutta percha completely <sup>[20]</sup>.

The gutta percha undergoes decomposition when the temperature was raised to 100C and heating to 130C causes chemical changes affecting its physical properties <sup>[19]</sup>.

### **External root surface and supporting structures**

The thermosoftening of gutta percha can lead to temperature rise on the root surfaces. It has been reported that the temperature elevations of 10C above body temperature of duration more than 1 minute is sufficient in causing injury to the bone and supporting structures <sup>[23]</sup>. Most thermal damage to tooth supporting tissue from warm compaction technique appears to be confined and short lived as no reports of damage has yet been reported.

The root dentine acts as a thermal insulator and thicker the dentine structure, less heat will be transferred to external root surface. The gutta percha is considered as a poor thermal conductor of heat and transmits less heat. It limits heat conduction from the canal by absorbing the heat and prevents heat rise on the root surface <sup>[24]</sup>. In clinical environment, the temperature rise on the root surface is less because of the periodontal blood flow and wetness of the dentine from dentinal fluids <sup>[25]</sup>.

The amount of injected heated gutta percha plays an important role on the temperature rise on the root surface. When the gutta percha was heated to 160C, the root surface temperature of maxillary central incisors resulted in increase of approximately 8.5C and the mandibular central incisors resulted in increase of 22.1C <sup>[26]</sup>. The temperature changes on the outer root surfaces in teeth with thin dentinal walls can show high values than the key values of causing injury to supporting structures. The temperature rise was higher in middle and coronal third rather than the apical third.

The heating time should be limited to 3seconds particularly in the area where the dentine thickness is less. When a plugger at 200C was activated for approx 3sec during compaction resulted in 9.9C temperature increase on periodontal ligament in the dangerous zone of the mesiobuccal root canal of mandibular first molar. When this plugger was activated for approximately 4 seconds, the temperature increase was 11.9C <sup>[27]</sup>.

## **2. Sealing ability**

Root canal obturation seals the root canal system to prevent its invasion and/or growth of microorganisms. An appropriate coronal seal and a complete apical seal greatly enhances the success of endodontic treatments.

The coronal leakage experimental model <sup>[28]</sup> of root canals filled by warm vertical compaction showed the sealing ability of these technique was comparable to cold lateral condensation <sup>[28]</sup>. The quality of endodontic sealing in the apical 4mm of narrow and curved canals <sup>[29]</sup> by measuring voids extension, voids maximum width, and dye penetration showed excellent adaptation of apical gutta percha to root canal walls and has shown least leakage over cold lateral condensation techniques <sup>[30]</sup>.

The sealing ability of obturation material can be assessed by

- Bond strength to Dentin
- Sealer penetration into dentinal tubules

## **Bond strength to dentin**

Gutta-percha does not have adhesive qualities and cannot provide a complete seal to the dentinal walls and results in poor sealing quality. Sealers are used as an adhesive to both the radicular dentin and the core filling for a hermetic seal. It fills the irregularities of the root canal system and resist disruption during tooth function. The increase adhesion of obturating material to the radicular dentin reinforce the restored tooth, provide a better resistance to root fracture<sup>31</sup> and results in clinical longevity.

Warm obturation techniques shown to effectively fill in canal irregularities, and form a thicker filling with less voids formation. The adhesion of endodontic sealer to root canal dentine found to be affected by the obturation technique. Warm vertical condensation technique produce greater bond strength of AH plus sealer to the intraradicular dentin <sup>[32]</sup>. The bond strength of total fill BC (Bioceramic) sealer was significantly higher than that of AH plus sealer <sup>[33]</sup>. The warm vertical compaction group of bioceramic group showed lower bond strength than cold lateral compaction group <sup>[33]</sup>. The push out bond strength of calcium silicate-based cements (MTA plus sealer and endosequence BC sealer) with thermoplasticized obturation technique was found to be lower when compared with single cone and cold lateral condensation (CLC) <sup>[34, 35]</sup>.

The thermoplasticized technique lowered the bond strength of the sealers especially endosequence BC sealer. This may be due to the chemical structure of bioceramic sealer (hydrated calcium silicate is composed of an inorganic matrix of calcium silicate hydrate enveloping unreacted silicate granules with water-filled microspaces in-between), when subject to heat application lead to water desorption, weight loss and microstructural changes in the cement. However, this water loss may be compensated by moisture from the root canal system during the setting reaction <sup>[33]</sup>.

## **Sealer penetration into dentinal tubules**

A closer approximation of gutta-percha to the canal wall and sealer penetration into the dentin would limit or restrict the invasion of microorganisms and their by-products responsible for periapical disease. The penetration of endodontic sealers into dentinal tubules is directly influenced by smear layer, physical and chemical properties of the sealer and root canal filling technique.

When the root canal is filled, the compaction forces on the gutta-percha cones produce pressure on the canal walls resulting in more interlinkage of the sealer and the root dentin <sup>[36]</sup>. The vertical compaction techniques has

shown the highest penetration of sealer into the dentinal tubules <sup>[32]</sup>. The greater penetration were observed for the cervical and middle thirds than for the apical third. This could be due to the quantity and diameter of the dentinal tubules of the root canal wall <sup>[32]</sup>.

The sealer penetration is primarily a function of dentinal tubules permeability and the properties of sealer used. The patent dentinal tubules and the sealer cements with sufficient flow, wetting and bonding potential should be able to penetrate and seal the canal. The frequency and depth of sealer penetration were unrelated to the obturation technique employed <sup>[37]</sup>.

Sealer enhances the sealing ability but to prevent disruption during function the obturation should have more volume of the core material and less amount of sealer. No material can completely seal the root canal and that no obturation technique completely avoids the microfiltration of microorganisms. The warm vertical condensation tech showed better sealing than lateral condensation. This may be due to the fact that thermoplasticized GP can easily reach the root canal irregularities and produces greater percentage of gutta percha in the canal.

### **3. Stresses generated during warm vertical condensation technique**

It has been observed by many investigators that stresses generated from excessive pressure during obturation can lead to vertical root fracture <sup>[38]</sup>. Studies have shown that vertical root fracture occurs most commonly in the buccolingual direction of the tooth, may start at or between the apex and the crown and is a root cause for 4.3% of endodontic failures <sup>[39]</sup>.

The stresses generated during warm vertical condensation technique has been investigated with different canal tapers and was found that the highest stresses were generated in the apical third of smallest taper canal during the insertion of first gutta percha increment. It was reported that root fracture originated at the apical third is likely to be initiated during filling and fracture originating at the cervical portion is likely caused by occlusal loads <sup>[39]</sup>.

The tooth with certain defects such as internal resorption, root perforation which might weakens the tooth and its supporting structures. Such teeth when filled by warm vertical compaction forces can survive the impact without premature root fracture provided the obturation is performed skillfully (without undue application of force through the tip of the plugger to the canal wall) <sup>[40]</sup>.

It was observed that the force generated and the heat transmitted by heated plugger during obturation creates undue stresses in the root dentin, affecting the fracture resistance adversely <sup>[3]</sup>. The different obturation techniques significantly influenced the root strains in maxillary central incisors when strain gauges were mounted on the coronal and apical one thirds of the root surface. The obtura system generated the highest strains. It was noted that the mean load required to cause vertical root fracture was significantly higher than the load used in obturation <sup>[38]</sup>.

The different taper canals having varying degree of curvature when subjected to vertical compaction obturation technique have shown different stress patterns <sup>[41]</sup>. There was no significant difference between the mean of fracture load of straight, moderate and severe curvature among the same group taper but 6% groups showed higher fracture resistance than 2% taper groups. Thus increasing the canal taper will decrease the internal stresses within the root canal. The forces generated during obturation in the root dentin can be minimized by plugger loading when kept within the safety range of compaction force.

#### **4. Treatment outcomes**

The objective of root canal obturation is to fill the root canal space and to seal the accessory canals between the main canal and the periodontium. The seal provides better prognosis for the tooth. A root canal filling should be well condensed, well adapted to canal walls, seal all canal irregularities and should terminate at the apical seat <sup>[42]</sup>. The treatment outcomes of obturation techniques can be assessed by clinical and radiographic success <sup>[45]</sup>.

The clinical outcomes have been assessed from

1. Postoperative pain prevalence <sup>[43, 44]</sup>
2. Clinical success rate <sup>[45, 46]</sup>

The clinical success was defined as functional and asymptomatic teeth after endodontic treatment.

The radiographic success outcomes were evaluated with <sup>[45]</sup>

1. The level of root canal filling in relation to the root apex
2. In cases without apical lesions, cessation of occurrence of periapical radiolucencies
3. In cases with apical lesions, reduction in size or complete resolution of periapical radiolucencies

The clinical studies add to the existing knowledge and provides pertinent recommendations. It has been shown that the maximum number of cases of chronic apical periodontitis develops at 1 year after filling <sup>[43]</sup>. The postoperative pain prevalence and long-term outcomes between the cold lateral condensation (CLC) and warm GP obturation <sup>[43]</sup> were studied in the meta-analysis of 9 out of 10 randomised clinical trial and found similar results between the two techniques. The postobturation pain after obturating with system B and obtura II in 60 patients shown no significant difference however the rate of pain was higher in obtura II than system B <sup>[44]</sup>.

The healing rate of periapical lesion 24 months after treatment with WVC and CLC technique shown the decrease of lesions was from 44 to 15% in the CLC whereas in WVC obturation from 59 to 5%. A difference of 10% was seen between the two technique groups <sup>[42]</sup>. The clinical and radiographic outcomes of lateral condensation and WVC in 290 patients with preoperative periapical lesions with a follow up of five years shown a significantly higher success rate for WVC <sup>[45]</sup>.

The root filling technique affects the treatment outcome and was found the cases filled with vertical compaction healed more (95%) than those filled with lateral condensation (85%) <sup>[46]</sup>. The effect of cold lateral condensation and obtura II condensation on the radiographic quality of obturation in molar teeth of 60 patients has shown similar results with postobturation voids and apical termination <sup>[47]</sup>.

The overextension in the warm GP obturation group was more often noticed than with the CLC group <sup>[42, 43]</sup> Proper caution taken during working length determination, apical width preparation and while depositing warm GP can lead to reduction in overextension of warm GP.

## **5. Various shapes of canals**

### **Oval shaped canals**

Oval-or ribbon-shaped canals may be seen in approximately 25% of teeth <sup>[48]</sup>. Because of the anatomy, oval shaped canals are difficult to clean and fill the root canal space. The prepared canal shows a central circular bulge with irregular shape <sup>[49]</sup>. The uninstrumented areas within the canals are often found. The nonuniform shape and poorly cleaned canal may impact the standards of root fillings.

Studies has been done to evaluate the obturation technique in oval canals of mandibular incisor <sup>[49]</sup>, mandibular premolar <sup>[50]</sup> and maxillary premolar <sup>[51]</sup> or artificially created canal <sup>[52]</sup>. The vertical compaction of warm gutta percha achieves a better quality of fill than cold lateral compaction of gutta-percha cones in oval canals <sup>[49]</sup>. The percentage of gutta

percha filled canal area was more appreciable in warm GP compaction than the cold GP compaction. The warm vertical compaction has significantly lower percentage volume range of voids than cold lateral [51].

The obturation of oval shaped canals is greatly demanding than the canals with round cross section. The vertical compaction of warm gutta percha shown superior results. The percentage of gutta percha area in an artificially created oval canals filled with gutta percha adopting continuous wave technique together with various plugger temperature setting and penetration depth was estimated and was found that it was affected by penetration depth of the plugger not the plugger temperature [52].

### **Lateral canals**

Numerous studies have shown that substantial proportion of lateral canals are found in apical thirds of the root [53]. The ability of root canal filling material to fill and seal the root canal system is important for the success of endodontic treatment. Various branching of the root canal system have a narrow orifices which measures from 50 to 150  $\mu\text{m}$  [54]. The smaller width together with their site within the root canal system poses inherent challenges in filling these branched canals.

Various studies [55, 56] have been done to evaluate the obturation techniques best suited for filling of lateral canals. The simulated lateral canals were created on the root surface by means of #15K files and were filled with different obturation technique and were subjected to three dimensional internal visualization of filling or to radiographic analysis. Warm compaction of filling materials has demonstrated its ability to seal lateral canals [55, 56]. Continuous wave of Condensation technique has manifested exceeding large amount of filled lateral canals. The coronal third of the canal produced many filled lateral canals than the remaining thirds [55]. The vertical compaction of warm gutta-percha filled the lateral canals more successfully than the lateral compaction of gutta percha [56].

### **Immature teeth**

The filling of teeth with immature apical formation presents challenges to the clinician. This is because the immature teeth have large open apices and have dentinal walls which are deviant and fragile. These walls if not treated properly may fracture during or after endodontic treatment. Such teeth were managed earlier by extended use of calcium hydroxide in the root canal space for apical hard-tissue blockade. With the development of bioceramic materials (MTA and biodentine) one-step insertion of bioceramic barrier in the apical one-third of the root canal and thermoplasticized gutta-percha filling of the remaining canal space is now widely used [57].

The variations of temperature on the external root surface of artificially reproduced immature teeth obturation using high heat thermoplasticized technique was contemplated and has shown that the insertion of thermoplastic gutta in the canal resulted in increase in temperature within a few seconds. Caution must be exercised while using high-temperature obturation methods in roots with thin dentinal walls <sup>[58]</sup>.

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## **Chapter - 6**

### **Implant Maintenance**

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# Chapter - 6

## Implant Maintenance

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### Abstract

Restoration of missing dentition with implants is currently the gold standard treatment. But, mere placement of the implant and its prosthetic rehabilitation does not ensure success in the long run. Maintenance of the osseointegrated implant and the prosthesis placed, does. Implant maintenance starts from the day of implant placement and continues throughout the life of the implant. It spans from meticulous assessment of the peri-implant tissues to instrumentation and most importantly implant home care carried out by the patient. This chapter discusses in detail about various aspects of implant maintenance.

**Keywords:** implant maintenance regimen, peri-implant instrumentation, implant home-care

### Introduction

Implant maintenance has evolved over decades from various supportive therapies to evidence-based protocols.

The peri-implant tissue system is similar yet different than our conventional periodontium surrounding the tooth. Tissues surrounding our tooth, i.e. periodontium are characterized by four types of tissues: periodontal ligament, cementum, alveolar bone, and gingiva. Whereas, tissue surrounding dental implants, known as peri-implant tissues are composed of implant supporting alveolar bone & surrounding mucosa (peri-implant mucosa) with absence of intercalated tissues between implant surface and bone, equivalent to periodontal ligament and cementum as in natural teeth.

### Need for implant maintenance

Despite the anatomical differences in supporting tissues, inflammation finds its way around dental implants just like natural teeth. Analogous to gingivitis and periodontitis affecting natural teeth, inflammation and

pathology of soft and hard peri-implant tissues is termed as peri-implant mucositis and peri-implantitis.

Peri-implant mucositis is a reversible condition characterised by peri-implant gingival inflammation without bone loss or loss of attachment. Clinically, bleeding on peri-implant probing may be present without suppuration. If peri-mucositis is not treated, it may progress to peri-implantitis which includes loss of bone and possible loss of osseointegration as well. Clinically, we may have mucosal swelling, deep probing depths, presence of pockets, suppuration, gingival recession accompanied by bone loss and, in extreme cases, implant mobility may be present.

Poor oral hygiene maintenance, among others (table 1) has been attributed as a major cause of peri-implant diseases. Poor oral hygiene maintenance leads to formation of biofilm, which contain microflora nearly identical to that found on adjacent teeth <sup>[1]</sup>. Natural teeth possess transseptal or dentogingival fibres (Sharpey's fibres) that insert into cementum and tend to form a seal against bacteria. These fibres are absent in implants and the fibres that exist are largely circumferential in nature causing implants to be susceptible to microbial invasion.

Laxity in implant maintenance by the patient, dentist or both can lead to such inflammatory conditions, eventually implant loss and treatment failure. (standby) Thus, thorough patient instructions and optimum recall and maintenance protocol is advised.

**Table 1:** Etiology of peri-implant diseases

• Poor oral hygiene causing accumulation of plaque and calculus
• Poor compliance with supportive procedures
• Poor prosthetic design
• Retained cement
• Unfavourable occlusal stress

### **Implant maintenance**

After successful implant placement and restoration, the longevity of the implant depends highly on the maintenance protocol followed. There is no definitive maintenance protocol advised for dental implants, instead, a suitable protocol tailored to the clinical situation is followed. Maintenance protocol is devised in accordance to the type of restoration, patients oral and systemic health, and past dental history.

Prior to maintenance the clinician should review the patients' medical, social and dental history. Any changes to patient history like diabetes,

smoking or occlusal interferences which can make the patient more susceptible to peri-implant diseases should be recorded and reviewed.

Alani *et al.* [2] suggest a 10 point inspection at recall and maintenance appointments (Table 2).

**Table 2:** Ten point inspection

<b>1. Plaque and calculus assessment</b>
Presence or absence of plaque, calculus or cement should be noted. Oral hygiene should be reinforced at this stage.
<b>2. Probing</b>
The implant should be probed at the same four points and angulations as the initial readings post restoration. If there has been an increase in probing then this may signify peri-implant mucositis or peri-implantitis.
<b>3. Bleeding or suppuration</b>
A positive finding of bleeding indicates inflammation with or without bone loss. Suppuration may mean the presence of advanced peri-implantitis. Pressing the gingival margin may be better to detect suppuration over probing.
<b>4. Recession</b>
The presence of progressing recession may either be a sign of progressive soft tissue changes or associated with mucositis or peri-implantitis.
<b>5. Mobility</b>
Any mobility with an implant must be investigated. This suggests either a restorative complication (loose abutment or screw) or complete loss of integration.
<b>6. Occlusion</b>
The occlusion of the implant should be kept light enough to allow three layers of shimstock to pass through with the patient in maximum intercuspation as well as in lateral excursions. Any faceting should be investigated.
<b>7. Contacts</b>
This should be assessed with floss. A definitive contact point is ideal. A loose or open contact may lead to food impaction which subsequently causes biofilm development on the implant or adjacent tooth.
<b>8. Percussion sensitivity</b>
A positive finding may be indicative of a biological or restorative complication.
<b>9. Radiographic assessment</b>
If findings from points 1-8 show the possibility of clinical changes relating to a peri-implant infection then a radiograph should be taken. This should be compared to previous radiographs to assess bone levels.
<b>10. Instrumentation</b>
This is performed supra-gingivally with a prophy cup and prophy paste. Sub-gingivally a titanium scaler can be used to dislodge any plaque, calculus or cement. A glycine-based air polishing powder can also be used to decontaminate subgingivally, as well as threads of exposed implants. A cotton pledget soaked in Chlorhexidine to swab the area may be utilised as the final step.

## Plaque and calculus assessment

Implants placed in the oral cavity represent artificial surfaces colonized by bacteria from saliva and ecologic niches such as periodontal pockets, tonsils, and crypts of the tongue. These bacterial colonization if left unmonitored and un-treated can lead to peri-implant inflammation. Thus, amount of plaque around implants and appearance of mucosal tissues should be evaluated and documented. Various indices can be used to record plaque and gingival status at every appointment. Mombelli and co-workers<sup>[3]</sup> modified the original Plaque Index introduced by Silness and Løe to assess biofilm formation in the marginal area around implants (Table 3). Lindquist and colleagues<sup>[4]</sup> (Table 4) have provided implant specific plaque index as well. Rougher implant and/or abutment surfaces have shown to accumulate higher amount of plaque as compared to smooth surfaces. ASPE and colleagues<sup>[5]</sup> have proposed an index to assess mucosal condition around dental implants. (Table 5) Rightly said by Humphrey, Consistent utilization of the selected index is more important than the choice of index<sup>[6]</sup>.

**Table 3:** Assessment of plaque accumulation with modified Plaque index (mPII) by Mombelli<sup>[3]</sup>

<b>Score 0</b>	<b>No detection of plaque</b>
Score 1	Plaque only recognized by running a probe across the smooth marginal surface of the implant
Score 2	Plaque which can be seen by the naked eye
Score 3	Abundance of soft matter

**Table 4:** Assessment of plaque accumulation around Implants by Lindquist<sup>[4]</sup>

Score 0	No visible plaque
Score 1	Local plaque accumulation (<25% of visible abutment area)
Score 2	General plaque accumulation greater than 25% (>25% of visible abutment area)

**Table 5:** Mucosal assessment index around Implants by ASPE<sup>[5]</sup>

<b>Score 0</b>	<b>Normal mucosa</b>
Score 1	Minimal inflammation with color change and minor edema
Score 2	Moderate inflammation with redness, edema and glazing
Score 3	Severe inflammation with redness, edema, ulceration and spontaneous bleeding without probing

## Probing

Peri-implant probing should be performed to determine the location of base of a pocket relative to a known and documented fixed landmark on the

implant or its supra-structure. Post-restoration, an initial probing depth reading should be obtained to serve as baseline data for monitoring implant and peri-implant tissue health. Probing around implants often tends to be more difficult than around teeth due to the need to navigate around the implant suprastructure. Where the restoration is bulky, reproducible probing depths may only be possible if the restoration is removed to assist direct visual examination. One suggestion has been to use plastic probes (TPS or WHO 621) due to their superior flexibility and ability to navigate around the implant suprastructure [7]. Where access to implant is not compromised, use of a metal probe is recommended. A probing force of 0.25 NCM same as that of natural teeth is recommended. Probing should be performed along the long axis of the implant and not that of the restoration, at four points; two buccally and two palatally/lingually [8]. Successful implants generally have a probing depth of 3 mm, whereas pockets of 5 mm or more serve as a protected environment for bacteria and can exhibit signs of peri-implantitis but is not a definitive indicator.

### Bleeding or suppuration

Bleeding on probing represents an inflammatory response of tissues to the presence of a biofilm. Bleeding on probing alone is a poor indicator of presence of periodontal disease but, absence of bleeding on probing on successive maintenance visit is a good negative indicator of attachment loss. Momebelli and colleagues [3] have proposed modified sulcus bleeding index specific to implants. (Table 6) Suppuration can be detected by lightly pressing the marginal gingival against the implant surface. Present of suppuration serves as a strong evidence of presence of infection or peri-implant disease.

**Table 6:** Modified Sulcus bleeding index (mBI) by Mombelli [3]

Score 0	No bleeding when a periodontal probe is passed along the mucosal margin adjacent to the implant
Score 1	Isolated bleeding spots visible
Score 2	Blood forms a confluent red line on mucosal margin
Score 3	Heavy or profuse bleeding

### Mobility

Unlike a tooth, for which mobility is not a primary factor for longevity, mobility is a primary determining factor for implant health. Rigid fixation is usually the first clinical criterion evaluated for a dental implant. The techniques to assess rigid fixation are similar to those used for natural tooth mobility. Two rigid instruments apply a labiolingual force of approximately 500 g. The amplitude of tooth mobility may be rated from 0 to 4 on an implant mobility scale given by Misch [8] (Table 7).

If mobility exists, the aetiology should be ascertained, specifically if its due to screw loosening or implant failure. Mobility of the prosthesis without any evidence of pain is indicative of screw loosening. However, if pain persists when the prosthesis is moved in a buccolingual or apical direction, then its most likely due to implant failure <sup>[8]</sup>.

Though the recording of implant mobility may be specific-but it is not a sensitive clinical parameter in detecting loss of osseointegration, this parameter more likely detects the final stage of osseo-disintegration and therefore, represents late implant loss.

An electronic device (Periotest) has been recommended to monitor initial degrees of implant mobility, but the prognostic accuracy of Periotest value for the diagnosis of peri-implantitis and early signs of implant failure has been criticized because of the lack of resolution, poor sensitivity, and susceptibility to operator variables <sup>[9]</sup>. Recently, a non-invasive device based on the principles of resonance frequency analysis (RFA) has been developed to measure primary implant stability and to monitor implant stability over time. This method not only evaluates the stiffness of the bone-implant interface but also allows the detection of any increase or decrease in implant stability that otherwise could not be clinically perceived.

**Table 7:** Clinical implant mobility scale by Misch <sup>[8]</sup>

Scale 0	Absence of clinical mobility with 500 g in any direction
Scale 1	Slight detectable horizontal movement
Scale 2	Moderate visible horizontal mobility up to 0.5 mm
Scale 3	Severe horizontal movement greater than 0.5 mm
Scale 4	Visible moderate to severe horizontal and any visible vertical movement

## **Occlusion**

Ideally, Implant protected occlusion should be present. Traumatic occlusion has shown to be a cause for peri-implant bone loss. Upon occlusion, natural teeth should contact before implant contact. During light contact, extra thin articulating paper should be easily pulled through the implant contact without any resistance. Whereas, during heavy contact, minimal resistance should be present. Any signs of occlusal disharmonies, such as premature contacts or interferences, should be identified and corrected to prevent occlusal overload which can in turn cause a host of problems, including loosening of abutment screws, implant failure and prosthetic failure.

## **Radiographic assessment**

Radiographs should be taken once the restorations are definitively placed to provide a baseline for future reference and help to confirm optimal

restoration seating. Marginal bone changes during the first year of restoration maybe related to physiological bone remodelling and establishment of biologic width, and should not be confused with peri-implant disease.

A radiograph only illustrates clearly the mesial and distal crestal levels of bone. However, early bone loss often occurs on the facial aspect of the implant. An absence of radiolucency around an implant does not mean bone is present at the interface, especially in the anterior mandible. As much as 40% decrease in density is necessary to produce a traditional radiographic difference in this region because of the dense cortical bone <sup>[10]</sup>.

Radiographs have their limitations when interpreting a three-dimensional pathologic process. For example, interproximal bone levels may appear to be intact radiographically but clinically a significant peri-implantitis lesion can be present, especially on the buccal aspect. The radiopacity of implants when compared to teeth may reduce the sensitivity of radiographs when attempting to detect peri- implant problems. Conventional radiography yields a high proportion of false negative findings, i.e., it has low sensitivity in the detection of early pathologic and/or bone remodeling changes. Therefore, radiographic methods are confirmatory rather than exploratory and should only be considered in conjunction with assessment of the clinical parameters.

Rensik <sup>[10]</sup> has suggested a comprehensive radiographic pre-operative, intra-operative and post-operative protocol. His post-operative protocol suggests, a peri-apical radiograph once annually for the first 3 years after implant prosthesis placement to monitor bone level. After 3 years, peri-apical radiograph every 2 years.

### **Maintenance therapy**

Following evaluation of the implant and peri-implant tissue status, the decision of performing maintenance therapy around the implant and peri-implant tissues should be undertaken. Mombelli <sup>[11]</sup> suggested a cumulative interceptive supportive therapy (CIST) for instrumentation protocol based on plaque index, Bleeding on probing and bone loss. (Chart 1) It is based on periodic monitoring with implementation of treatment as thresholds for a particular condition are met. The first step is protocol (A), then (B) and, if conditions continue to worsen, the patient may require more advanced treatment, i.e. execution of protocol (C), and finally (D). To control inflammation in peri- implant mucositis, that is, implants with minimal increase in pocket depth, slight (+) bleeding on probing, marginal erythema, plaque, and/or calculus, Protocol (A) is implemented.

The endpoint of the therapy is resolution of inflammation with careful mechanical debridement, swabbing with 0.12% chlorhexidine twice daily, and

a review of home care and patient motivation. Protocol (B) is carried out for conditions that exhibit features similar to mucositis but with deeper pocket depths (4-5 mm) but without loss of supporting bone.

Protocol (C) consists of a more intensive approach and is used in conditions where there is radiographic evidence of osseointegrated bone loss of <2 mm and probing pocket depths >5 mm. The strategy should comprise a combination of the modalities for protocols (A) and (B) with the addition of systemic antibiotic therapy.

In cases of frank peri-implantitis that reveal probing depths (>5 mm), (+) bleeding on probing, plaque/calculus, and peri- implant bone loss of >2 mm, Protocol (D) is initiated along with the other three protocols.

In 2004, Lang *et al.* [12] modified the CIST protocol and called it the AKUT protocol. (Table 8) The basis of this concept is a regular recall of the implanted patient and repeated assessment of plaque, bleeding, suppuration, pockets, and radiological evidence of bone loss.

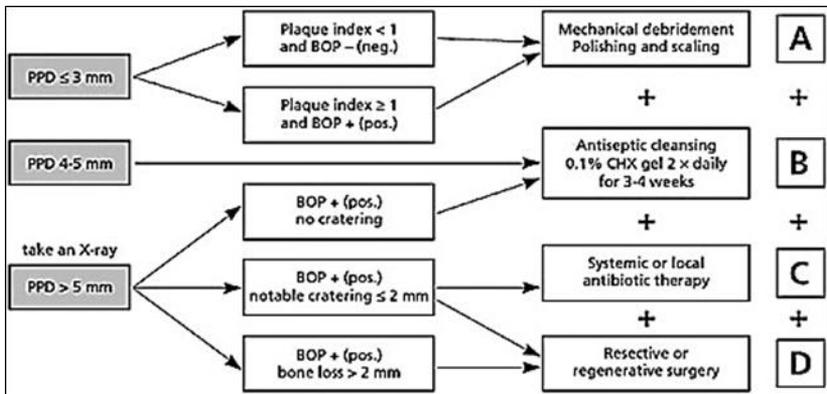


Chart 1: CIST protocol by Mombelli [12]

Table 8: AKUT protocol by Lang [12]

Stage	Result	Therapy
	Pocket depth (PD) < 3 mm, no plaque or bleeding	No therapy
A	PD < 3 mm, plaque and/or bleeding on probing	Mechanically cleaning, polishing, oral hygienic instructions
B	PD 4-5 mm, radiologically no bone loss	Mechanically cleaning, polishing, oral hygienic instructions plus local anti-infective therapy (e.g. CHX)
C	PD > 5mm, radiologically bone loss <2mm	Mechanically cleaning, polishing, microbiological test, local and systemic

		anti-infective therapy
D	PD > 5 mm, radiologically bone loss > 2 mm	Resective or regenerative surgery

### Instrument selection

Rendering the implant surface free of plaque, debris and eradication of pathogenic microbes around the implant surface and in the peri-implant tissues, is the aim of instrumentation. But, if our instruments end up creating micro-scratches on the implant or abutment surface thereby creating niches for biofilm adherence would lead to a diametrically opposite effect. Materials like stainless steel which are harder than Titanium, scratch the titanium surface. Thus, the material of the instrument used plays a major role. For mechanical debridement, Scalers and curettes or ultrasonic scalers can be used. Ultrasonic scalers are recommended to be used only when the stainless-steel tip is covered with a protective sleeve. Mechanical debridement instruments are available in a variety of materials listed in Table 8.

**Table 8:** Materials for Instrumentation

Material of the instrument	Merits and demerits
Stainless steel	Much harder than titanium alloy; not recommended as they may alter the surface
Titanium coated curettes	Recommended; similar hardness as that of titanium surface and will not scratch the surface.
Carbon fiber	Softer than implant surface; will not damage the implant surface; prone to fracture
Teflon	Will not scratch the surface of the implant
Amorphous resin (Unfilled and filled resin)	Softer than titanium; recommended
Plastic	Recommended; leaves residue around the implant surface which can be removed during resective

### Instrumentation

To prevent trauma to the delicate peri-implant sulcus, instrumentation should be carried out using light pressure and horizontal, oblique, or vertical short working strokes. Upon insertion of the instrument, the blade should be closed against the abutment and then opened past the deposit, engaging it apically with the stroke extending coronally. When instrumentation needs to be carried out subgingivally to remove calculus or excess cement, it should be carried out with light strokes in a semi-circular pattern. Prostheses can sometimes limit access of the scaler, and, in such cases, an ultrasonic or sonic scaler covered with a plastic sleeve can be used to remove deposits. The

nonporous titanium surface calculus that forms around implants tends to be softer than calculus adhering to a natural tooth and is mostly supragingival.

## **Polishing**

Low-abrasive amino acid glycine powder has been shown to be an effective treatment for removing biofilm without damaging the implant surface or hard and soft tissues. This piezo instrument (Hu-Friedy, Chicago, Ill.) uses a special handpiece with a plastic tube nozzle with three orthogonally oriented holes. An air-powder mixture with reduced pressure is expelled through the nozzle, which prevents the formation of air emphysema complications. The nozzle is moved in a circumferential movement around the implant surface. The clinician should be careful to use the powder only in areas where access is available and a post-treatment rinse can remove any residue.

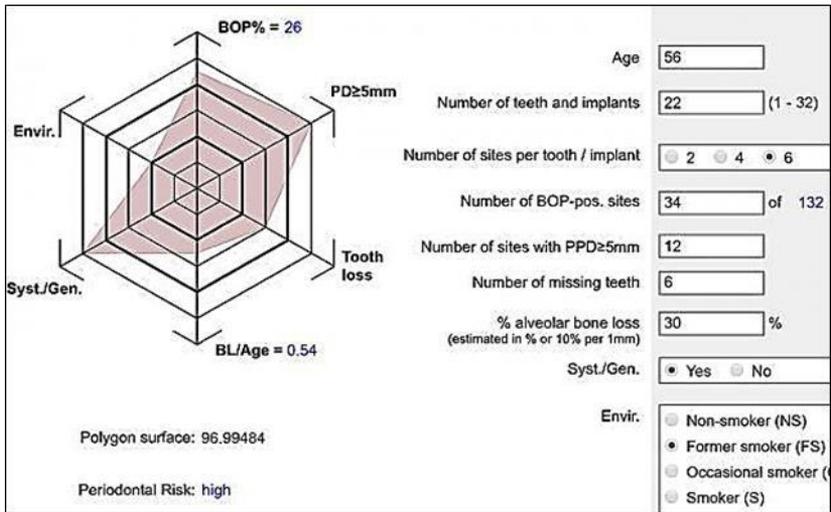
## **Maintenance protocol**

U Bagger and colleagues <sup>[13]</sup> and Mombelli <sup>[14]</sup> suggest using Periodontal risk assessment tool by Lang & Tornetti <sup>[15]</sup> for deciding upon a maintenance interval. The tool help's visualise a patients individual risk for disease recurrence using a spider- chart (Figure 1)-a graph showing 6 variables, potentially increasing the risk on axes, all starting from a single point in the middle.

The variables are:

- The percentage of bleeding on probing
- The number of residual pockets > 4 mm
- The number of lost teeth
- Loss of periodontal support in relation to the patient's age
- Systemic and genetic conditions
- Environmental factors, such as cigarette smoking

Data suggesting an effect on risk for disease recurrence have been presented for each of these criteria. The area of the polygon formed by connecting the data values on each axis is assumed to represent the overall risk of a person to experience disease recurrence. The tool considers overall dentition along with the implants (and not implants individually) to determine the recall frequency, serving as a major drawback.



**Fig 1:** Periodontal risk assessment tool (Photograph courtesy; perio-tools.com)

### Home care instructions

The patient must initiate the implant care regimen immediately after surgical placement with one-stage system, after exposure of the implant site in the two-stage system and upon premature exposure of the implant healing screw in the two-stage system. However, during healing periods, when mechanical plaque control is contraindicated, chemical agents (e.g., chlorhexidine) should be used. After every maintenance appointment, oral hygiene instructions should be re-enforced depending upon the oral hygiene status of the individual.

### Brushing

Twice daily cleaning of implants to remove bacterial plaque accumulations should be accomplished using a soft toothbrush or a very gentle power brush. The modified Bass technique should be used or a short, horizontal, back-and-forth movement may be incorporated into the hygiene regimen. The brush should be held at a 45-degree angle to the gingival tissue. Studies have shown electromechanical brushes to be superior over manual brushes for implant maintenance.

In difficult to access areas, small diameter toothbrushes like end tufted toothbrush or interdental brushes are recommended for use. A hollowed rubber cup may be used on the facial and lingual aspects of the implant and prosthesis. Interdental tooth brushes used should be plastic coated as metal may damage the implant surface. For an interdental brush, the tip should be

inserted tip interproximally in an occlusal direction and gentle rotary motion against the gingiva should be used. A low abrasive toothpaste is recommended to ensure no scratching of any exposed implant surface. Toothpastes containing 0.3% triclosan have been recommended in cases where inflammation is present.

### **Floss**

Floss is ideally used interproximally when a splinted prosthesis is present. There are many types of floss on the market, and generally it is highly recommended to use unwaxed tape or implant-specific floss in order to protect the tissue surrounding the implant. Alternatively for a bar-retained prostheses, full fixed prostheses, or wider interproximal spaces, a floss threader or a specialized floss that has a built-in threader is necessary. It is difficult to manoeuvre the floss in cases of over-contoured prosthesis. It is imperative that the patient is instructed on the proper technique of flossing around dental implants. Improper or over-aggressive flossing may lead to tissue trauma and resultant peri-implant soft tissue lesions.

### **Oral irrigator**

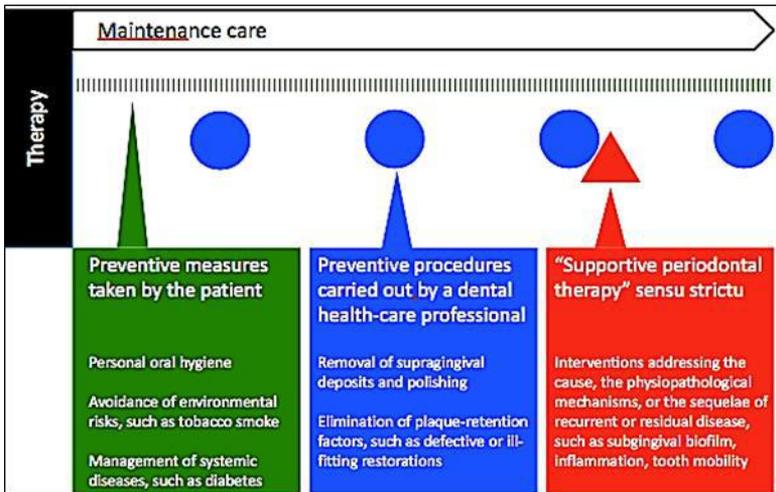
Oral irrigators like Air floss or waterpik may be beneficial in removing supra-gingival debris and in difficult to access areas. Oral irrigators should be advised to be used with a non-metal tip, once to twice daily in low to medium speeds to avoid damage to gingival tissues. In cases where inflammation is present, an antimicrobial like chlorhexidine can be suggested to be used as an irrigant.

### **Anti-microbial rinses**

Owing to its substantivity, Chlorhexidine gluconate is the most recommended mouth rinse. Studies have shown that a 30-second rinse of chlorhexidine inhibits 90% of oral bacteria for more than 5 hours. Chlorhexidine or cetylpyridinium chloride may be locally applied with a cotton swab or may be used as a rinse twice daily.

### **Conclusion**

The ongoing maintenance of dental implants is one of the most important factors for long-term health. Implant survival is a result of cumulative effort by the patient and the dental professional. As rightly mentioned by Mombelli<sup>[14]</sup>, implant maintenance consists of 3 components, namely, Preventive measures taken by the patient, preventive procedures carried out by dental health-care professional and supportive periodontal therapy. (Fig 2).



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## **Chapter - 7**

### **Growth Factors**

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# Chapter - 7

## Growth Factors

Dr. Shubham Kumar

### Abstract

Injury to the tissue initiates a cascade of events including inflammation, new tissue formation, and tissue remodelling, which finally leads to partial reconstruction of the wounded area. Wound healing involves an orderly sequence of events, which includes migration of specialized cells, angiogenesis and nerve sprouting occurring at the wound edge. Finally, a transition from granulation tissue to mature scar occurs, characterized by continued collagen synthesis and collagen catabolism. These processes at least in part are mediated by a series of low molecular weight polypeptides produced and released from the inflammatory cells, serum of injured blood vessels & from degranulating platelets and are referred to as *Growth Factors*. This chapter discusses about their role in wound healing.

**Keywords:** growth factors, wound healing, PDGF, FGF, BMP, TGF- $\beta$

### Introduction

Wound healing is characterized by an orchestrated cell proliferation, migration, adhesion and differentiation of into various tissues. The cells and their matrix synthesis are affected by a variety of polypeptide factors present in the local environment known as Growth Factors, which are derived from inflammatory cells, serum of injured blood vessels & from degranulating platelets during wound healing. Discussion of all the growth factors and their specific role in wound healing is beyond the scope of this chapter; however brief description of the following growth factors has been done:

- A. Platelet Derived Growth Factor (PDGF) Family
- B. Fibroblast Growth Factor (FGF) Family
- C. Epidermal Growth Factor (EGF) Family
- D. Vascular Endothelial Growth Factor (VEGF) Family
- E. Insulin like Growth Factor (IGF)
- F. Transforming Growth Factor- $\beta$
- G. Bone Morphogenic Proteins (BMP)

## H. Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF)

### A. Platelet Derived Growth Factor (PDGF) Family

PDGFs comprise a family of homo or heterodimeric growth factors (PDGF-AA, PDGF-AB, PDGF-BB, PDGF-CC, and PDGF-DD) and they exert their functions by binding to three different transmembrane tyrosine kinase receptors, which are homo- or heterodimers of an  $\alpha$  and a  $\beta$ -chain <sup>[1]</sup>. PDGF was the first growth factor shown to be chemotactic for cells migrating into the healing skin wound, such as neutrophils, monocytes, and fibroblasts. In addition, it enhances proliferation of fibroblasts and production of extracellular matrix by these cells. Finally, it stimulates fibroblasts to contract collagen matrices and induces the myofibroblast phenotype in these cells <sup>[1, 2]</sup>. Upon injury, PDGF is released in large amounts from degranulating platelets <sup>[3]</sup>, and it is present in wound fluid, particularly early after injury <sup>[4]</sup>. Furthermore, expression of PDGFs and their receptors has been demonstrated in various cells of murine, pig, and human wounds using *in situ* hybridization and immunohistochemistry.

The patterns of PDGF and PDGF receptor expression suggest a paracrine mechanism of action, since the ligands are predominantly expressed in the epidermis, whereas the receptors are found in the dermis and the granulation tissue. Interestingly, expression of PDGFs and their receptors was reduced in wounds of healing-impaired genetically diabetic mice and glucocorticoid treated mice <sup>[5, 6]</sup>, indicating that a certain expression level of PDGFs and their receptors is essential for normal repair.

On the other hand, augmented PDGF production might be involved in the pathogenesis of hypertrophic scars and keloids as suggested by the potent effect of PDGF on fibroblast proliferation and extracellular matrix production by these cells (see above), the presence of enhanced levels of this growth factor in hypertrophic scar tissue <sup>[7]</sup> and the increased responsiveness of keloid fibroblasts to PDGF <sup>[8]</sup>.

Based on its expression pattern in the healing wound and its known *in vitro* activities, PDGF has been suggested to have two major but distinct roles in wound repair: an early function to stimulate fibroblast proliferation and a later function to induce the myofibroblasts phenotype <sup>[2]</sup>.

### B. Fibroblast Growth Factor (FGF) Family

FGFs comprise a growing family of structurally related polypeptide growth factors, currently consisting of 18 members that are grouped into 6 subfamilies based on differences in sequence homology and phylogeny <sup>[9]</sup>.

FGFRs (Fibroblast Growth Factor Receptors) belong to the family of RTKs (Receptor Tyrosine Kinases) that consist of an extracellular ligand-binding domain linked to an intracellular catalytic protein kinase core, via a single-pass TM (Transmembrane) domain.

Classically, FGFRs are activated when two FGF molecules (in concert with heparan sulfate proteoglycans) bind to the extracellular domains, facilitating receptor dimerization. Ligand-induced dimerization of FGFRs leads to a conformational shift in the receptor structure and release of kinase auto-inhibition. This results in a 50-100-fold increase in kinase activity of the receptor, and consequential signal transduction primarily through the MAPK (mitogen-activated protein kinase) pathway, but also acting via PI3K (phosphoinositide 3-kinase), PLC $\gamma$  (phospholipase C $\gamma$ ) and STATs (signal transducers and activators of transcription), that ultimately orchestrate key processes such as proliferation, growth, differentiation, migration and survival <sup>[10]</sup>.

Additional complexity is achieved by alternative splicing in the extracellular domains of FGFR1–3, which dramatically affects their ligand binding specificities. Most FGFs bind to a specific subset of FGF receptors. FGF1, however, binds to all known receptors, and FGF7 specifically interacts with a splice variant of FGFR2, designated FGFR2IIIb <sup>[11]</sup>. A characteristic feature of FGFs is their interaction with heparin or heparan sulfate proteoglycans, which stabilizes FGFs to thermal denaturation and proteolysis, and which strongly limits their diffusibility. Most importantly, the interaction with heparin or heparan sulphate proteoglycans is essential for the activation of the signalling receptors <sup>[12]</sup>.

Most members of the FGF family have a broad mitogenic spectrum. They stimulate proliferation of various cells of mesodermal, ectodermal, and also endodermal origin. The only exception is FGF7 (Keratinocyte Growth Factor, KGF), which seems to be specific for epithelial cells, at least in the adult organism <sup>[93]</sup>. In addition to their mitogenic effects, FGFs also regulate migration and differentiation of their target cells, and some FGFs have been shown to be cytoprotective and to support cell survival under stress conditions <sup>[13]</sup>. Numerous *in vivo* effects of FGFs have been demonstrated, which suggest a role of these growth factors in wound repair. In particular, FGF1 and FGF2 were shown to stimulate angiogenesis in various assay systems <sup>[14]</sup>. Furthermore, FGFs are mitogenic for several cell types present at the wound site, including fibroblasts and keratinocytes. Thus FGFs are clear candidates for contributing to the wound healing response, and this hypothesis has been corroborated by a number of studies where local

application of FGF1, FGF2, FGF4, FGF7 or FGF10 stimulated tissue repair [13].

Some FGFs have been detected at the wound site, indicating that the endogenous proteins are also regulators of wound healing. FGF2 was found in human and porcine wound fluid, particularly at early stages after injury [15]. Using immunohistochemistry, FGF has been localized in injured adult mice skin but not in fetal wounds where FGF2 immunoreactivity was undetectable. It was suggested that this difference could explain at least in part the reduced amount of capillary formation seen in the foetal versus adult wounds [16]. In rat burn wounds, FGF2 immunoreactivity was detected in the regenerated epidermis, in a bandlike zone near the regenerated epidermis, in renewed capillaries, and in cells infiltrating in the granulation tissue [17].

In addition to FGF2, several studies have provided evidence for an important role of FGF7 and its receptor (FGFR2IIIb) in cutaneous wound repair. FGFR2IIIb is expressed in keratinocytes of the normal and wounded epidermis as well as in hair follicles of murine, porcine, and human wounds [18]. Impaired wound healing was seen in aged mice, and this impairment was associated with reduced levels of FGF2 and with a reduced angiogenic response in the skin of these mice upon addition of FGF2 [19]. The strong upregulation of this FGF in fibroblasts and DETCs ( $\gamma\delta$  T Cell receptor-bearing Dendritic Epidermal T - Cells) after skin injury and the expression of its receptor in keratinocytes suggested that FGF7 stimulates wound reepithelialisation in a paracrine manner.

Guo *et al.* [20] used embryonic stem cell technology to generate mice lacking FGF7. Most surprisingly, the healing process of full-thickness incisional wounds was not obviously affected by the lack of FGF7, and the proliferation rate of the keratinocytes at the wound edge was not altered. These data demonstrate that incisional wounds can heal in the absence of FGF7. Although FGF7 might normally be the most important ligand of FGFR2IIIb in the skin, the lack of this gene could be compensated for by other known ligands of this receptor. More recent data suggest that FGF10 is the principal candidate for effecting this compensation, since it is also expressed in normal and wounded skin [21].

The involvement of FGF signalling in human disease is well documented. Many studies have addressed the role of cell autonomous alterations of FGFR signalling pathways in cancer and many excellent reviews extensively cover the mutations and alterations of members of the FGFR subfamily of RTKs in human disease. Of the non-synonymous

mutations, FGF signalling was one of the most commonly mutated pathways with more than 1000 somatic mutations found in the coding exons of 518 protein kinase genes from over 200 different cancers [22].

### C. Epidermal Growth Factor (EGF) Family

The Epidermal Growth Factor (EGF) family of mitogens comprises several members including EGF, Transforming Growth Factor- $\alpha$  (TGF- $\alpha$ ), Heparin-Binding EGF (HB-EGF), Amphiregulin, Epiregulin, Betacellulin, Neuregulins, the recently discovered Epigen, as well as proteins encoded by Vaccinia virus and other poxviruses [23, 24, 25]. In addition, more distantly related proteins known as neuregulins (heregulins, neu differentiation factors, NDF 1-4) can also bind to some EGF receptor family members [25]. All these growth factors exert their functions by binding to four different high-affinity receptors.

The epidermal growth factor receptor (EGFR) was the first receptor tyrosine kinase (RTK) to be discovered and it is a transmembrane receptor of the ErbB family. This family is comprised of four related receptors: the epidermal growth factor receptor itself (EGFR/ErbB1/HER1), ErbB2 (HER2/neu), ErbB3 (HER3), and ErbB4 (HER4) [26]. These receptors trigger downstream signaling pathways that are not linear but consist of rich multilayered and cross-connected networks, which allow for horizontal interactions and permit multiple combinatorial responses. This may explain the variety of biological outcomes to activation of a specific receptor in a specific cell. Receptor activation leads to recruitment and phosphorylation of several intracellular substrates, which, in turn, engage mitogenic signaling and other tumor promoting activities.

Upon ligand binding, these receptors form homo- or heterodimers [25]. Over expression of these receptors, in particular of HER2, is often found in human cancers and is likely to have a causative role in tumorigenesis. In addition, a series of experimental and clinical studies have demonstrated a positive effect of EGF, TGF- $\alpha$  and HB-EGF on wound repair, suggesting that the endogenous growth factors are also involved in the healing process [27].

Grotendorst *et al.* [28] detected EGF-like factors in wound fluid collected from rats. In addition, substantial levels of EGF and TGF- $\alpha$  were found in wound fluid from skin graft donor site wounds in patients with small to moderate sized burn injuries [29]. Several publications report on the presence of HB-EGF in wound fluid. Thus this growth factor was shown to be present at high levels in human burn wound fluid [30]. Because HB-EGF is mitogenic

for fibroblasts and keratinocytes, it was suggested to play an important role in re-epithelialization and granulation tissue formation. Interestingly, it was shown to act synergistically with insulin-like growth factor-I (IGF-I), another growth factor present in wound fluid, in stimulating keratinocytes proliferation *in vitro* <sup>[31]</sup>.

In a search for the cellular source of these EGFR ligands in wounds, Rappolee *et al.* <sup>[32]</sup> detected TGF- $\alpha$  mRNA in isolated wound macrophages. With the use of *in situ* hybridization and immunohistochemistry, this growth factor was also detected in eosinophils in a rabbit cutaneous open wound model and also in hamster wounds <sup>[33, 34]</sup>. In addition, epidermal keratinocytes at the wound edge as well as hair follicle epithelial cells were identified as a source of TGF- $\alpha$  in partial-thickness murine burn wounds, in particular during the phase of keratinocytes proliferation <sup>[35]</sup>. HB-EGF was localized in the advancing epithelial margin, islands of regenerating epithelium within human burn wounds, and in eccrine sweat glands <sup>[30]</sup>.

In addition to these correlative data, recent functional studies revealed an important role of EGFR ligands in wound repair. All EGFR ligands are synthesized as membrane-anchored forms, which are proteolytically processed to the bioactive soluble forms <sup>[36]</sup>. Interestingly, the transmembrane forms are also able to stimulate the growth of adjacent cells in a juxtacrine manner, indicating that both transmembrane and soluble forms might play a role in wound healing. However, processed HB-EGF was detected in wound fluid <sup>[37]</sup>, suggesting that ligand shedding could play an important role in wound healing. These results indicate an important role of EGFR ligand shedding for keratinocyte migration *in vitro* and *in vivo* <sup>[38]</sup>.

#### **D. Vascular Endothelial Growth Factor (VEGF) Family**

Humans are complex multicellular organisms, and all cells require a dependable, finely controlled supply of oxygen. Therefore, a highly developed vascular system has evolved to ensure oxygen delivery to all the cells. The system needs to be maintained through angiogenesis, the process of new blood vessel development from pre-existing vasculature. This involves endothelial cell division, selective degradation of the basement membrane and the surrounding extracellular matrix, endothelial cell migration, and the formation of a tubular structure. Once blood vessels have been established, the endothelial cells undergo tissue-specific changes to generate functionally distinct vessels. Angiogenesis is subject to a complex control system with proangiogenic and antiangiogenic factors. In adults, angiogenesis is tightly controlled by this “angiogenic balance”, i.e., a

physiological balance between the stimulatory and inhibitory signals for blood vessel growth. In normal circumstances, the formation of new blood vessels occurs during wound healing, organ regeneration and in the female reproductive system during ovulation, menstruation, and the formation of the placenta. It is also an important factor in several pathological processes such as tumor growth, rheumatoid arthritis, diabetic retinopathy, and psoriasis.

Vascular Endothelial Growth Factor (VEGF), also called vascular permeability factor, has emerged as the single most important regulator of blood vessel formation in health and disease. The VEGF family currently comprises seven members: VEGF-A, VEGF-B, VEGF-C, VEGF-D, VEGF-E, VEGF-F, and PlGF (Placental Growth Factor). They exert their biological functions by binding to three different transmembrane tyrosine kinase receptors, designated VEGFR-1, VEGFR-2, and VEGFR-3 [39]. VEGF induces proliferation, sprouting, migration and tube formation of endothelial cells [40]. VEGF is also a potent survival factor for ECs during physiological and tumor angiogenesis and it has been shown to induce the expression of antiapoptotic proteins in the endothelial cells [41,42]. VEGF was originally described as a permeability factor, as it increases permeability of the endothelium through the formation of intercellular gaps, vesicovascular organelles, vacuoles and fenestrations [43]. VEGF also causes vasodilatation through the induction of the endothelial nitric oxide synthase (eNOS) and the subsequent increase in Nitric Oxide production [44, 45].

The biological functions of VEGF-A and its receptors VEGFR-1 and VEGFR-2 have been characterized in most detail. Based on a series of *in vitro* and *in vivo* studies, VEGF-A has been identified as a major regulator of vasculogenesis and angiogenesis during development [39], indicating that it might also be involved in the regulation of angiogenesis during wound healing. Besides angiogenesis, VEGF induces Haematopoietic Stem Cell mobilization from the bone marrow, monocyte chemoattraction, osteoblast-mediated bone formation and neuronal protection [40, 46]. Furthermore, VEGF stimulates inflammatory cell recruitment and promotes the expression of proteases implicated in pericellular matrix degradation in angiogenesis [47].

VEGF-A is a 34- to 42-kDa, dimeric, disulfide-bound glycoprotein. In normal tissues, the highest levels of VEGF-A mRNA are found in adult lung, kidney, heart, and adrenal gland. Lower, but still readily detectable, quantities of VEGF-A transcript levels occur in liver, spleen, and gastric mucosa. VEGF-A exists in at least seven homodimeric isoforms. VEGF-B was discovered in 1995. It is abundantly expressed in the adult myocardium, skeletal muscle, and pancreas. In mouse embryonal tissues, high expression

is seen in the developing heart, brown fat, muscle (including the smooth muscle layer in embryonic arteries) and in the spinal cord. In adult tissues, VEGF-C is expressed most prominently in heart, placenta, ovary, small intestine, and the thyroid gland, whereas in embryonal tissue, expression occurs where lymphatic vessels undergo sprouting from embryonic veins, such as the paramesonephric, axillary, and jugular areas. VEGF-D is found in adult tissues, particularly lung, heart, skeletal muscle, colon, and small intestine. In embryonal tissues, it is abundant in the developing lung. VEGF-E is an Orf virus-encoded VEGF (NZ-strains). The gene products have only 19 to 25% amino acid identity with VEGF, have no apparent basic domain, and seem to be involved in the process of pathological angiogenesis in virus-infected lesions. PlGF is predominantly expressed in the placenta, heart and lungs [48].

The important role of VEGF-A in wound healing was recently revealed in a study where application of neutralizing VEGF-A antibodies caused a striking reduction in wound angiogenesis, fluid accumulation, and granulation tissue formation in a pig wound model [49]. Furthermore, the angiogenic activity present in human wound fluid from later time points after injury was strongly inhibited by VEGF neutralization [50]. Expression of PLGF mRNA and protein was strongly upregulated in migrating keratinocytes of acute human skin wounds. Furthermore, endothelial cells of capillaries adjacent to the wound expressed PLGF [51]. A synergy between VEGF-A and PLGF was detected in these studies, indicating that the presence of both growth factors is important for normal wound angiogenesis. Besides the formation of new blood vessels, lymphangiogenesis occurs during the healing of skin wounds. Several groups have shown the formation of lymphatic vessels to be regulated via VEGFR-3 and its ligands VEGF-C and VEGF-D [52]. In a recent study using a pig wound model, VEGFR-3-positive lymphatic vessels were found in the wound granulation tissue [53]. Taken together, members of the VEGF family are likely to be major regulators of angiogenesis and lymphangiogenesis not only during development but also during cutaneous wound repair.

### **E. Insulin like Growth Factor (IGF)**

IGF-I and IGF-II are potent stimulators of mitogenesis and survival of many different cells types, and they exert their functions in an autocrine, paracrine, or endocrine manner. Their actions are mediated through the Type I IGF receptor, a tyrosine kinase that resembles the insulin receptor. In addition, IGF-II also binds to the IGF type II/mannose-6-phosphate receptor, which results in internalization and degradation of IGF-II [54]. The

availability of free IGF for interaction with the IGF-I receptor is modulated by six IGF-binding proteins (IGFBPs). In addition, IGFBPs have also been shown to have IGF independent effects on cell growth <sup>[55]</sup>. Several studies have revealed a beneficial effect of exogenous IGF-I on wound healing, in particular in combination with other growth factors <sup>[56]</sup>. In addition, liposome-mediated IGF-I gene transfer improved the pathophysiology of a thermal injury <sup>[57]</sup>. These findings suggested important activities of IGFs in the healing wound.

Several study group demonstrated expression of IGF-I and IGF-II in wounds of different species. In a rat ear freeze-thaw injury model immunohistochemical expression of IGF-I was seen only a few cells in the dermis and epidermis. However, all epidermal cells as well as macrophages and some other inflammatory cells were positive within 1-3 days after wounding <sup>[58]</sup>. Gartner MH (1992) used an incisional wound model as well as a subcutaneous sponge implant model to determine expression of IGF-I and IGF-II in the wound and found that mRNA levels of both IGFs increased significantly after injury in both models <sup>[59]</sup>. Increased IGF-I mRNA levels but unaltered IGF-I receptor expression were observed in a rat wound model where steel wire mesh cylinders were implanted in the subcutaneous tissue of the back <sup>[60]</sup>. Finally, in situ hybridization studies on porcine wounds revealed expression of IGF-I, IGF-I receptor, and IGF-II receptor mRNAs in epithelial cells of normal and wounded skin.

Several studies suggest a role of the IGF system in the wound healing abnormalities associated with diabetes and glucocorticoid treatment. One group found that streptozotocin-induced diabetes in rats caused a 42% reduction in wound fluid IGF-I levels <sup>[61]</sup>. Others analyzed the expression of IGF-I and IGF-II during wound healing in normal and genetically diabetic mice <sup>[62]</sup>. The normal induction of IGF-I mRNA expression was severely delayed and reduced in diabetic mice. Delayed induction was also seen for IGF-II, although peak concentrations of IGF-II mRNA were higher in diabetic compared with control mice. Consistent with the RNA data, a delayed appearance of the proteins was noted in diabetic animals. These findings are likely to be important for the pathogenesis of chronic human wounds, since IGF-I protein was absent in the basal layer of the epidermis and in fibroblasts of diabetic patients but not of healthy control patients. Furthermore, it was absent in the basal keratinocyte layer at the edge of human diabetic foot ulcers <sup>[63]</sup>.

Taken together, these studies suggest that reduced expression of IGFs and/or their receptors leads to impaired wound healing. On the other hand,

enhanced expression of IGF-I might lead to excessive scarring as suggested by the observed overexpression of IGF-I in postburn hypertrophic scar tissue compared with control skin. Because IGF-I was shown to increase the expression of the pro  $\alpha$  1(I) chain of type I procollagen and the pro  $\alpha$  1 (III) chain of type III procollagen in cultured dermal fibroblasts, these findings indicate a causative role of elevated IGF-I levels in the pathogenesis of hypertrophic scars <sup>[64]</sup>.

## **F. Transforming growth factor- $\beta$**

The TGF- $\beta$  superfamily encompasses a diverse range of proteins, many of which play important roles during cell proliferation, differentiation and apoptosis, homeostasis, disease, and repair. In the early 1980s, it had become apparent that cell growth is controlled by many polypeptides and hormones. A new hypothesis of 'autocrine secretion' was postulated, which suggested that polypeptide growth factors are able to cause malignant transformation of cells. A new polypeptide called SGF (Sarcoma Growth Factor) was discovered in cultures of transformed rat kidney fibroblasts <sup>[65]</sup>. Soon it became apparent that this factor is a mixture of at least two substances with different functions. They were called Transforming Growth Factor- $\alpha$  (TGF- $\alpha$ ) and Transforming Growth Factor- $\beta$  (TGF- $\beta$ ) <sup>[66]</sup>. TGF- $\beta$  was further described by Roberts and Sporn as a secreted polypeptide capable of inducing fibroblast growth and collagen production <sup>[67]</sup>. Soon after its discovery, TGF- $\beta$  was found to inhibit cell proliferation as well; thus, a dual role of this cytokine was recognized <sup>[68]</sup>.

The TGF- $\beta$  superfamily is composed of a large group of proteins, including the Activin/Inhibin family, Bone Morphogenetic Proteins (BMPs), Growth Differentiation Factors (GDFs), the TGF- $\beta$  subfamily, and the Glial Cell Line Derived Neurotrophic Factor (GDNF) family. The TGF- $\beta$  proteins have been discovered in a variety of species, including invertebrates as well as vertebrates. There are three known isoforms of TGF- $\beta$  (TGF- $\beta$ 1, TGF- $\beta$ 2 and TGF- $\beta$ 3) expressed in mammalian tissues; they contain highly conserved regions but diverge in several amino acid regions. All of them function through the same receptor signaling pathways <sup>[69]</sup>.

TGF- $\beta$ 1, the most abundant and ubiquitously expressed isoform, was cloned from human term placenta mRNA. In mouse development, Tgf- $\beta$ 1 mRNA and/or protein have been localized in cartilage, endochondral and membrane bone and skin, suggesting a role in the growth and differentiation of these tissues <sup>[70]</sup>. TGF- $\beta$ 2 was first described in human glioblastoma cells. It was found that TGF- $\beta$ 2 is capable of suppressing interleukin- 2-dependent

growth of T lymphocytes. Thereby, it was named Glioblastoma-derived T cell Suppressor Factor (G-TsF). Physiologically, TGF- $\beta$ 2 is expressed by neurons and astroglial cells in embryonic nervous system [71]. It is also important in tumor growth enhancing cell proliferation in an autocrine way and/or reducing immune surveillance of tumor development [72]. The third isoform, TGF- $\beta$ 3, was isolated from a cDNA library of human rhabdomyosarcoma cell line; it shares 80% of amino acid sequence with TGF- $\beta$ 1 and TGF- $\beta$ 2. Studies on mice demonstrated essential function of Tgf-  $\beta$ 3 in normal palate and lung morphogenesis and implicate this cytokine in epithelial-mesenchymal interaction [73, 74]. Its mRNA is present in lung adenocarcinoma and kidney carcinoma cell lines; interestingly, umbilical cord expresses very high level of TGF- $\beta$ 3 [75].

In most cells, three types of cell surface proteins mediate TGF- $\beta$  signaling: TGF- $\beta$  receptor I (T $\beta$ RI), II (T $\beta$ RII) and III (T $\beta$ RIII). Out of these three receptors, T $\beta$ RIII, also called betaglycan, is the largest (250-350 kD) and most abundant binding molecule. This cell-surface chondroitin sulfate/heparan sulfate proteoglycan is expressed on both fetal and adult tissues and most cell types. T $\beta$ RI and T $\beta$ RII mediate signal transduction. Both receptors are transmembrane serine/threonine kinases, which associate in a homo or heteromeric complex and act as tetramers.

SMADs are intracellular proteins that transduce extracellular signals from transforming growth factor beta ligands to the nucleus where they activate downstream gene transcription [76]. TGF- $\beta$  interacts with TGF- $\beta$  receptors and its effects are mediated via SMAD dependent & SMAD independent pathways [77]. The SMAD proteins are the only known latent cytoplasmic transcription factors that become directly activated by serine phosphorylation at their cognate receptors. SMADs can be classified into 3 groups based on their functions [78]:

- 1. Receptor-Regulated SMADs (R-SMADS):** SMAD1, SMAD2, SMAD3, SMAD5 and SMAD8.
- 2. Common SMAD (Co-SMAD):** SMAD4.
- 3. Inhibitory SMADs (I-SMADs):** SMAD6 and SMAD7.

Nearly 30 proteins have been identified as members of the TGF-beta superfamily in mammals, and can be classified based on whether they activate TGF- $\beta$ -specific R-Smads (AR-Smads) or BMP-specific R-Smads (BR-Smads). R-Smads form complexes with Co-Smads and translocate into the nucleus, where they regulate the transcription of target genes. AR-Smads bind to various proteins, including transcription factors and transcriptional

co-activators or co-repressors, whereas BR-Smads interact with other proteins less efficiently than AR-Smads. I-SMADs function as intracellular antagonists of RSMADs. Through stable interactions with activated serine/threonine receptors, they inhibit TGF- $\beta$  family signaling by preventing the activation of R-SMADs and Co-SMADs. Understanding the mechanisms of TGF-beta superfamily signalling is thus important for the development of new ways to treat various clinical diseases in which TGF-beta superfamily signalling is involved [79].

Immediately after wounding, TGF- $\beta$ 1 is released in large amounts from platelets [80]. This initial kick-start of active TGF- $\beta$ 1 from platelets serves as a chemoattractant for neutrophils, macrophages, fibroblasts, and these cell types further enhance TGF- $\beta$ 1 levels in various cell types. As well as active forms, latent TGF- $\beta$ s are also produced and sequestered within the wound matrix, allowing sustained release by proteolytic enzymes. This combination of different cellular sources and temporary storage ensures a continuous supply of TGF- $\beta$  throughout the repair process [81]. Several publications have reported on the presence of TGF- $\beta$ s in wound fluid of different species and expression of all three isoforms was detected in many different cell types during repair, with each isoform having a characteristic distribution in the wound tissue [82,83].

In most studies, a rapid induction of TGF- $\beta$ 1 and TGF- $\beta$ 2 was observed, in early stages of wound repair while an increase in TGF- $\beta$ 3 expression was seen at later stages [84]. On the basis of the expression pattern of TGF- $\beta$ s and their receptors in the healing skin wound and of exogenous TGF- $\beta$ , it has been suggested that the effect of TGF- $\beta$  on reepithelialisation appears paradoxical. The inhibitory effect of TGF- $\beta$  on keratinocyte proliferation after wounding *in vitro* and *in vivo* suggests TGF- $\beta$  as a negative regulator of reepithelialisation [85]. On the other hand, it also induces the expression of integrins necessary for keratinocyte migration across the fibronectin-rich provisional wound matrix [86]. Complementary to these data are findings suggesting that aberrant expression of TGF- $\beta$ s is associated with the wound healing defect seen in glucocorticoid-treated [87] and aged mice [88] as well as in diabetic rats [89].

Brown *et al.* [90] wounded transgenic mice deficient in TGF- $\beta$ 1 due to a targeted disruption of the *tgf- $\beta$*  gene. These animals were wounded at day 10 after birth. Full-thickness excisional wounds healed almost normally for the first few days in the TGF- $\beta$ 1 deficient mice. However, histological analysis of the wounds at day 10 after injury revealed a thinner, less vascular granulation tissue in the knock-out mice, which was dominated by a marked

inflammatory cell infiltrate. Furthermore, decreased reepithelialization and collagen deposition were. Superficially, this suggests that other TGF- $\beta$  isoforms or even different growth factors can compensate for the lack of TGF- $\beta$  1 in early wounds, but implies that TGF- $\beta$  1 plays a crucial role later in the repair process.

Several studies support an important role of TGF- $\beta$ s in cutaneous scarring. Strong and persistent expression of TGF- $\beta$ s and their receptors was detected in fibroblasts of human post burn hypertrophic scars <sup>[91]</sup> and over expression of TGF- $\beta$ 1 and TGF- $\beta$ 2 was found in keloid tissues and keloid derived fibroblasts <sup>[92]</sup>. Treatment of fetal wounds with different concentrations of TGF- $\beta$ 1 caused marked scarring of these wounds, demonstrating a direct involvement of TGF- $\beta$ 1 in cutaneous scarring <sup>[93]</sup>. In yet another study, topical application of a synthetic TGF- $\beta$  antagonist reduced scarring in porcine burn and excisional wounds as well as in rabbit skin excisions <sup>[94]</sup>.

Thus TGF- $\beta$  signaling is complex and finely regulated fundamental pathway, which has an important role during human development and adult life. It is broadly intertwined with other signaling pathways. Moreover, it is involved in carcinogenesis of solid tumors as well as hematological malignancies. Paradoxically, TGF- $\beta$  is both a tumor suppressor and tumor promoter.

### **G. Bone Morphogenic Proteins (BMP)**

Bone morphogenetic proteins (BMPs) are multi-functional growth factors that belong to the transforming growth factor beta (TGF- $\beta$ ) superfamily. They were originally discovered by their ability to induce formation of bone and cartilage, but are now considered to constitute a group of pivotal morphogenetic signals, orchestrating tissue architecture throughout the body. The ability of BMPs to induce a cellular response resulting in new bone tissue formation was first observed and researched extensively by an orthopedic surgeon, Dr. Marshall Urist, Director, Bone Research Laboratory, University of California in 1965.

BMPs play a role in the differentiation, proliferation, growth inhibition, and arrest of maturation of a wide variety of cells, depending on the cellular microenvironment and the interactions with other regulatory factors <sup>[95]</sup>. In vertebrates, BMPs act as signals of epidermal induction and BMP-2 directs the development of neural crest cells into neuronal phenotypes (Christiansen *et al.*, 2000), while BMP-4 and 7 specifically induce a sympathetic adrenergic phenotype <sup>[96]</sup>.

The human genome encodes for 20 BMPs. BMPs are synthesized inside the cell in a precursor form with a hydrophobic stretch of about 50-100 amino acids. Prior to secretion, BMPs consists of a signal peptide, pro-domain, and mature peptide. Following cleavage of the signal peptide, the precursor protein undergoes glycosylation and dimerization. On secretion of the mature bioactive dimeric BMP by the cell, the pro-domain is cleaved. The mature BMP derives from the carboxy terminal region by proteolytical cleavage and are secreted as either heterodimers or homodimers <sup>[97]</sup>. Comparisons among the derived amino acid sequences of the BMPs found in osteoinductive extracts of bone indicate that they fall into 3 subclasses <sup>[98]</sup>:

**Subclass A:** BMP-2 & BMP-4-80% homology

**Subclass B:** BMP-5, BMP-6 & BMP-7-78% homology

**Subclass C:** BMP-3-Significantly different from other members of BMP family

The first subclass contains BMP-2 and BMP-4, highly related molecules that differ mainly in the amino terminal region, with BMP-2 containing a heparin binding domain. In the second subclass are BMP-5, BMP-6, and BMP-7, also known as osteogenic protein - 1 (OP-1), and BMP-8 (OP-2). These are slightly larger proteins than BMP-2 and BMP-4, and there is an approximate 78% amino acid identity between the subgroups. In the third subclass, and more distantly related to these factors, is BMP-3, also called osteogenin. Proof that these proteins were responsible for the bone inductive activity in bone matrix was found in the recombinant expression of each of these proteins <sup>[99]</sup>.

Receptors for BMPs are complexes of two different types of membrane-bound serine/threonine kinases: Type I BMP receptors (BMPR-1A and BMPR-1B) and type II receptors. After ligand binding, the type II receptor phosphorylates the type I receptor. The activated type I receptor then phosphorylates a member of the SMAD family of intracellular proteins, which are the functional signal transducers of the TGF- $\beta$ /BMP family. At the receptor level itself, the oligomerization mode of the receptors determines the specificity of the activation of the signaling pathway. Into intracellular compartment, the signal can be modulated by the activation of inhibitory SMAD proteins (ISMAPDs).

BMP-2, BMP-4, and BMP-7 are expressed in normal and wounded adult mouse skin, although their expression is not regulated by skin injury <sup>[100]</sup>. Exogenous BMP-2 induced massive dermal and epidermal growth in foetal wounds of lambs and an adult like pattern of scar formation <sup>[101]</sup>. In

contrast to other BMPs, the expression of BMP-6 in healing skin wounds has been well documented. It is highly expressed in the regenerating epidermis at the wound edge as well as in fibroblasts of the granulation tissue. After completion of wound closure, BMP-6 accumulated throughout the suprabasal layers of the newly formed epidermis [102].

To determine the activities of BMP-6 in the skin, Blessing *et al.* [103] generated transgenic mouse lines overexpressing this protein in the suprabasal layers of the epidermis. Interestingly, strong and uniform expression of the BMP-6 transgene inhibited cell proliferation but had little effect on differentiation, whereas weak and patchy expression resulted in keratinocyte hyperproliferation and in a psoriasis-like phenotype. Most importantly, reepithelialisation was significantly delayed in the transgenic mice that overexpress low levels of BMP-6 in the epidermis [102], suggesting that this protein inhibits keratinocytes proliferation in wounded skin and is necessary for the reestablishment of a fully differentiated epidermis.

#### **H. Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF)**

GM-CSF is a pleiotropic cytokine that was shown to be mitogenic for keratinocytes and to stimulate migration and proliferation of endothelial cells. Together with its potent effect on hematopoietic cells, it has been suggested to play an important role in cutaneous wound repair. Indeed, a series of animal experiments and clinical studies have demonstrated a beneficial effect of GM-CSF for the treatment of normal wounds and chronic ulcers.

Recently, Mann *et al.* [104] demonstrated a strong increase in the levels of GM-CSF in skin extracts after generation of full-thickness excisional wounds in mice, although the cellular source has not been determined. In order to gain further insight into the possible role of GM-CSF in skin wound healing, the same group generated transgenic mice that overexpress this cytokine in the epidermis and generated full-thickness excisional wounds in these animals. Interestingly, these animals displayed accelerated wound reepithelialization as a result of increased keratinocyte proliferation. Furthermore, neovascularization and granulation tissue formation were strongly enhanced. Interestingly, several cytokines that are known to be important for wound healing such as TGF- $\beta$ 1 were elevated in the wounds of these animals, indicating that GM-CSF stimulates wound repair directly but also indirectly via induction of secondary cytokines.

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**Chapter - 8**  
**Endoscopic Surgery in Oral and Maxillofacial  
Surgery**

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# Chapter - 8

## Endoscopic Surgery in Oral and Maxillofacial Surgery

Dr. Abhishek Kumar

### Abstract

Minimally invasive surgery has caused a change in the route of access, has significantly and irrevocably changed the surgical treatment of most disease processes. Through the innovation of digital imaging technology, combined with optical engineering and improved video displays, a surgeon can reach inaccessible areas for therapeutic intervention without the larger incisions previously deemed mandatory to allow the access. Endoscopic surgery has a vast scope in oral and maxillofacial surgery in arthroscopy, facial fracture management, functional endoscopic sinus surgery, orthognathic surgery, sialendoscopy and implant placement. Accurate visualization, minimal external incision, reduced soft tissue dissection, smaller aesthetic scars, lesser chances of nerve damage, bruising, bleeding and swelling, reduced hospital stay and surgeries performed on an outpatient basis are the main advantages of endoscopic surgeries.

**Keywords:** endoscopic surgery, oral and maxillofacial surgery, minimally invasive surgery

### Introduction

Surgery has traditionally been a specialty within the medical profession that has revolved around invasive procedures to treat various anomalies. Initially, trauma induced by the therapeutic procedure was unavoidable to provide benefit to the patient. But now, through the innovation of digital imaging technology, combined with optical engineering and improved video displays, a surgeon can reach inaccessible areas for therapeutic intervention without the larger incisions previously deemed mandatory to allow the access. Rather than creating large incisions several inches long to gain access to underlying tissues, minimally invasive surgical techniques typically rely on small half-inch incisions encircling the surgical field in order to insert small scopes and instruments. Minimally invasive surgery has caused a change in the route of access and has significantly and irrevocably changed the surgical

treatment of most disease processes. Patients still undergo interventions to treat disease, but minimally invasive surgery makes possible a reduction or complete elimination of the "collateral damage" required to gain access to the site requiring surgery.

While the benefits of this approach were numerous for the patient, early technology limited the application of minimally invasive surgery to some procedures. Specifically, surgeons using standard minimally invasive techniques lost the value of a natural three dimensional image, depth perception, and articulated movements. Basically, Endoscopic surgery uses scopes going through small incisions or natural body openings in order to diagnose and treat disease.

### **Endoscopic terms**

Endoscopy can involve Gastrointestinal tract (Small intestine-Enteroscopy, Colon and Large intestine-Colonoscopy, Sigmoidoscopy), Rectum-Rectoscopy and Anus-Anoscopy both also referred to as-Proctoscopy, Respiratory tract (Nose-Rhinocopy, Lower Respiratory tract-Bronchoscopy), Ear-Otoscopy, Urinary tract-Cystoscopy, Abdominal or Pelvic cavity-Laparoscopy, Interior of a joint-Arthroscopy, Organs of the chest-Thoracoscopy and Mediastinoscopy, During pregnancy (Amnion-Amnioscopy, Fetal-fetoscopy), Panendoscopy (or triple endoscopy) combines Laryngoscopy, Esophagoscopy, and Bronchoscopy, Epidural space-Epiduroscopy, Female Reproductive system-Gynoscopy (Cervix-Colposcopy, Uterus-Hysteroscopy).

### **Advantages**

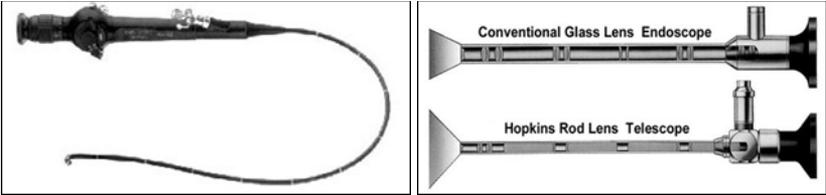
Accurate visualization, Minimal external incision, Visualization around corners, Reduced soft tissue dissection, Smaller scars, Less chance of nerve damage, Less bruising, bleeding and swelling, Reduced hospital stay and Surgeries performed on an outpatient basis are the main advantages of endoscopic surgeries.

### **Endoscope**

An instrument used to examine the interior of a hollow organ or cavity of the body. Basically, two types of endoscopes are used-

- a) **Flexible endoscope:** Useful for respiratory endoscopy or gastrointestinal endoscopy. The main disadvantage is the poorer image quality
- b) **Rigid endoscope:** Most commonly used endoscope

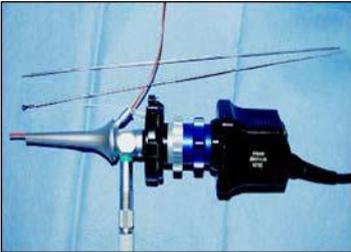
Advantage of this endoscope is that the rod lens system has greater light transmission, better image resolution, wider field of view and image magnification.



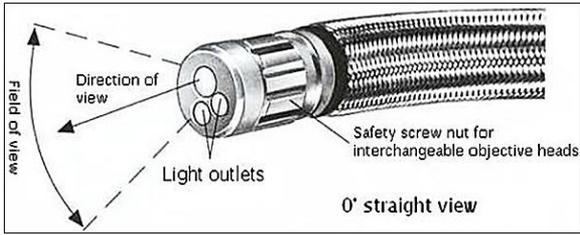
**Endoscopy equipments**



Monitor is very useful for viewing by the surgical team or to operate at a second site. Cameras are analog, but more modern ones have digital capability that permit recording of digital images. Digital images are preferred when for later presentation and publications.



**Camera and light cable**



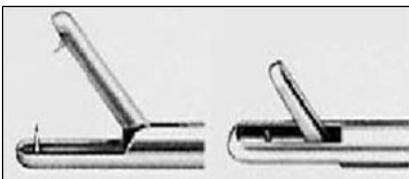
5 and 10 mm scopes. 0 and 30 degree scopes.

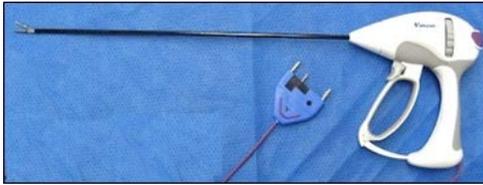
Light Sources are high intensity such as xenon or halogen.

Trocar cannula are the portals through which the endoscope and terminal operative instrumentation are passed.



Grasping and dissecting forceps, as well as scissors and biopsy forceps have connections for cautery to coagulate prior to cutting, thus reducing blood and visibility loss. Terminal instruments for grasping, dissection and cutting Endoscopic forceps is for lymph node dissections and vascular dissections.

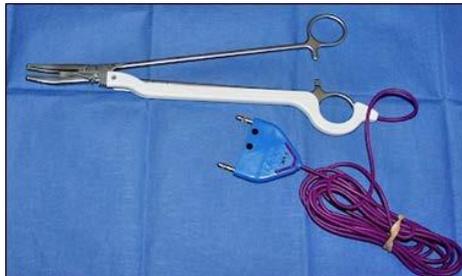




Endobag is a retriever bag for specimens from the cavities in endoscopic surgeries.



Handpiece is comprised of a stainless-steel handpiece with inserts for energy delivery



Use of endoscope in oral and maxillofacial surgery

1. Arthroscopy
2. In Fractures
  - Orbital floor fracture
  - Medial orbital wall fracture

- Zygomatic fracture
  - Frontal sinus fracture
  - Condyle fracture
  - Angle fracture
3. Functional Endoscopic Sinus Surgery (FESS)
  4. Orthognathic surgery
  5. Sialendoscopy
  6. Facial Aesthetic Surgery
  7. Implant placement

**Arthroscopic surgery:** Arthroscopy is a technique of introducing an optical instrument into the joint allowing direct visual examination of its internal surfaces. Kenji Takagi in 1918 used cystoscope to visualize cadaveric knee joint. He was the first true innovator and developer of arthroscopy. Arthroscopic examination of temporomandibular joint was first described by Ohnishi using the Number 24 arthroscope developed by Watanabe.

### **Indications of arthroscopy**

- Internal derangement
- Osteoarthritis
- Arthritides (rheumatoid and psoriatic)
- Pseudotumor
- Post traumatic complaints

### **Contraindications of arthroscopy**

#### **Absolute**

- Bony ankylosis
- Advanced resorption of the glenoid fossa
- Infection around joint area
- Malignant tumours

#### **Relative**

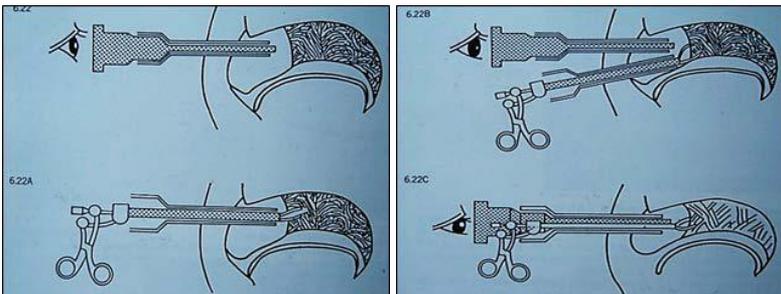
- Increased risk of haemorrhage
- Increased risk of infection
- Fibrous ankylosis



**Arthroscopic instruments**

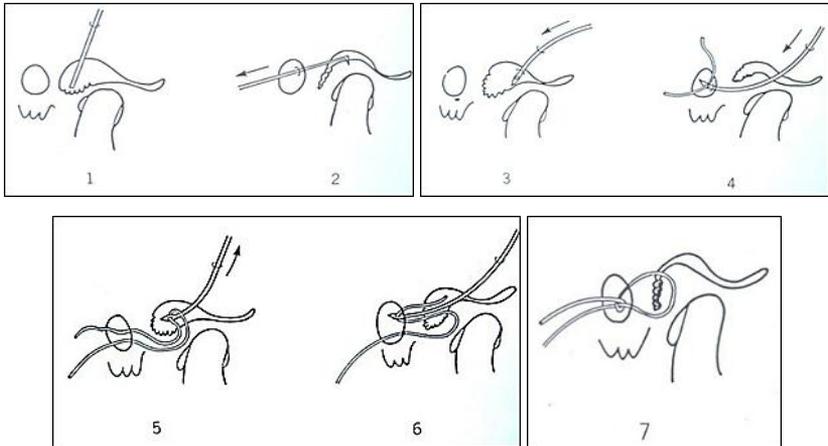
**Joint entry technique**

Superficial temporal artery is palpated and located. Upper joint space is distended with 2ml of 2% Lignocaine using 18 gauge needle with a 30 degree anterior and superior direction until resistance is felt. A 2mm skin incision is made approx 5mm anterior to the 18m gauge needle. Arthroscopic sheath is introduced through the incision with a sharp trocar and inserted into the joint cavity passing through the capsule in the same direction as the needle



Double-channel sheath can be used not only for diagnostic but also for arthroscopic surgery. In particular, it has a hole for surgical device insertion which enables parallel insertion of device. This makes it easy to always observe the advancing edge of surgical device making any manipulation simple.

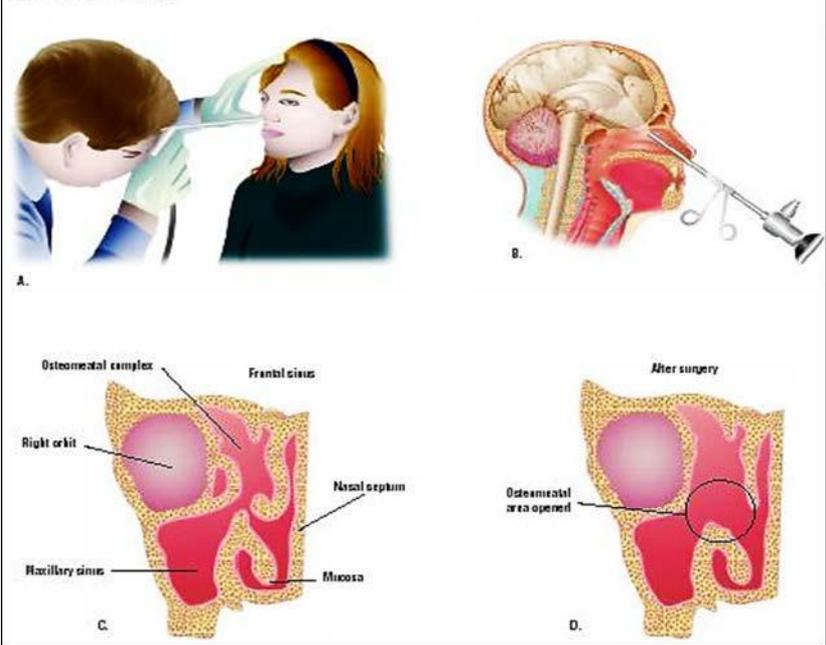
**Laser:** A quartz fibre probe is indicated. Burning, evaporation, and coagulation all occur. Physiologic saline solution is perfused for cooling the surgical site. Nd-YAG laser is the most suitable for this technique as it can pass through fibres. Arthroscopic suturing is done as shown below-



**Complications of arthroscopic surgery:** Main complications of arthroscopic surgery are extravasation, neurologic injury, vascular injury, intra-articular injury, instrument breakage, otologic infections, burns and anaesthetic complications.

**Endoscopic sinus surgery (Sinuscopy):** Minimally invasive surgical procedure that opens up sinus air cells and sinus ostia (openings) with an endoscope. Hirschmann first attempted sinus endoscopy with cystoscope in 1901. The term Sinuscopy was coined by a facial plastic surgeon Maxwell Maltz in 1925.

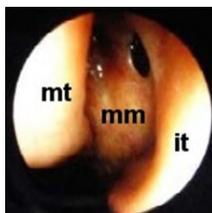
## Endoscopic sinus surgery



**Indications of sinuscopy:** Polyposis, Obstructed nasal respiration, Recurrent and Chronic sinusitis, Epiphora, Anosmia, Chronic headaches, Mucocele Retention cyst, Mycoses, Orbital complication of acute sinusitis, Eustachian tube problems, Post nasal drip, continuing complaint after Caldwell-luc operation. Intranasal fenestration, Allergies, Sinobronchial syndrome, Bronchial asthma, Recurrent pharyngitis, Phonation disturbances and Snoring are the conditions where sinuscopy is advised.

**Contraindications of sinuscopy:** Extensive invasive procedures like Osteoma, coarse bony inflammatory stenosis of the ostium, acute sinusitis with central complications (meningitis, epidural abscess, cavernous sinus thrombosis), evidence of osteomyelitis and chances of vision loss are the conditions where sinuscopy is contraindicated.

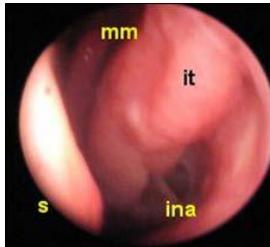
### Procedure of sinuscopy



Normal opening into left maxillary sinus (the natural ostium) seen through a nasal endoscope (mt = middle turbinate, mm = middle meatus, it = inferior turbinate).



Polyps and persistent thick sticky secretions in the ethmoid two years following Functional Endoscopic Sinus Surgery, seen through an endoscope. This asthmatic patient was pleased with the improvement in his ability to breathe through the nose, but still suffered from thick postnasal drip.



Intra nasal antrostomy, left inferior meatus, seen through a 30 degree rigid nasendoscope, s = nasal septum, mm = middle meatus, it = inferior turbinate, ina = intranasal antrostomy.

**Complications of sinuscopy:** Bleeding, Blindness, Closure of antrostomy, Diplopia, Cerebrospinal fluid leak, Orbital injury, Orbital hematoma, Direct brain injury and Nasolacrimal duct injury/epiphora are the common complications noted during sinuscopy.

**Image-guided endoscopic surgery:** Image guidance techniques feature a three-dimensional mapping system combining CT scanning and real-time data acquisition. It confirms the location of the surgical instruments during the procedure and navigates more precisely at the desired site. It monitors the exact location of vital sites to avoid the injury. Balloon catheter dilatation for sinusitis (Balloon sinuplasty): Introduced in 2005, the aim is to stretch and widen narrowed openings into the sinuses. It guides a narrow, flexible wire up the nose and into the sinus. A balloon catheter is slid over the wire, until it sits in the sinus opening.

The balloon is then inflated with liquid, stretching and widening the sinus opening. Once the opening has been enlarged, the wire and balloon are removed. In the UK, balloon sinus dilatation was given official approval as a safe and effective procedure to treat chronic sinusitis by NICE (National Institute of Clinical Excellence) in September 2008.

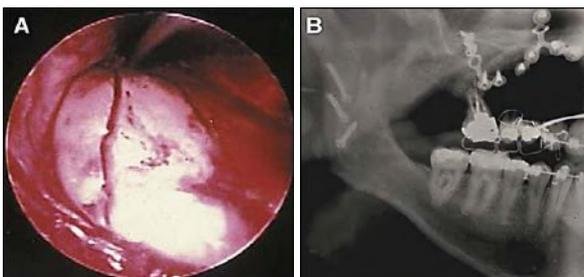
**Endoscopy in maxillary orthognathic surgery:** Sakai and colleagues extended endoscopic applications to the management of craniofacial disorders, performing a Le Fort I level osteotomy. It minimizes the access and to optimize the vascularization (risk of injury to the descending palatal artery), should be the aim of future treatments. The use of this technique for the surgically assisted rapid palatal expansion (SARPE) could be one of the main indications.

**Advantages & disadvantages of endoscopy in maxillary orthognathic surgery:** The vertical direction of the incisions preserves the anastomotic network between branches of the facial artery and branches of the maxillary artery on the gingiva and buccal mucosa, reduces blood loss, prevents swelling and edema, decrease the risk for postoperative infection, accelerates the recovery and allows for correct reattachment are the basic advantages. But disadvantages are extended time of surgery, disturbed visibility, higher technical challenge and more expensive treatment.

### **Endoscopy in mandibular orthognathic surgery**

Mandibular prognathism or asymmetry cases who refuse maxillomandibular fixation, are not willing to accept the risks of inferior alveolar nerve injury, allow for mandibular setback without the need for extraction of well-developed mandibular third molars, which are associated intimately with the IAN. will be the minimally invasive alternative to the sagittal split osteotomy.

### **Endoscopic orthognathic surgery**



- A) Endoscopic view of right lateral ramus with completed osteotomy, extending from sigmoid notch to angle
- B) Close-up panoramic view showing vertical ramus osteotomy with setback and rigid fixation

**Endoscopic condylar fracture repair:** It allows the surgeon to produce anatomic fracture alignment and to avoid the negative sequelae of condylar malunion.

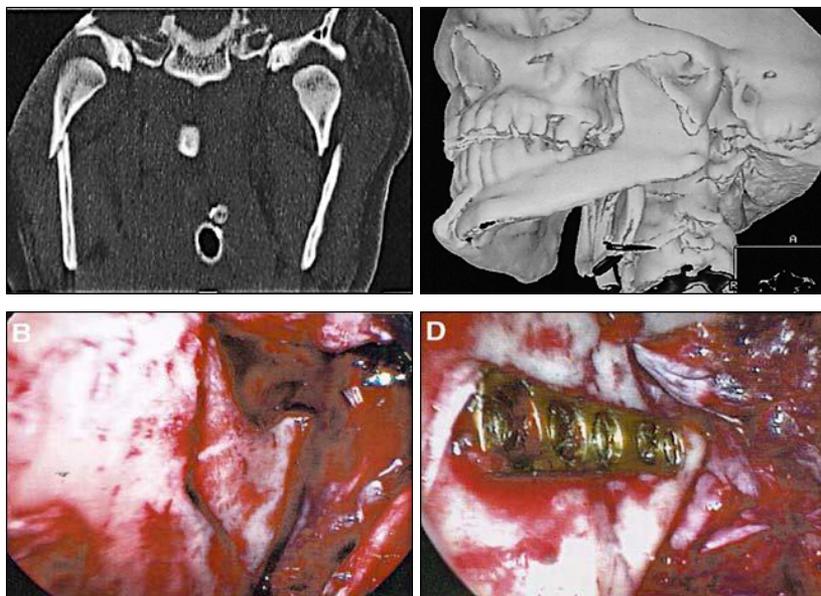
**Advantages of endoscopic condylar fracture repair:** To reduce morbidity by limiting scars, reducing the risk to the facial nerve, eliminating the need for MMF and anatomic reduction and rigid fixation are some advantages.

**Indications & Limitations endoscopic condylar fracture repair**

**Fracture displacement:** Lateral override fractures are the easiest to approach but medial override is difficult. The management of medial override injuries is by first reducing them to the lateral override category.

**Fracture comminution:** Comminution is a relative contraindication.

**Condyle-fossa relationship:** Non-dislocated condylar heads are the most favorable but displaced condylar head without dislocation usually can be relocated. Dislocation of the condylar head are significantly more challenging.



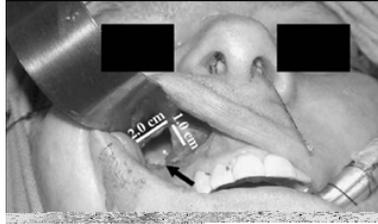
## Endoscopic condylar repair procedure

A view of the anatomically reduced and rigidly fixated left condylar fracture using the endoscopic technique.

## Endoscopic repair of orbital floor fractures

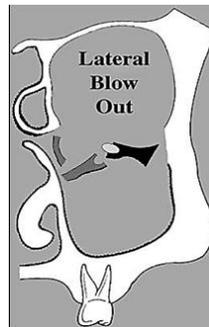
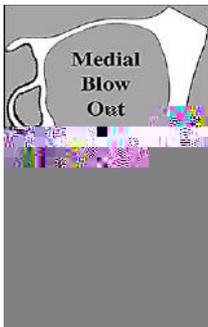
### 2 Approaches

1. Caldwell-Luc approach
2. Transnasal approach



Indications and Limitations-Trap door fracture and medial blow-out fracture are indications. In early repairs it offers excellent fracture visualization.

Lateral blow-out fracture and hyphema are contraindications.



Endoscopic Repair of Medial Orbital Wall Fractures: Variable sizes of the medial orbital wall fractures and fractures involving the superior and posterior medial orbits can be repaired and transcaruncular endoscopic approach is used to correct late enophthalmos caused by uncorrected displacement of medial wall or previously inadequate reconstruction of medial wall defects.

## Procedure endoscopic repair of medial orbital wall fractures

Two approaches

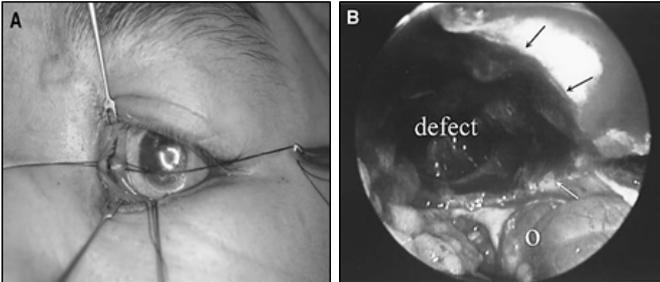
**1. Intranasal (transethmoidal):** It involve partial ethmoidectomy.

It assist in placement of an orbital implant by means of a periorbital incision.



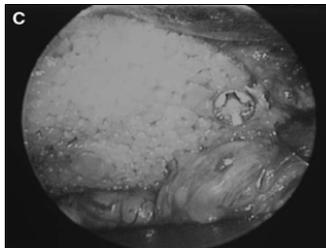
- A) Bony defect of the lamina papyracea
- B) Medpor implant in proper position

## Endoscopic transcaruncular approach



- Transcaruncular incision posterior to caruncle
- Transcaruncular incision posterior to caruncle

## Endoscopic view of the bone defect of the orbital medial wall



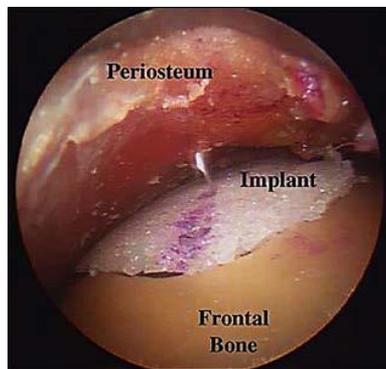
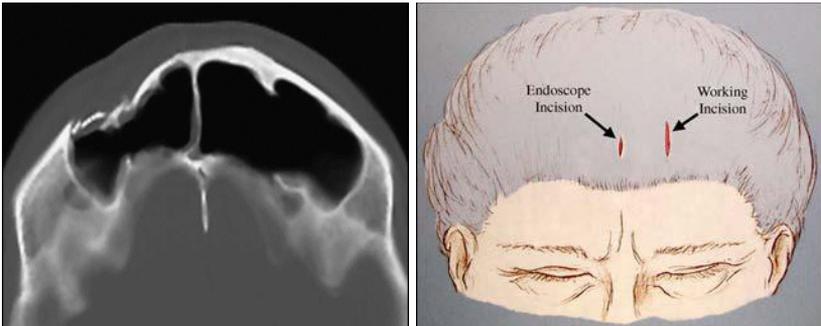
- Endoscopic view of Medpor implant placed
- Endoscopic Repair of Frontal Sinus Fractures

**Acute fracture reduction with or without fixation:**

It involves exposure of the fracture in the acute setting, reduction of the bone fragments, and application of internal fixation as needed to maintain.

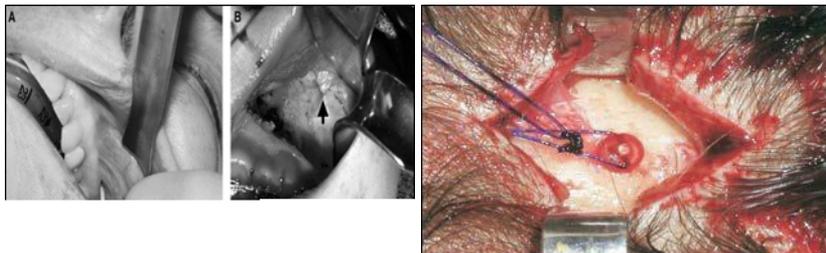
**Fracture camouflage:** It involves an observation period to allow resolution of facial edema, followed by recontour with an alloplastic implant. Exposure is easier, because the bone fragments are not mobile and technically less challenging. Need not be done in the acute setting of the defect.

Disadvantage of the this technique is the need for an alloplastic implant

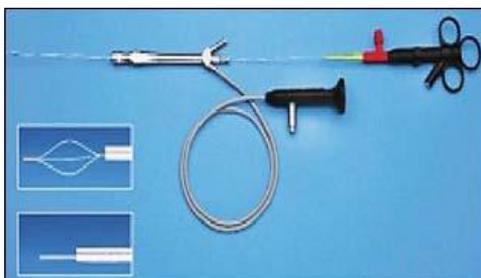


**Endoscopic Facial Aesthetic Surgery**

Series of small incisions that are much less Invasive, less problem with supraorbital and supratrochlear anesthesia and paresthesia, hair loss and bleeding is a rare problem, scars are rarely seen.



**Sialendoscopy:** To visualize the lumen of the salivary ducts and their pathologies. Indicated in all salivary gland swellings of unclear origin. Limitations are sharply bent curvature.



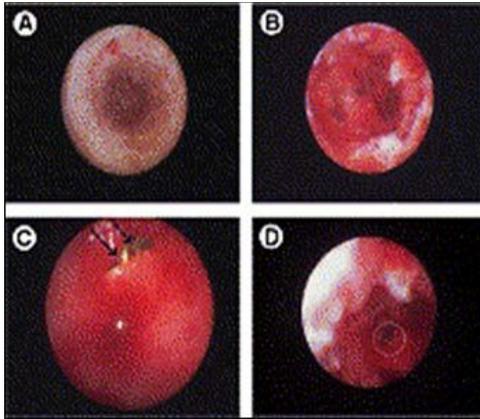
### Interventional Sialendoscopy



### Endoscopic approach to dental implantology

In 2006, a microendoscope (Visio Scope) was introduced for multidisciplinary use in dentistry, including dental implantology. The

Modular Implant Endoscope is a semirigid microendoscope with an objective to increase the longevity of oral implants by securing proper implant placement into bone of sufficient density.



With the advent of Capsule Endoscopy and robotic systems, telesurgery was introduced. The first transatlantic surgery has been called the Lindbergh Operation.

A new endoscopy technology using Magnetically Guided Capsule Endoscopy (MGCE) for wireless control, monitoring and imaging. Robotic surgery is an extension of minimally invasive techniques. Surgeon uses robotic arms instead of endoscopes and other tools.

The future of Endoscopic surgery i.e. Minimally Invasive surgery is changing into the Least Invasive surgery. Natural Orifice Transluminal Endoscopic Surgery (NOTES) is the least invasive surgery performed without giving external incision leaving no scars (surgeons without scalpel) through natural orifice (mouth, anus, vagina, urethra). NOTES is an entirely novel method of surgical therapy with future prospects in oral and maxillofacial surgery.

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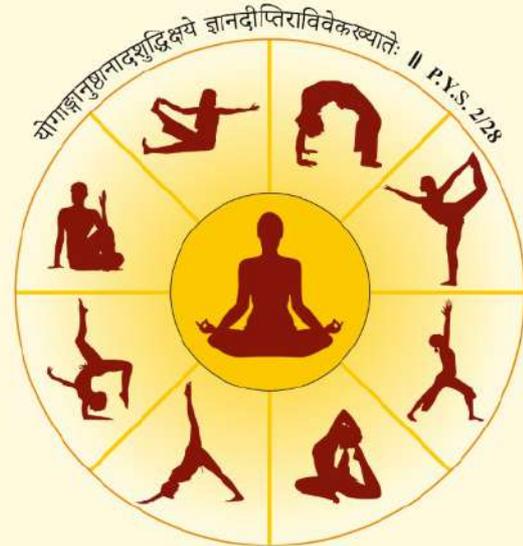


YOGA AND WELLNESS

# YOGA AND WELLNESS

YOGA AND WELLNESS

• DR. SANJEEV S. TONNI



योगस्यः कुरु कर्माणि सङ्गं त्यक्त्वा धनञ्जय ।

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## *List of Contents*

Sl.No	Name of the Content	Page. No
1.	Introduction to Yoga & Wellness	11
2.	Definition of Wellness	11
3.	Yogakshema	12
4.	Various definitions of Yoga	12
5.	Yoga as a Preventive Medicine ; Concept of Wellness in Yoga	13
6.	Yoga as a LIFESTYLE - Role of yoga in Health Promotion	14
7.	Personality development through Yoga	15
8.	Pre-requisites of yoga (Rules and Regulations of Yoga practice)	16
9.	Shithilikarana vyayama or Loosening exercises	18
10.	Practice of Suryanamaskara	29
	<b>Practice of Yogasana - Standing Series Asana</b>	<b>35</b>
11.	- Practice of Taadasana	37
12.	- Practice of Utkatasana	39
13.	- Practice of Ardha-chakrasana	41
14.	- Practice of Prasarita paadottanasana	43
15.	- Practice of Trikonasana	45
16.	- Practice of Parivrutta Trikonasana	47
17.	- Practice of Ardha-kati chakrasana	49
18.	- Practice of Vrikshasana	51
19.	- Practice of Veerasana	53
20.	- Practice of Garudasana	55
21.	- Practice of Natarajasana	57
22.	- Practice of Upavishta-konasana	59
23.	- Practice of Parshwa konasana	61
24.	- Practice of Veerabhadrasana	63
	<b>Practice of Supine Series Asna</b>	<b>65</b>
25.	-Practice of Shavasana	65
26.	- Practice of Ardha-halasanana	67
27.	- Practice of Vipareetakarani	69

28.	- Practice of Sarvangasana	71
29.	- Practice of Pavana-muktasana	73
30.	- Practice of Jathara-parivartanasana	75
31.	- Practice of Setubandhasana	77
32.	- Practice of Naukasana	79
33.	- Practice of Matsyasana	81
34.	- Practice of Anantasana	83
35.	- Practice of Vashishtasana	85
	<b>Practice of Prone Series Asana</b>	<b>87</b>
36.	- Practice of Makarasana	87
37.	- Practice of Bhujangasana	89
38.	- Practice of Dhanurasana	91
39.	- Practice of Ardha-shalabhasana	93
	<b>Practice of Sitting Series Asana</b>	<b>95</b>
40.	- Practice of Dandasana	95
41.	- Practice of Padmasana	97
42.	- Practice of Vajrasana	99
43.	- Practice of Marjaalasana	101
44.	-Practice of Ushtrasana	103
45.	-Practice of Simhasana	105
46.	-Practice of Baddha-konasana	107
47.	-Practice of Baalasana	109
48.	-Practice of Gomukhasana	111
	<b>Practice of Pranayama</b>	<b>113</b>
49.	- Practice of Suryabhedana Pranayama	115
50.	- Practice of Chandrabhedana pranayama	117
51.	- Practice of Naadishuddhi pranayama	119
52.	- Practice of Sheetali pranayama	121
53.	- Practice of Sitkari pranayama	123
54.	- Practice of Bhramari pranayama	125
55.	- Practice of Bhastrika pranayama	127
56.	- Practice of Ujjayi pranayama	130





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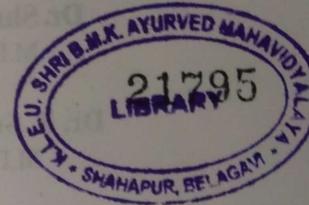
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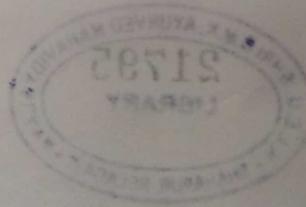
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# CONTENTS

Abbreviations	(iii)
Transliteration	(iv)

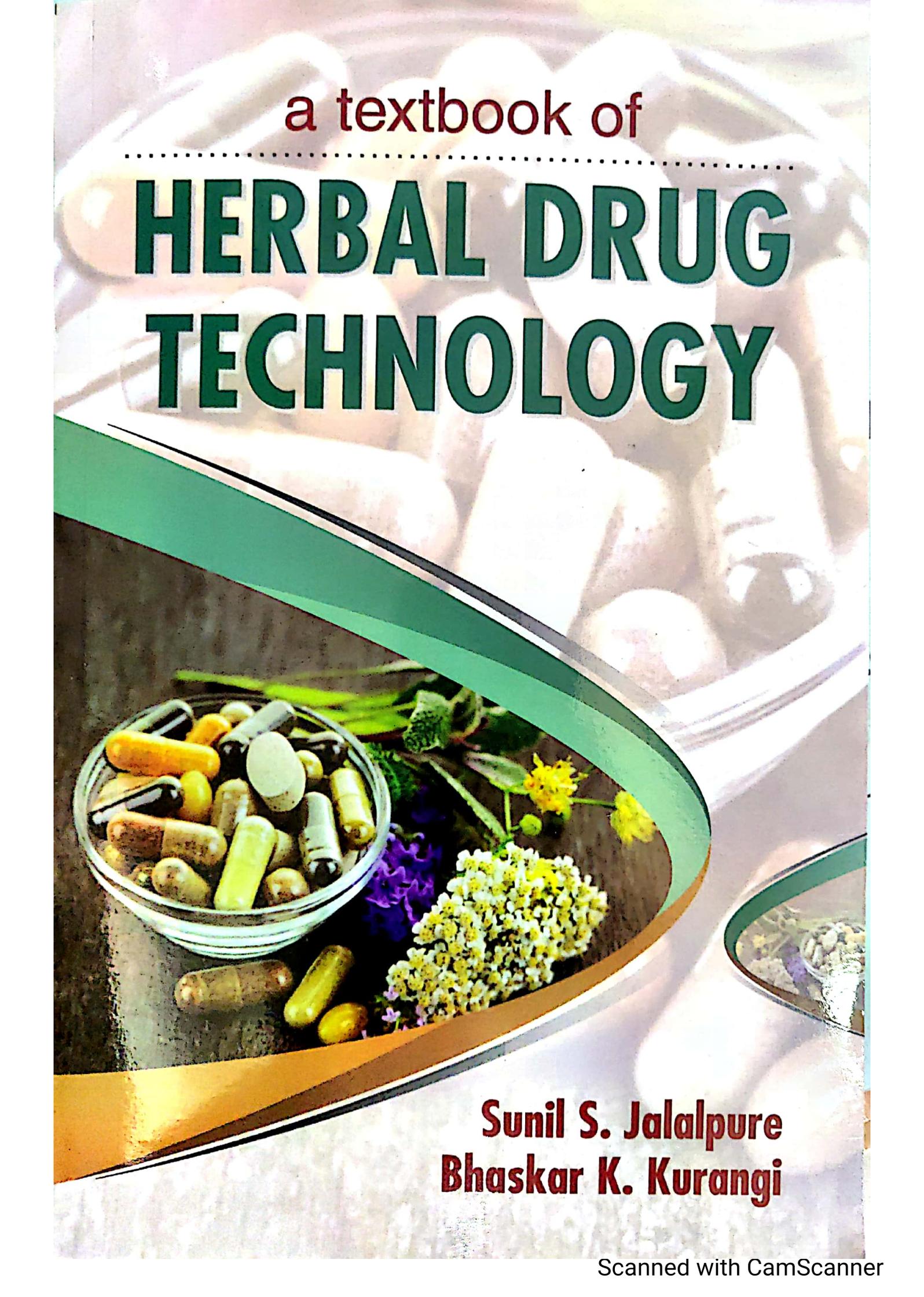
Sl.No	Chapter	Page No.
<b>Section 1</b>		
	Preface	
1.	ADR in Current scenario	1
2.	ADR in <i>Āyurveda</i>	8
3.	Pharmacovigilance related terms in <i>Āyurveda</i>	12
4.	<b>Drug related ADR</b>	19
4.1	<i>Abhesaja</i>	22
4.2	Tangible properties of Drug	25
4.3	Drug Quality Concern	37
4.4	Idiosyncrasy & Pharmacogenomics in <i>Āyurveda</i>	42
4.5	<i>Anupāna</i>	44
5.	<b>Iatrogenesis</b>	45
5.1	<i>Viruddhadravayaprayoga</i> (Drug interaction-incompatibility) on stage of Disease)	48
5.2	<i>Avasthanusāradravayaprayoga</i> (Administration of Medicine based on stage of Disease)	59
5.3	<i>Atimātradravayaprayoga</i> (Over dose)	63
5.4	Iatrogenicity Due to Procedural Therapy.	67
6	<b>Patient related ADR</b>	72

## Detection and Prevention of Āyurvedic ADR

### Section 2

7	Detection of ADR	73
8	Assessment and Evaluation of ADR	79
9	Preventive measures	86
	References	88
	Reference books of Tables	91
	Appendix : NPP - ASU Form	93
	Alphabetic Index	96





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For Undergraduate & Postgraduate Nursing Students

(As per the Syllabus of Indian Nursing Council)



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# Plant Ecophysiology and Adaptation under Climate Change: Mechanisms and Perspectives I

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# Plant Ecophysiology and Adaptation under Climate Change: Mechanisms and Perspectives I

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# Chapter 12

## High-Temperature Tolerance of Flowers



Satisha Hegde, Yui Umekawa, Etsuko Watanabe, and Ichiro Kasajima

### Contents

12.1	Introduction: High Temperature Affects Floricultural Production.....	344
12.2	High-Temperature Response of Long-Day and Short-Day Plants.....	346
12.2.1	Long-Day Plant.....	346
12.2.2	Short-Day Plant.....	348
12.3	High-Temperature Effects on Petal Colors.....	350
12.3.1	Anthocyanin Synthesis.....	350
12.3.2	Decoloration of Petals.....	352
12.3.3	Color Influences Flower Temperature.....	353
12.4	Heat Production in Flowers.....	355
12.4.1	Heat-Producing Flowers.....	355
12.4.2	Biochemical Basis of Thermogenesis.....	357
12.4.3	Significance of Self-Produced Heat.....	360
12.5	Genetic Approaches to Attenuate High-Temperature Effects.....	361
12.6	Physiological Treatments to Attenuate High-Temperature Effects.....	364
12.7	Conclusion: Strategies to Attenuate High-Temperature Effects.....	365
	References.....	366

**Abstract** Similar to the other crops, production of floricultural plants (crops for ornamental purposes) is susceptible to high temperature. High temperature changes flowering time, causing problems in the schedule of shipment to the market.

---

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343

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Consistent with the idea of plant adaptation to climate, induction of long-day spring flowers (*Arabidopsis/thale cress*) is accelerated by high temperature, whereas induction of short-day autumn flowers (*chrysanthemum*) is delayed by high temperature. High temperature also reduces flower size and causes paler petal colors (e.g. *chrysanthemum*, rose, and Eustoma) and fruit skin colors (e.g. grape and apple), thus decreasing the quality of flowers and fruits. The reasons for high-temperature caused disorders are not necessarily clear, but high temperature influences part of gene expressions involved in flowering time (*FT*, *Flowering Locus T*) and pigment synthesis (such as *CHS*, *chalcone synthase*). High-temperature-tolerant cultivars are identified or selected in floricultural and pomological (fruit) crops. High-temperature effects could be alternatively attenuated by shading or supplementation of magnesium. Heat is sometimes required for flowers: some plant species generate heat in flowers by themselves. Petal color affects flower temperature. Relationships between flower and heat in these various aspects are illustrated by photographs and illustrations of the representative studies in this research field.

**Keywords** Extreme temperature · Flowering habit · Flower coloration · Heat stress

## 12.1 Introduction: High Temperature Affects Floricultural Production

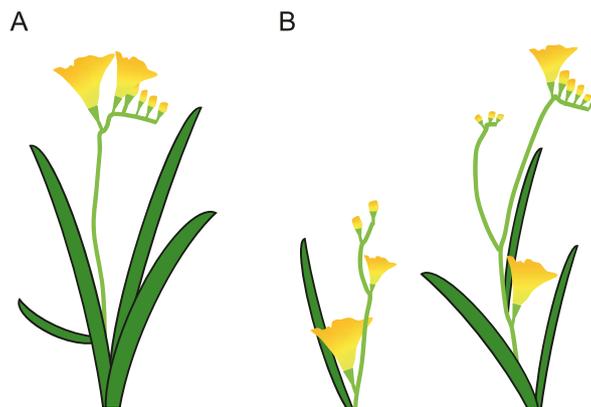
The global temperature is gradually rising by 0.02 °C every year (Berkeley Earth 2019). High atmospheric temperatures caused by global warming will be a great risk for production of most crops, but the effects of high temperature on crop production and breeding of high-temperature tolerant cultivars have just started to be widely studied in recent years. In the present report, we will focus on the effect of high temperature on the production of flowers (floriculture), to discuss necessary solutions to overcome adverse effects of future high temperature on flower production. The number of reference papers is limited on this topic, but representative papers will be reviewed in precision to learn high-temperature response and tolerance of flowers. Reference photographs of flowers will be also cited from representative papers, as long as copyright permission is given from the publishers.

High temperature affects both quality and quantity of flower production. As for the quantity of flower production, short period (3 days) of very high temperature (35 °C maximum for 6 h each day) during early flowering period was enough to reduce flower yield of pyrethrum (*Tanacetum cinerariifolium*). *Pyrethrum* flower is the source of the production of pyrethrin, a natural insecticide. In addition to the yield of flowers, pyrethrin content in the flower (achene) is also reduced by heat stress, causing the problem of unstable pyrethrin production in the main producer country Australia (Suraweera et al. 2016). Reduction of the number of flowers is also observed in groundnut (*Arachis hypogaea* cultivar 'ICGV 86015'): the number

of flowers decreases as the day temperature is raised from 28 to 48 °C (Prasad et al. 2000).

As for the quality of flowers, flower diameter is reduced by 16% and petal number is reduced by 23% in rose (*Rosa* sp., cultivars ‘M4-4’, ‘J06-20-14-3’, ‘97/7-2’, ‘Red Fairy’, ‘Sweet Chariot’, ‘Vineyard Song’, ‘Old Blush’, and ‘Little Chief’), only by 1-h heat shock at 44 °C. Although severe heat shock will be better for estimation of heat tolerance, heat-tolerant trait of rose is heritable (Liang et al. 2017). The shape of freesia (*Freesia refracta* cultivar ‘Blue Heaven’) inflorescence is affected by high temperature. Juvenile plants of freesia generated from corms are usually chilled at 10 °C. When juvenile plants are treated at 24 °C for 1, 2, or 3 weeks, abnormal (malformed) inflorescences are formed on mature plants, and the ratio of abnormal inflorescences rises with the longevity of heat stress at 24 °C. Abnormal inflorescences have different (vertical) angles of flower stalks or form aberrant flowers at the base of inflorescence (Fig. 12.1). The formation of abnormal inflorescences is correlated with faster development of floral meristems (Motozu et al. 2000).

Heat stress affects floral scent (fragrance) as well. The production of phenylpropanoid-based volatiles was reduced in petunia (*Petunia × hybrida*) flowers (cultivars ‘P720’ and ‘Blue Spark’) when day/night temperature was raised from 22 °C/16 °C to 28 °C/22 °C (Cna’ani et al. 2015). Floral scent will not be important for petunia as an ornamental flower, but decrease of floral scent is critical for excellently fragrant species such as sweet pea, freesia, and fragrant rose. Other damages to flowers by heat stress include decoloration of petals and altered time of flowering. These topics will be described in the other sections of this chapter. Heat stress causes sterility in flowers (Yang et al. 2009; Ishimaru et al. 2016; Hakata et al. 2017; Zhang et al. 2018), but this is not within the focus of the present chapter. Interestingly, heat does not always have negative influences on flower production. When rose cultivars ‘Meirutral’ and ‘Meidanclar’ are grown at the day/night



**Fig. 12.1** Abnormal inflorescence of freesia. (a) Normal inflorescence. (b) Abnormal inflorescences. These figures illustrate data in Motozu et al. (2000)

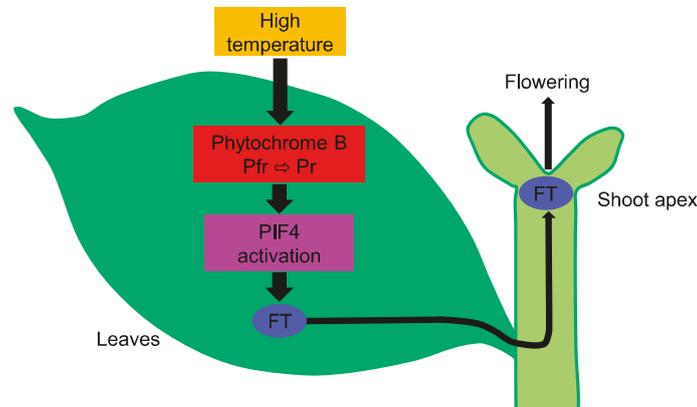
temperature of 24 °C/18 °C or 29 °C/24 °C, longevity of open flowers was increased, and the ratio of bud drop was decreased at higher temperature. Most notably, flower longevity was increased from 2 to 9 days and bud drop was decreased from 61 to 5% in ‘Meirutral’, when plants were heated at green-bud stage. ‘Meidanciar’ also enjoyed similar effects of high temperature, but malformed flowers were increased in this cultivar. Although high temperature induces smaller flowers, high temperature is beneficial for some rose cultivars (Monteiro et al. 2001). Such benefits of high temperature should be also remembered to promote flower production under high temperature. After listing heat effects to flowers, we will also review physiological or chemical treatments and genetic approaches to alleviate heat damages.

## 12.2 High-Temperature Response of Long-Day and Short-Day Plants

### 12.2.1 Long-Day Plant

The time required from germination to reproductive growth (flowering) is the important trait for plants to survive in the environment (Song et al. 2015). Flowering time is principally regulated by the length of light and dark conditions in a day (photoperiod), although regulation of flowering time is much more complicated. Thale cress (*Arabidopsis thaliana*) is a “facultative” long-day plant: thale cress flowers much earlier under long-day conditions than under short-day conditions. Studies of thale cress have demonstrated that abiotic stresses also control time of flowering, in addition to photoperiod. The reason for the response of flowering time to abiotic stresses is considered that plants try to generate seeds before they are fatally damaged by stresses (Takeno 2016).

Temperature is one of such environmental stresses that accelerate flowering in thale cress. Thale cress flowering is accelerated by high temperature (Song et al. 2015). Here, we will review how thale cress plants sense temperatures. Plants sense both temperature and photoperiod by the same mechanism. Protein called “Phytochrome B” usually senses the “quality” of light, i.e. the ratio between red light and far-red light. Also wave lengths of lights, Phytochrome B also senses the temperature through its temperature-dependent reversion from the active “Pfr state” to the inactive “Pr state” (Fig. 12.2; Legris et al. 2016; Kreslavski et al. 2018). Thus, Phytochrome B is considered to work as a temperature sensor by this conformational change. Phytochromes interact with phytochrome-interacting factors (PIFs), the transcriptional factor proteins with the basic helix-loop-helix (bHLH) DNA binding domain. PIF4 protein is actually reported to be involved in acceleration of flowering by high temperature in thale cress: flowering is no longer accelerated in the *pif4* mutant of thale cress which lack the function of PIF4, under high temperature (Kumar et al. 2012).



**Fig. 12.2** Activation of FT by high temperature in thale cress: schematic representation

The expression of the *FT* (*Flowering Locus T*) gene, encoding florigen, takes place in the vascular tissues of leaves, and the *PIF4* gene is also expressed in the same tissues. In “chromatin immuno-precipitation” assay, PIF4 protein binds to the promoter DNA region of the *FT* gene. This indicates that heat-activated Phytochrome B activates PIF4, which enhances expression of the *FT* gene (Kumar et al. 2012). Here, florigen is the master regulator that transmits flowering-inducing stimuli in higher plants (Tsuji 2017). The *FT* gene of thale cress and the *Heading Date 3a* (*Hd3a*) gene of cultivated rice (*Oryza sativa*) encode phosphatidylethanolamine binding-like proteins, which are the realities of florigen (Kardailsky et al. 1999; Kobayashi et al. 1999; Kojima et al. 2002). These proteins are expressed in leaves and then translocated to shoot apices via the phloem and promote flowering in shoot apices (Corbesier et al. 2007; Tamaki et al. 2007).

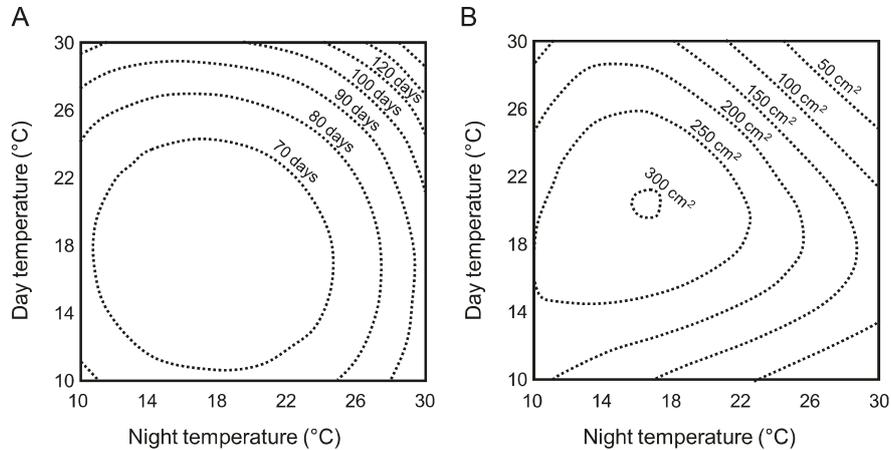
High temperature also accelerates the heat-stress responsive pathway, e.g. upregulation of heat shock proteins (HSPs) which help the folding of proteins, and HSPs are related to flowering as well. Once HSPs are activated, plants can adapt to the secondary heat stresses. This is called “adaptation to heat stress.” HSP90 is highly induced during adaptation of thale cress. HSP90 is quite abundant in normal temperature to help the protein folding. Mutation in the *HSP90* gene affects a variety of “quantitative life-history traits,” including delay of flowering, reduction of total seed set, and increase in morphological diversity (Sangster et al. 2007, 2008). Then, HSP90 might regulate the flowering time by modulating several proteins. Candidates of such target proteins of HPS90 are an F-box protein ZTL involved in photoperiod regulation (Kim et al. 2011) and Heat Shock Transcription Factor A1 (HSFA1) involved in high-temperature tolerance together with HSP90 (Yamada et al. 2007). In summary, Phytochrome B and PIF would regulate high-temperature-induced change of flowering time through regulation of the expression of the *FT* gene in the vein of leaves (Fig. 12.2), and HPS will also influence this response.

### 12.2.2 Short-Day Plant

Data indicate that flowering induction of short-day plants such as chrysanthemum responds to high temperature oppositely from long-day plants such as thale cress. *Chrysanthemum* is the most popular cut flower in Japan: it occupies more than one-third of cut flower production, followed by rose, carnation, Gerbera, Statice, Eustoma, and gentian. Chrysanthemum is produced in many areas of Japan but is most produced in warm or semi-tropical areas such as Aichi and Okinawa (<http://www.e-stat.go.jp/SG1/estat/Pdfdl.do?sinfid=000031665471>). *Chrysanthemum* also occupies 18% of all sales of ornamental plants in Japan (<http://www.maff.go.jp/e/policies/agri/attach/pdf/index-5.pdf#search=%27chrysanthemum+production+d+ata%27>). Chrysanthemum originates in East Asia and first cultivated in China. Data on the response of short-day plants to high temperature is practically restricted to chrysanthemum, but the other species may respond to high temperature in the same way.

Carvalho et al. (2005) reported high-temperature response of chrysanthemum cultivar 'Reagan Improved'. They test cultivated chrysanthemum under 15, 18, 21, or 24 °C and compared flower traits. As in the other reports, they observed smaller but larger number of flowers per plant at higher temperatures. They also reported that the pink color of the petal was lighter (paler) at higher temperatures, similar to the other reports. On the other hand, they did not observe great difference in flowering time (days from the start of short-day treatment to anthesis). This range (15–24 °C) of moderate stimulus will not have significant effect on the induction of chrysanthemum flowering.

An interesting survey was performed on the response of *chrysanthemum* cultivar 'Bright Golden Anne' to high temperature by Karlsson et al. (1989). They changed day temperature and night temperature independently from 10 to 30 °C. Clear difference in flowering time was observed in this wide range of temperatures (Fig. 12.3a). The optimum temperature for shortest flowering time of *chrysanthemum* is both day and night temperatures of 18 °C, which requires 60 days to flowering. The flowering time becomes longer when temperatures are more different from this optimum level. The flowering time is even 120 days, the double of the shortest case at high temperatures such as day temperature of 30 °C and night temperature of 26 °C. The "total flower area" per plant was also measured in their analysis. This is the output of the balance between flower size and flower number, but the optimum temperatures are day temperature of 20 °C and night temperature of 16 °C, at which temperature the flower area is 300 cm<sup>2</sup> (Fig. 12.3b). This value is also much affected by high temperature, for example, the values is more than halved (less than 150 cm<sup>2</sup>) at day temperature of 28 °C and night temperature of 22 °C. Virtually no flower is generated at both day and night temperatures of 30 °C. Light intensity also matters. The above data were obtained at light intensity (photosynthetic photon flux, PPF) of 15 mol day<sup>-1</sup> m<sup>-2</sup>. Flowering is delayed, and flower area is reduced in darker conditions.



**Fig. 12.3** Response of chrysanthemum to high temperature (1). Days needed to anthesis from the start of short day (a) and total flower area per plant (b), shown as the function of day temperature and night temperature. Data were acquired for plants grown in PPF of  $15 \text{ mol day}^{-1} \text{ m}^{-2}$ . These figures illustrate data in Karlsson et al. (1989). (a) Expression inductions (in short-day condition) of the *AP3/AG/SEP/PI* homologs was analyzed every week at 20 or 30 °C. (b) Expression induction of the *CsFTL3* gene was analyzed every week at 20 or 30 °C. Data were cited from Nakano et al. (2013) under the Creative Commons CC-BY conditions

Genetic analysis of the generally observed flowering retardation of chrysanthemum at high temperature was performed on the cultivar ‘NIFS-3’ (Nakano et al. 2013). In *chrysanthemum* shoot apices, expressions of meristem identity genes *SOC1* (*Suppressor of Overexpression of Constans 1*), *LFY* (*Leafy*), *API* (*Apetala 1*), and *FUL* (*Fruitful*) and floral homeotic genes *AP3* (*Apetala 3*), *AG* (*Agamous*), *SEP* (*Sepallata*), and *PI* (*Pistillata*) are induced within 3 weeks in short-day condition at 20 °C. Expression inductions of four *SOC1/LFY/API/FUL* homologs were not significantly affected by high temperature at 30 °C, although expression inductions of two *API/FUL* homologs were delayed. Consistent with this, there was no clear delay in the induction of floral meristems at high temperature, in microscopic analyses. On the contrary, expression inductions of all four *AP3/AG/SEP/PI* homologs examined were delayed by high temperature (Fig. 12.3a). As a result, development of floral organs after generation of floral meristem is delayed in chrysanthemum. The delay of the expressions of these genes is seemingly caused by the delay in the expression induction of the *CsFTL3* gene, one of the *FT* (*Flowering Locus T*) homologs, in leaves at high temperature (Fig. 12.3b). This is consistent because *FT* is florigen, the inducer of flowering. Expression of the *CsTFL1* gene, a homolog of flowering suppressor *TFL1* (*Terminal Flower 1*), was not altered by high temperature at shoot apices, indicating that *FT* pathway is solely inhibited by high temperature. They also confirmed this phenomenon by grafting between high-temperature sensitive cultivar ‘Mona Lisa’ and high-temperature

tolerant cultivar 'Kurarisu', where high-temperature retardation of flowering occurred depending on root-stock cultivars.

In summary, cultivation of chrysanthemums is the best around 18–20 °C. Symptoms are observed at higher temperatures, such as retardation of short-day induced flowering, reduction in flower area, and reduction in pigment synthesis. Physical treatments should be performed to reduce temperature in the greenhouse, or high-temperature-tolerant cultivars should be used/bred to avoid symptoms, when chrysanthemums are grown at high temperatures. Knowledge on the other short-day plants is nearly lacking, but a similar phenomenon is observed in *Eustoma*: elongation of inflorescence stem is inhibited at high temperatures in *Eustoma* seedlings, causing rosette-like structure without flowers. Thus, mechanisms of high-temperature inhibition of flowering must be also analyzed in the other plant species.

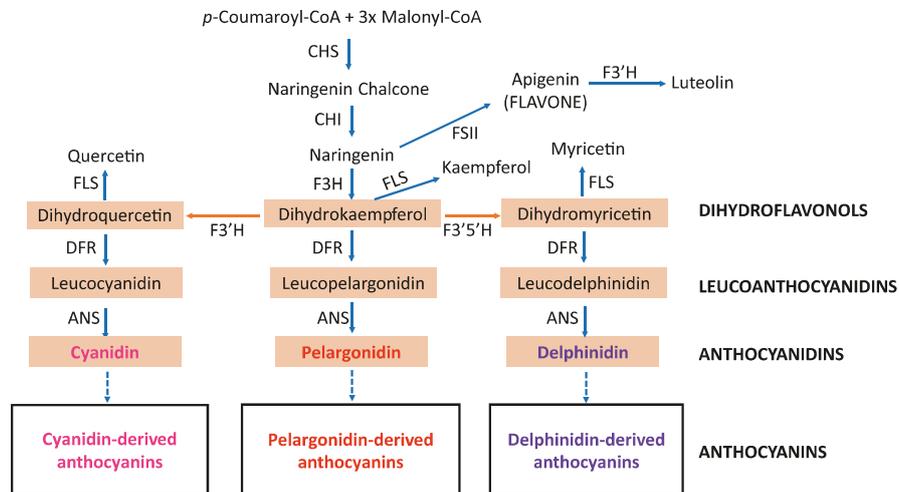
## 12.3 High-Temperature Effects on Petal Colors

### 12.3.1 Anthocyanin Synthesis

Another problematic effect of high temperature to flowers is decoloration. Anthocyanin is a flavonoid subclass which is the pigment present in flowers responsible for color variations. Temperature is a key factor reducing biosynthesis of anthocyanin (Puangkrit et al. 2018), but we have to understand the process of anthocyanin synthesis first.

Animal pollinators are generally the cause of color polymorphism in flowers (Mu et al. 2010). Seed production in plant species is correlated with the flower color, size, and visitation rates of pollinators. Conversely, recent studies provided the information that flower color diversity is related to the physical factors of the environment (Mu et al. 2010). The different color polymorphism is directly proportional to the specialized metabolite anthocyanin in many of red, purple, and blue flowers, together with yellow/orange carotenoid and yellow/pink betalain. Decoloration of flowers in high temperature may affect pollination in nature, but decoloration affects sales of ornamental flowers in the market.

Cyanidin, pelargonidin, and delphinidin are the main anthocyanidins present in higher plants (Schwinn and Davies 2004). The first step of anthocyanin synthesis is catalyzed by chalcone synthase (CHS), which synthesizes naringenin chalcone from *p*-coumaroyl-CoA and three molecules of malonyl-CoA. Then the naringenin chalcone is catalyzed to naringenin in presence of chalcone isomerase followed by further synthesis of dihydrokaempferol in presence of flavonoid 3'-hydroxylase (F3'H; Fig. 12.4). Naringenin is also catalyzed to apigenin (flavone) which is catalyzed by flavone synthase. Again, in the presence of flavonoid 3'-hydroxylase (F3'H), apigenin is catalyzed to luteolin. In addition, dihydrokaempferol produces leucopelargonidin and further catalyzed to pelargonidin in presence of



**Fig. 12.4** Biosynthesis pathway of anthocyanins. *CHS* chalcone synthase, *CHI* chalcone isomerase, *F3H* flavanone 3-hydroxylase, *DFR* dihydroflavonol 4-reductase, *ANS* anthocyanidin synthase, *FLS* flavonol synthase, *F3'H* flavonoid 3'-hydroxylase, *F3'5'H* flavonoid 3',5'-hydroxylase, *FSII* flavone synthase. This figure was generated based on the data in Berman et al. (2016)

dihydroflavonol 4-reductase (*DFR*) and anthocyanidin synthase, respectively. Meanwhile, dihydroquercetin synthesized by dihydrokaempferol in the presence of *F3'H*. Dihydroquercetin is catalyzed to both quercetin and leucocyanidin by flavonol synthase (*FLS*) and dihydroflavonol 4-reductase (*DFR*), respectively. Cyanidin synthesis is catalyzed from leucocyanidin by anthocyanidin synthase. Dihydrokaempferol is responsible for synthesizing dihydromyricetin and myricetin which is catalyzed by flavonoid 3',5'-hydroxylase (*F3'5'H*) and *FLS*. Further, leucodelphinidin and delphinidin are synthesized in the presence of *DFR* and *ANS*, respectively. Finally, anthocyanins are synthesized by glycosylation of cyanidin, pelargonidin, and delphinidin (Fig. 12.4). Anthocyanins derived from cyanidin, pelargonidin, and delphinidin are typically pink, red, and violet, but colors (hues) are variable depending on the type of glycosylation and chemical environment in plant cell (vacuole).

For the synthesis of kaempferol, quercetin, and myricetin in gentian, flavonol synthase (*FLS*) is essential. Pelargonidin, cyanidin, and delphinidin (anthocyanidins) are altered by the sugars and other moieties binding to form anthocyanins in a species-specific manner. For example, different colors of the petals accumulate different anthocyanin like pink-flowered gentians (*Gentiana*) petals contains gentiocyanin, blue-flowered contains gentiodelphin and orange-flowered contains solely pelargonidin glycosides in their petals. In the case of *aurantiaca* and *lutea* types of gentian, similarities in amino acid sequences were revealed at *CHS*, *CHI*, *ANS1*, and *ANS2* loci, while *F3H* and *DFR* loci showed variation in amino acid sequences. Relatively high levels of transcripts are detected for *DFR*, *F3H*, *CHS*,

*ANS*, and *UDP-glucose: flavonoid-3-O-glucosyltransferase* genes in *aurantiaca* petals in comparison with *lutea* petals (Berman et al. 2016).

However, structural genes above themselves do not always regulate the anthocyanin accumulation. For example, the study conducted by Fatihah et al. (2019) in *Nicotiana benthamiana* and *Lilium* flowers describes that *ROSEA1* (*ROS1*, a *MYB*-type transcription factor) and *DELILA* (*DEL*, a bHLH-type transcription factor) regulate the biosynthesis of anthocyanin. There are myeloblastosis protein (*MYB*) complexes, *WD40*, and helix-loop-helix (*bHLH*) transcription factor families (Quattrocchio et al. 1998; Koes et al. 2005). Out of these three transcription factors, *WD40* is required for stabilization of “*MBW* complexes,” and *MYB* and *bHLH* co-expression is essential for activation of the structural genes for anthocyanin synthesis (Bovy et al. 2002; Hichri et al. 2011). In the process of regulating anthocyanin production, *MYB* plays a key role (Hichri et al. 2011). In many plant species, *MYB* alone is enough to stimulate anthocyanin production (e.g. *Anthocyanin1*(*ANTI*) of tomato (Schreiber et al. 2012) and *MYB10* of apple, strawberry, and potato (Kortstee et al. 2011)). In the case of maize *CI*, *MYB* is unable to stimulate anthocyanin without *bHLH* (Bovy et al. 2002). Therefore, biosynthesis of anthocyanin is regulated by both *MYB*- and bHLH-type transcription factors, whereas in some cases only one transcription factor is sufficient.

### 12.3.2 Decoloration of Petals

Anthocyanin content/accumulation varies from developmental stages and is induced by many factors including cold temperature (Chalker-Scott 1999). In other words, anthocyanin content in flowers is less at high temperatures. Conditioned low-temperature environments of petunia (Shvarts et al. 1997) and rose flowers (Biran and Halevy 1974) showed increased synthesis of anthocyanin content. In a study conducted on ‘Jaguar’ rose flowers by Dela et al. (2003) showed the long-term noticeable effect on concentration of anthocyanin when high temperature is applied. The anthocyanin synthesis enzymes (CHS and DFR) in ‘Jaguar’ were decreased by 50% after treatment of heat, revealing that declined anthocyanin content is because of reduced transcription rates of these genes. Therefore, even after the treatment with high temperature, the inhibition of anthocyanin accumulation continues by decreased levels of CHS and DFR (Dela et al. 2003). Similar studies on strawberries showed that inhibition of anthocyanin accumulation is caused by the decrease in the phenylalanine ammonia lyase (PAL) and CHI activities (Civello et al. 1997).

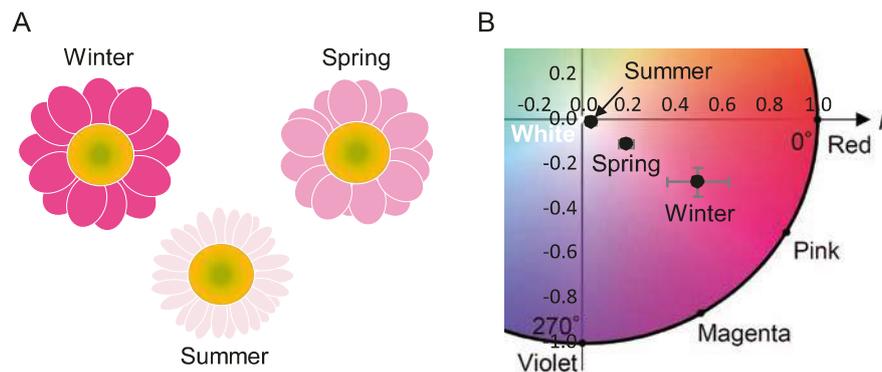
An interesting study by Nozaki et al. (2005, 2006) on *Chrysanthemum morifolium* Ramat. (pink flower genotype of *chrysanthemum*) revealed differential anthocyanin content under different temperatures or seasons. At 30 °C, the poor flower coloration was observed except for one genotype ‘Chatoo’ out of six pink-flower genotypes in greenhouse. Especially great difference in petal color was visible for ‘Sei-Monako’ genotype. In ‘Sei-Monako’, chroma (vividness) values were low under high temperature. The overall illustration of this phenomenon is shown in Fig. 12.5. In

addition, contents of cyanidin3-*O*-(6"-*O*-monomalonyl-beta-glucopyranoside) and cyanidin3-*O*-(3',6"-*O*-dimalonyl-beta-glucopyranoside) were lower at higher temperature (Nozaki et al. 2006). This study also indicated that the mean temperature is the key factor rather than day or night temperatures, to determine the coloration of flower.

Another study conducted on pink-flower chrysanthemum by Puangkrit et al. (2018) describes the effect of high temperatures on pigmentation, petal coloration, and flavonoid biosynthesis genes during the developmental stages of inflorescence. Exposures to 20 and 30 °C revealed that anthocyanin levels (cyanidin3-*O*-(6"-*O*-monomalonyl-beta-glucopyranoside) and cyaniding3-*O*-(3',6"-*O*-dimalonyl-beta-glucopyranoside)) at 20 °C were much higher than those at 30 °C. Observation throughout the "bud break to vertical stages" at 20 or 30 °C revealed the maximum temperature sensitivity of "petal extension to vertical stage" and its importance for pigmentation. The structural genes of anthocyanin biosynthesis (*CmplCHS1*, *CmplCHS2*, *CmplCHI*, *CmplF3H2*, *CmplC3'H*, *CmplDFR1*, *CmplDFR2*, and *CmplANS*) were heat-sensitive.

### 12.3.3 Color Influences Flower Temperature

Floral color (hue) is also adjusted based on the temperature of the environment (Dela et al. 2003; Stiles et al. 2007). Study was conducted on petal color changes and pigment concentrations (i.e. pelargonidin/cyanidin ratio) of Baccara rose by Biran and Halevy (1974) at different temperature ranges. The inner (reddish with major pelargonin) and outer (bluish with major cyanin) side of Baccara rose petals was examined under low (14 °C/20 °C) and high (18 °C/25–30 °C) temperatures.

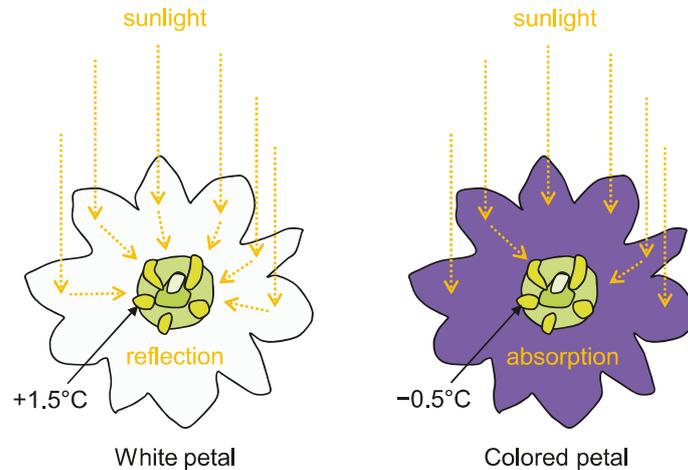


**Fig. 12.5** Decoloration of chrysanthemum. (a) Difference in the shape and color of cultivar 'Sei Monako' depending on the seasons. (b) Petal colors of cultivar 'Sei Monako' grown in winter, spring, or summer. Colors were plotted on color circle (Kasajima 2016, 2019). Saturation (vividness) is higher at edges of the circle, and the center of the circle is white/gray. The pictures in (a) illustrate data in Nozaki et al. (2005)

The result showed that ratio among cyanin and pelargonin was high in low temperature as compared to high-temperature conditions. Lacey and Herr (2005) reported that multiple floral parts of *Plantago lanceolata* produce maroon to black (dark-colored) spots in spring and autumn when the temperature is cool. The closely clustered spikes in the inflorescence are dark in these tiny flowers. These spikes are more reflective and lighter at summer due to reduced pigmentation (Stiles et al. 2007). Dark-colored spikes produced under cool temperatures absorb solar radiation more efficiently, and thereby they produce warm condition for seed development. On the contrary, less radiation is absorbed by light-colored spikes in summer, which is effective to cool flowers (Stiles et al. 2007). Thus, flower color influences temperature conditions of the flower itself.

Petal colors influence flower interior temperature due to the variance in absorption and reflection of the light in a bit different manner as well (Seymour et al. 2009b; Mu et al. 2010). This effect can be of significance for the adaptation of plants living in stressful conditions. For example, in drought- and heat-stressed conditions, individuals with pigmented flowers usually survive better than anthocyanin-free or less ones (Steyn et al. 2002), and white-flowered individuals are frequently susceptible to the stress and therefore suffer a large loss in fitness benefit (Coberly and Rausher 2003; Mu et al. 2010). In contrast to this, in arctic or cold alpine areas, flower color may have evolved to become white to help keep interior temperatures warm and stable against fluctuating ambient temperatures (Seymour and Schultze-Motel 1998). This adaptation is essential to the development of pollen, ovules, and fertilization (Mu et al. 2010). For example, the white petals of *Crocus chrysanthus*, an arctic herb species, reflect light into flower interiors to warm. Simultaneously, at ambient temperature, white flowers are generally warmer compared to yellow or purple flowers in interior structures but not in corolla, since white petals reflect light more efficiently than dark ones (Fig. 12.6; McKee and Richards 1998; Mu et al. 2010). Studies examining the relationships between petal colors, interior temperature of flower, and pollinator visitation rates usually employ a comparative methodology like between varieties of a single species. However, the different factors involved in these studies may be confusing. For example, the three varieties of *Crocus* differ in both flower structure and petal color (McKee and Richards 1998). Hence, further studies will be necessary to obtain direct evidence as to the effects of petal colors on flower temperature, by using genetic mutants or transformants.

In summary, high temperature reduces anthocyanin synthesis in flowers. High-temperature effects on carotenoids and betalains are not clear. If syntheses of these pigments are not susceptible to high temperature, flowers synthesizing these pigments do not show decoloration symptom in high temperature, unlike the flowers accumulating anthocyanin in petal. Reports on the effect of petal color on the temperature of flower interiors are also meaningful. White petals are cooler than colored petals in accordance with our imaginations, but flower interior is oppositely cooler in flowers with colored petals. This is thought to be a consequence of lower light reflectance on the colored petal. Consistently, colored flowers seem to survive better than white flowers in heat (Steyn et al. 2002).



**Fig. 12.6** Effect of petal color on flower temperature. Pictures illustrate reflection of sunlight on petals of *Gentiana leucomelaena*, an Alpine herb. White petals reflect more sunlight than deep-colored petals. Anthers are warmed by approximately 1.5 °C above the ambient temperature in white flowers, whereas anthers are cooled by approximately 0.5 °C in purple flowers; thus petal colors cause 2 °C difference in anther temperatures. This figure was generated based on the data in Mu et al. (2010)

## 12.4 Heat Production in Flowers

### 12.4.1 Heat-Producing Flowers

We are showing examples of heat damage to flowers, but adequate level of temperature is necessary for plants. Especially pollination seems to be dependent on relatively higher temperatures in many plant species. Some plants also heat themselves to tolerate cold temperature. In this section, we will review such examples where plants generate high temperature by themselves. Several seed plants actively elevate their body temperature above the surrounding environment. The first discovery of such plant thermogenesis was made by Jean-Baptiste de Lamarck in the eighteenth century (Lamarck 1778), who documented the thermogenesis in the inflorescence of European arum lily during blooming. To date, floral organ-specific thermogenesis (i.e. single flowers, inflorescences consisting of many florets, or cones) has been found in plants from diverse range of plant taxa, including the monocotyledon families Araceae, Arecaceae, and Cyclanthaceae; dicotyledon families Annonaceae, Aristolochiaceae, Hydnoraceae, Magnoliaceae, Nelumbonaceae, Nymphaeaceae, Rafflesiaceae, and Schisandraceae; and gymnosperm families Cycadaceae and Zamiaceae (Seymour 2010).

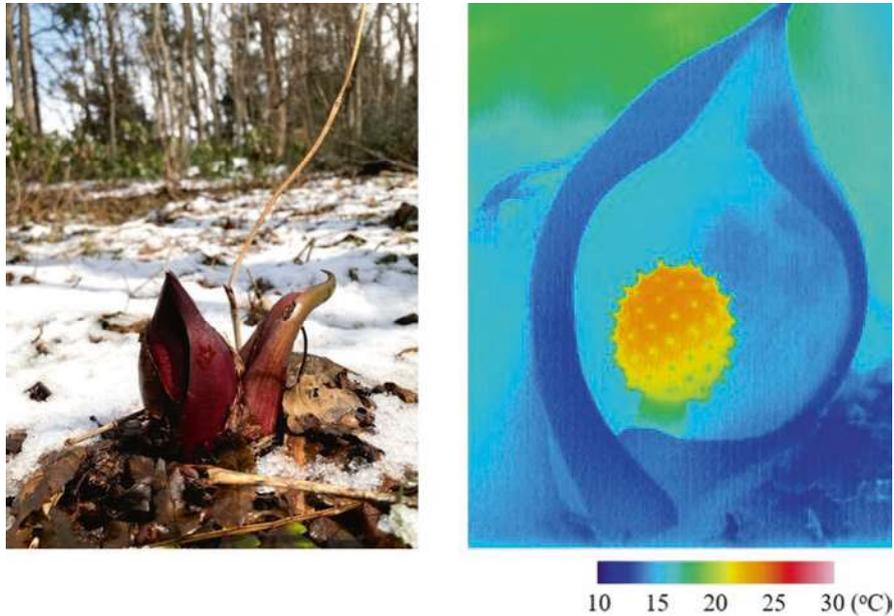
Heat production occurs by massive increase of cellular respiration rate in flowers (Meeuse 1975). Based on the pattern of heat production, the thermogenic plants are categorized into two groups: thermoregulatory and non-thermoregulatory (Seymour

et al. 2010; Kakizaki et al. 2012). Thermoregulatory plants can regulate floral temperatures to a constant level for several days during blooming, even if ambient temperature fluctuates. Thermoregulation has been observed in a few species of thermogenic plants, *Philodendron*, *Symplocarpus*, and *Dracunculus* belonging to the family Araceae and *Nelumbo* belonging to the family Nelumbonaceae. In contrast, most thermogenic plants are non-thermoregulatory which cannot maintain the floral temperature, namely, thermogenesis occurs explosively and transiently.

Plant thermogenesis is closely associated with floral development (Seymour 2010; Kakizaki et al. 2012). Although the molecular mechanism for the initiation of thermogenesis has not been fully understood, some physiological experiments demonstrated that salicylic acid, which is a well-known plant hormone, is the trigger of heat production in thermogenic inflorescence of voodoo-lily (*Sauromatum guttatum*; Raskin et al. 1987; Raskin et al. 1989). Salicylic acid begins to dramatically increase in appendix of the inflorescence, the main thermogenic organ, in the late afternoon of the day before blooming, and immediately reaches 100 times higher than the basal level. In the next morning, blooming starts with the exposure of appendix by unfolding the “spathe” (a large bract that encloses the inflorescence), which is followed by the extensive thermogenesis in appendix, and the peak of its temperature reaches 10 °C above the ambient temperature. The salicylic acid-induced heat production in appendix is not observed when appendix is exposed to constant darkness, suggesting that thermogenesis is regulated by photoperiod (day/night length) as well (Raskin et al. 1989).

Other example of well-studied thermogenic plants includes sacred lotus (*Nelumbo nucifera*). About a century after observation of thermogenesis in sacred lotus by Miyake (1898), Seymour and Schultze-Motel discovered the physiological thermoregulation of its flower (Seymour and Schultze-Motel 1996, 1998). Here, it was demonstrated that the receptacle inside the petals is the main thermogenic organ. The period of thermoregulation is basically related to their pattern of “protogynous” (pistil maturing earlier than stamen) anthesis in this plant. The lotus bud initiates thermogenesis in early summer when the petals are still closed, and then thermogenesis continues when the petal opens slightly to reveal the stigmas. The thermoregulatory capacity is finally lost when flower fully opens to expose the stamens. The temperature of the thermogenic receptacle is typically around 30–36 °C within 2–4 days sequence of flowering, although the ambient temperature fluctuates between 10 and 45 °C. Moreover, the receptacle temperature is completely regulated even in constant darkness for over 3 days; thus thermoregulation of sacred lotus depends on temperature and is not influenced by photoperiod (Seymour and Schultze-Motel 1998).

Skunk cabbage, a member of Araceae family, is the only plant species demonstrating the thermogenesis at cold environment, at least at the moment (Fig. 12.7; Knutson 1974). There are species from eastern Asia (*Symplocarpus renifolius*) and eastern North America (*S. foetidus*), both of which are thermoregulatory and naturally growing on wetland (Nie et al. 2006). During blooming in early spring, they produce enough heat to melt snow (Kamata et al.

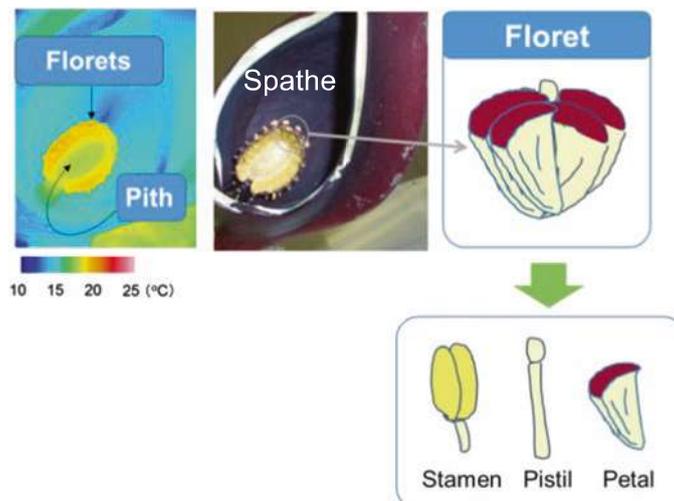


**Fig. 12.7** Thermogenesis of skunk cabbage. Left: The blooming stage of skunk cabbage in the field. Right: Thermography of the skunk cabbage. One of the spathe surrounding the spadix was cut off to display the spadix

2009). The thermogenesis occurs in its inflorescence (spadix), especially in florets (Fig. 12.8; Onda et al. 2008; Sayed et al. 2016). Interestingly, skunk cabbage maintains their spadix temperature at around 23 °C even if ambient temperature drops below zero (Seymour et al. 2009a). The thermoregulation of spadix continues during the fertilizable female phase for around 1-week period, which is the longest-term thermoregulation among all currently known plant species.

#### 12.4.2 Biochemical Basis of Thermogenesis

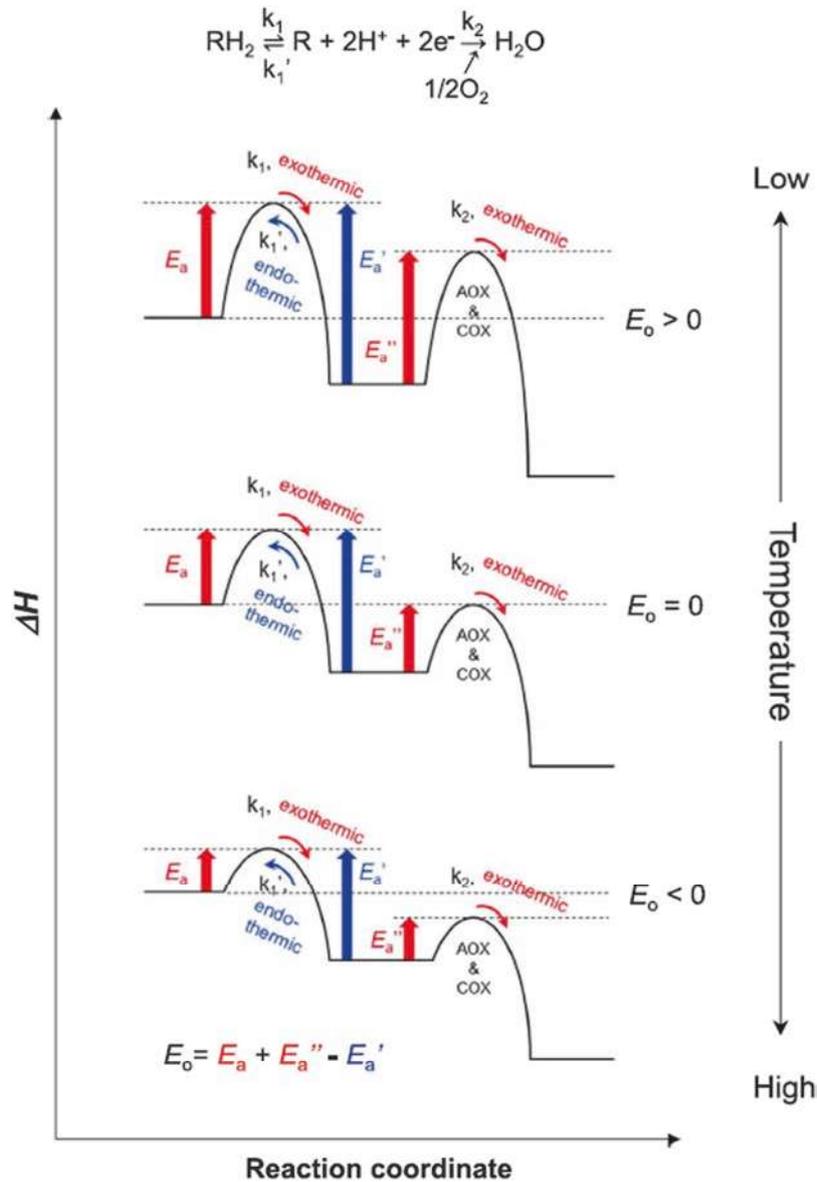
Biochemical mechanisms for thermogenesis of flowers are reported. Thermogenesis is associated with the metabolic heat production through the increase of respiration rate in flowers, especially with the “cyanide-resistant respiration pathway” via alternative oxidase (AOX; Moore et al. 2013). AOX is a mitochondrial enzyme in plants, fungi, and nematodes, and its expression is induced by several environmental stresses. AOX accepts electrons from the “ubiquinone pool” and uses them to reduce oxygen to water without generating ATP. Thus, the chemical energy is transformed to heat in AOX reaction. In thermogenic plants, the abundant AOX protein exists as the reduced (active) form in floral organ (Elthon et al. 1989; Umbach and Siedow 1993; Onda et al. 2007), probably due to the reduction via mitochondrial *o*-type



**Fig. 12.8** Structure of the spadix of skunk cabbage. Spadix is composed of a pith and numerous florets. Spathes are surrounding spadix. Thermogenesis is mainly observed at the florets of spadix. Each floret contains stamens, a pistil, and petals. This figure was cited from Sayed et al. (2016) under the Creative Commons CC-BY conditions

thioredoxin “Trx *o*” (Umekawa and Ito 2018). Therefore, not only the level of respiration rate, which is comparable to most animals, but also relatively high proportion of AOX-mediated respiration within the total respiration allow the thermogenic plants (flowers) to generate heat.

In the thermoregulatory flowers, thermoregulation is achieved by the temperature-dependent control of respiration in flowers: the floral respiration rate decreases as flower temperature rises and vice versa (Seymour et al. 2010). It is noteworthy that the temperature responses of the respiration in these flowers are opposite to the general chemical reactions where the reaction rate increases as temperature rises. Recently, we performed thermodynamic analysis on the respiration in thermogenic spadices of skunk cabbage (Umekawa et al. 2016). The results indicated that the thermoregulation is achieved by temperature-dependent change of cellular biochemical equilibrium comprising “exothermic (heat producing) and endothermic (heat absorbing) reactions” in the respiratory metabolism of skunk cabbage. Namely, the cellular equilibrium is formed by an exothermic pre-equilibrium reaction which consists of a fast-reversible step (reverse reaction is endothermic) that precedes formation of unstable intermediates ( $k_1$  and  $k_1$ ), and the following rate-limiting exothermic step determines the entire reaction rate ( $k_2$ ; Fig. 12.9). The occurrence of the reverse (endothermic) reaction in the pre-equilibrium reaction needs relatively high temperature due to its high activation energy (Fig. 12.9); thus the rate of the reverse (endothermic) reaction increases as temperature increases. Therefore, higher temperature increases the rate of reverse (endothermic) reactions and reduces the concentration of intermediates, and finally the entire reaction rate decreases. The

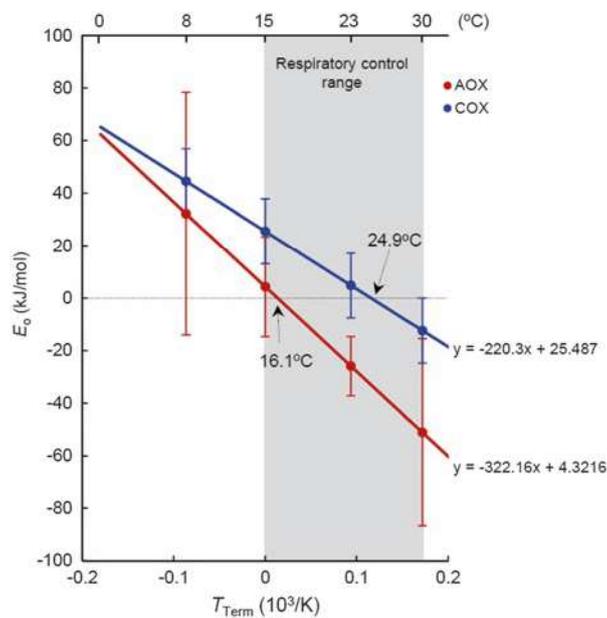


**Fig. 12.9** Model of the temperature-dependent respiratory control in thermogenic spadices of skunk cabbage. The model is composed of a leading fast-reversible step that forms equilibrium ( $k_1$  and  $k_1'$ ) and a final step of oxygen consumption through mitochondrial terminal oxidases (AOX and COX) ( $k_2$ ). The activation energies of the exothermic reactions with reaction constants  $k_1$  ( $\text{RH}_2 \rightarrow \text{R} + 2\text{H}^+ + 2\text{e}^-$ ) and  $k_2$  ( $1/2\text{O}_2 + 2\text{H}^+ + 2\text{e}^- \rightarrow \text{H}_2\text{O}$ ) are expressed as  $E_a$  and  $E_a''$ , respectively. The endothermic reaction with reaction constant  $k_1'$  ( $\text{R} + 2\text{H}^+ + 2\text{e}^- \rightarrow \text{RH}_2$ ) is indicated as  $E_a'$ . The overall activation energy ( $E_o$ ) is expressed as:  $E_o = E_a + E_a'' - E_a'$ . This figure was cited from Umekawa et al. (2016) under the Creative Commons CC-BY conditions

involvement of the endothermic reaction (NADPH production catalyzed by mitochondrial isocitrate dehydrogenase) in the respiratory control was a new concept for understanding the physiological thermoregulation. Here, both AOX- and COX-mediated reactions can be rate limiting steps in the pre-equilibrium reaction. To evaluate the contribution of those pathways to respiratory control, further studies on the temperature response of overall activation energy of AOX-/COX-mediated respiration were conducted (Fig. 12.10; Umekawa et al. 2016). The results indicated that AOX pathway is more sensitive to the temperature change than COX pathway. AOX-mediated respiration seems to be involved in the fast response of thermoregulation to the temperature fluctuations.

### 12.4.3 Significance of Self-Produced Heat

The biological significance of thermogenesis for plants has been of great concern to the researchers since its discovery. In some of the thermogenic plants, heat production initiates after flower opening; therefore thermogenesis may not be required for anthesis but is required for reproduction. Pollinator attraction is one of the most reasonable explanations so far (Meeuse and Raskin 1988). Most



**Fig. 12.10** Comparison of the temperature responses of  $E_o$  for mitochondrial respiration mediated by the AOX- or COX-respiratory pathways.  $E_o$  values of NADPH-NDA/ICDH-mediated respirations through AOX (red) or COX (blue) pathways. This figure was cited from Umekawa et al. (2016) under the Creative Commons CC-BY conditions

non-thermoregulatory species increase the scent production by volatilization during thermogenesis that makes flowers more attractive to insects. For example, titan arum (*Amorphophallus titanum*), which possesses the largest flower in the world (a maximum height of 3 m), also transiently produces heat and the animal-like odor in its inflorescence at night (Barthlott et al. 2009). The temperature gap between the warmed large inflorescence and the cool air in its natural rain forest habitat may cause heat convection. This could enhance the transport of scent far away. Moreover, thermoregulatory flowers can offer the energy reward for insect pollinators. Flying beetles, the main pollinators of thermoregulatory plants, require high body temperatures of their flight muscles to produce sufficient power; thus the constant warm environment inside the floral chamber makes the beetles save the energy cost for their activities (Seymour et al. 2003).

Thermoregulation is more directly important for the success of fertilization in some flowers. As mentioned above, skunk cabbage begins to bloom in early spring when pollinators are not in the field and pay massive energy cost to maintain their floral temperature for about 1 week. The optimal temperature for pollen germination and pollen tube growth is 23 °C, which is the same as the temperature regulated in the spadix of the skunk cabbage (Seymour et al. 2009a). Interestingly, no pollen germination or pollen tube growth was observed at 8 °C, which is higher than the average of ambient temperature during blooming of skunk cabbage (Onda et al. 2008). This suggests that physiological temperature regulation is crucial for the fertilization of skunk cabbage in their natural habitat.

In the present section, we showed that heat is not always harmful to flowers: optimal thermogenesis has essential roles in pollination and fertilization in some occasion. Heat may also benefit floral traits in the other aspects, although they are not basically the subject of this chapter. On the contrary, plants should be cooled to attenuate the harmful effects of high temperature. Plants decrease leaf temperatures through transpiration (Cook et al. 1964; Negi et al. 2008), although there is a risk to wither by losing leaf water. Thermoregulation by chemical equilibrium may be a clue for self-cooling of plants. If plants can heat themselves by chemical reactions, they would be also able to cool themselves. It is desirable to identify such a self-cooling mechanism of plants to attenuate heat stress.

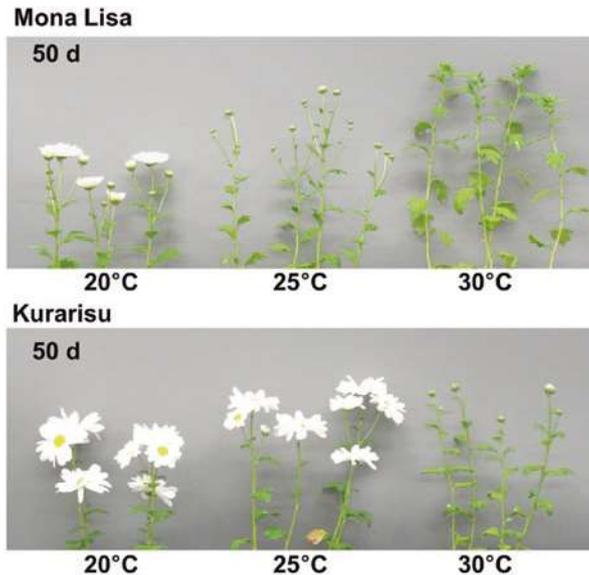
## 12.5 Genetic Approaches to Attenuate High-Temperature Effects

There seems to be no specific gene identified to function for flower tolerance to high temperature up to date. Nevertheless, there exists difference between cultivars as to flower tolerance to high temperature, and then some genes or genetic loci function for attenuating high-temperature effects on flowers, such as reduction of pigmentation and acceleration/delay of flowering. Such genes/loci should be identified in future studies. For example, some allele of the *MYB* gene encoding transcription factor

may function for high-temperature tolerance of pigment synthesis, and some allele of the *FT* gene encoding florigen may function for high-temperature tolerance of flower induction. Genetic studies on high-temperature tolerance of flowers are quite limited, but we will overview a few related studies in the present section. These will give good hints for future breeding of high-temperature-tolerant cultivars of ornamental/floricultural plants (flowers).

As already described in a previous section, flowering of chrysanthemum is delayed by high temperature, and this is due to the reduction in the expression of the *FT* gene (Nakano et al. 2013). In this report, they also showed that there is difference in high-temperature tolerance between chrysanthemum cultivars. Cultivar ‘Mona Lisa’ was bred in the Netherlands and relatively susceptible to high temperature. The optimum growth condition of chrysanthemum is 18–20 °C. *FT* expression is half reduced at 25 °C compared with 20 °C and dramatically reduced at 30 °C in this cultivar. This results in delay of flowering even at 25 °C (Fig. 12.11). In contrast, cultivar ‘Kurarisu’ was bred for summer production in Japan and then is tolerant to high temperature to some extent. The expression of *FT* is not affected at 25 °C, but it is dramatically reduced at 30 °C. Consistent with this, flowering is not delayed in ‘Kurarisu’ at 25 °C, although it is delayed at 30 °C (Fig. 12.11).

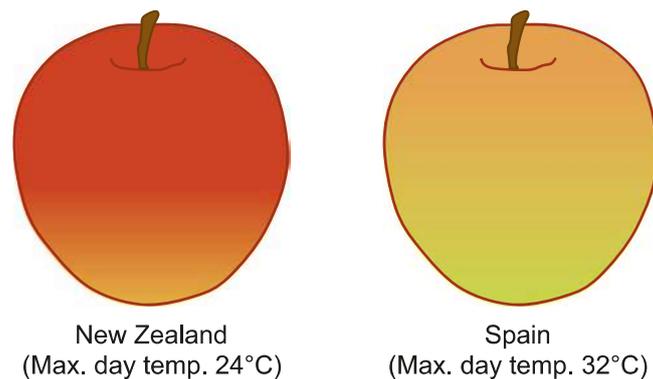
In *Eustoma (Lisianthus)*, rosette-like leaves are formed at high temperatures such as 25 or 28 °C, depending on cultivars. Thus, high temperature has deadly effect on flower production: plants do not form flowers until the next year. This will



**Fig. 12.11** Response of chrysanthemum to high temperature (3). Photographs of cultivars ‘Mona Lisa’ and ‘Kurarisu’, grown at 20, 25, or 30 °C. Photographs were taken 50 days after starting short-day treatment. Data were cited from Nakano et al. (2013) under the Creative Commons CC-BY conditions

be a protective mechanism of *Eustoma* plants against heat conditions, but agriculturally unfavorable trait. Some high-temperature-tolerant cultivars are reported such as ‘Florida Blue’ and ‘Florida Pink Frill’ (Harbaugh and Scott 2005). These cultivars can be grown at 28–31 °C without rosetting. The mechanism of their tolerance to high temperature is not clear, but *FT* pathway may be also involved in this phenomenon.

Fruits show similar symptoms as flowers in high temperature as well. Reports on genetic effects in fruits will benefit genetic approaches to attenuate the effect of high temperature in flowers. In the skin (surface) of apple fruits, synthesis of red anthocyanin pigment is inhibited by high temperature. Figure 12.12 illustrates decoloration of apple skin under high-temperature condition during fruit maturation. Anthocyanin content is reduced to approximately a quarter when this cultivar is grown in high temperature (Lin-Wang et al. 2011). In high temperature, expressions of all tested genes involved in anthocyanin synthesis, such as *chalcone synthase* (*CHS*), were suppressed. The *MYB1* gene (also called the *MYB10* gene) is responsible for the regulation of these genes and for red skin color of apple fruits (Takos et al. 2006; Kikuchi et al. 2017). Consistently, the expression of *MYB1* was reduced by high temperature, as well as the other regulatory genes. These trends were regenerated by artificial heating of fruits. Although high-temperature-tolerant apple cultivar is not identified, screening of apple cultivars may identify cultivars with strong allele of the *MYB1* gene, which can generate red fruits even in high temperature. Such trial to genetically enforce anthocyanin synthesis is performed in grape. In grape, *MYB* alleles regulate hue of skin anthocyanin (red or purple), and alleles of the *O-Methyl Transferase* (*OMT*) gene regulate anthocyanin concentration. Selection of purple *MYB* allele and strong *OMT* allele by DNA markers will generate dark-purple grape even in high temperature (Azuma et al. 2015). Identification of such “strong” alleles of the regulatory genes of anthocyanin will also improve flower tolerance as to decoloration in high temperature.

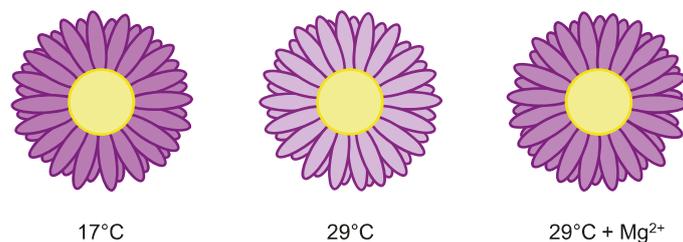


**Fig. 12.12** Decoloration of apple skin. Mature fruits of cultivar ‘Mondial Gala’ grown in orchards of New Zealand and Spain. The averages of maximum day temperature during fruit maturation in the orchards are indicated in the figure. The pictures illustrate data in Lin-Wang et al. (2011)

## 12.6 Physiological Treatments to Attenuate High-Temperature Effects

Chemical, physical, or physiological treatments have been also tested to attenuate unfavorable effects of high temperature on flowers. Cooling the greenhouse by air circulation and water mist is a basic treatment to avoid high temperature. Other additional strategies are taken when plants are not cooled enough by these methods. An interesting effect of magnesium on flower color was observed in aster (Fig. 12.13; Shaked-Sachray et al. 2002). In the cultivar ‘Sungal’ of aster, anthocyanin concentration of petals is approximately halved when growth temperature rises from 17 to 29 °C. The authors hypothesized that magnesium ion protects anthocyanin from degradation at high temperature, and actually anthocyanin concentration was nearly recovered to the original level when they applied 0.8 mM of magnesium ion to aster. It will be important to test whether this kind of approach is also effective in other floricultural plant species.

Shading (cutting off sunlight) with shading net is a popular approach to avoid high-temperature effects. In rice, the temperature of flower was decreased by 2.4 °C (Ishimaru et al. 2016). Due to this treatment, heat sterility of rice cultivar ‘Thadokkham1’ was reduced from 23.3 to 10.0%. Zhao et al. (2012) shaded herbaceous peony cultivar ‘Dafugui’ (Fig. 12.14; Zhao and Tao 2015). By cutting off 60% of sunlight, the day temperature was reduced by 3 °C. The decreased temperature itself will merit plant growth, but reduced intensity of sunlight affected both photosynthesis and flower color: the color of petal was clearly lighter in shaded plant, due to less accumulation of anthocyanin. We can learn from this phenomenon that the deepness of flower color is increased by both lower temperature and higher light intensity, and higher light intensity is more important at least in some cases. The same phenomenon was also observed in tuberose (Huang et al. 2000). The pink flower color of tuberose cultivar ‘77A05’ is lost at 30 °C. The color remains white with 45% shading. In addition, the pink color at 25 °C is also reduced (become lighter) with 45% shading, indicating that high light intensity is necessary to



**Fig. 12.13** Decoloration of aster. Colors of the petals of aster flowers are illustrated. Flowers were grown at 17 °C/9 °C or 29 °C/21 °C day/night temperatures in left or center, respectively. Flowers were grown at 29 °C/21 °C day/night temperatures, with treatment (drench for 3 times, a week apart) of 0.8 mM of  $\text{Mg}(\text{NO}_3)_2$  in right. This illustration was prepared based on the data in Shaked-Sachray et al. (2002)

**Fig. 12.14** Decoloration of herbaceous peony. Flowers of herbaceous peony cultivar ‘Dafugui’ grown with or without shading (‘shade’ and ‘sun’, respectively). Data were cited from Zhao and Tao (2015) under the Creative Commons CC-BY conditions



generate pink color of the flowers. The effect of shading on flower color is not clearly detected at 20 °C. Flower colors of the other plants may be also regulated by the balance between temperature and light intensity.

High temperature affects deepness of flower colors, but it may merit flower fragrance. Studies of Hirata et al. (2016) observed decoloration and decrease of rose petals in summer (Fig. 12.15), just like the other plant species. On the contrary, they noticed that the fragrance of this rose cultivar is stronger in summer. They analyzed that a different bioanalytic pathway of flower scent is active in summer. This will be because rose flowers try to compensate for the smaller size of flowers to attract pollinators.

## 12.7 Conclusion: Strategies to Attenuate High-Temperature Effects

Flowers change or modulate themselves in response to temperatures much more than we imagined before starting to write the present chapter together. Many parts of the changes under high temperatures are unfavorable for production of ornamental flowers, such as deformation of flowers (Fig. 12.1), but some changes may be beneficial such as increased fragrance in rose and increased number of flowers in chrysanthemum. Heat is also beneficial in heat-producing flowers, for pollinator



**Fig. 12.15** Decoloration of rose. Flowers of rose cultivar ‘Yves Piaget’ grown in winter and summer. Average ambient temperatures were 6 or 26 °C in winter or summer, respectively. Data were cited from Hirata et al. (2016) under the Creative Commons CC-BY conditions

attraction and pollination reaction. Plants respond to high temperature through Phytochrome B pathway (Fig. 12.2). This pathway will be responsible for high-temperature-induced changes at least in some cases. One of the typical symptoms of high temperature is heat delay of flowering in short-day plant (chrysanthemum), although flowering is accelerated in long-day plant (thale cress). High temperatures in both day and night delay flowering of chrysanthemum (Fig. 12.3); nevertheless high-temperature-tolerant cultivars can express the *FT* gene in leaves even in moderately high temperature and can avoid heat delay of flowering (Fig. 12.11). Another typical symptom of high temperature is decoloration of anthocyanin pigment in the petal (Fig. 12.5). Magnesium treatment is potentially effective for avoiding this effect (Fig. 12.13). There are also genetic differences in tolerance to decoloration: strong alleles of *MYB* or *OMT* genes are beneficial for tolerance to decoloration. Data indicate that dark-colored petals are good at cooling interior structure of flowers (Fig. 12.6). This mechanism will function for seed production in high temperature in the field. Simple cooling of plants is certainly good to avoid high-temperature effects. For example, low-temperature treatment of *Eustoma* seeds and seedlings are good to avoid rosetting (Fukushima et al. 2009), although cooling needs energy and cost. Shading with shading net is an ecology way to cool plants, but decreased light intensity may cause decoloration (Figs. 12.14 and 12.15). The entire picture of the relationship between flowers and high temperatures is not still clear, but there actually exist genetic variations and physiological treatments which are effective to avoid high-temperature effects as above. Plants may be also able to cool themselves by unknown reactions, if they can heat themselves (Fig. 12.7).

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