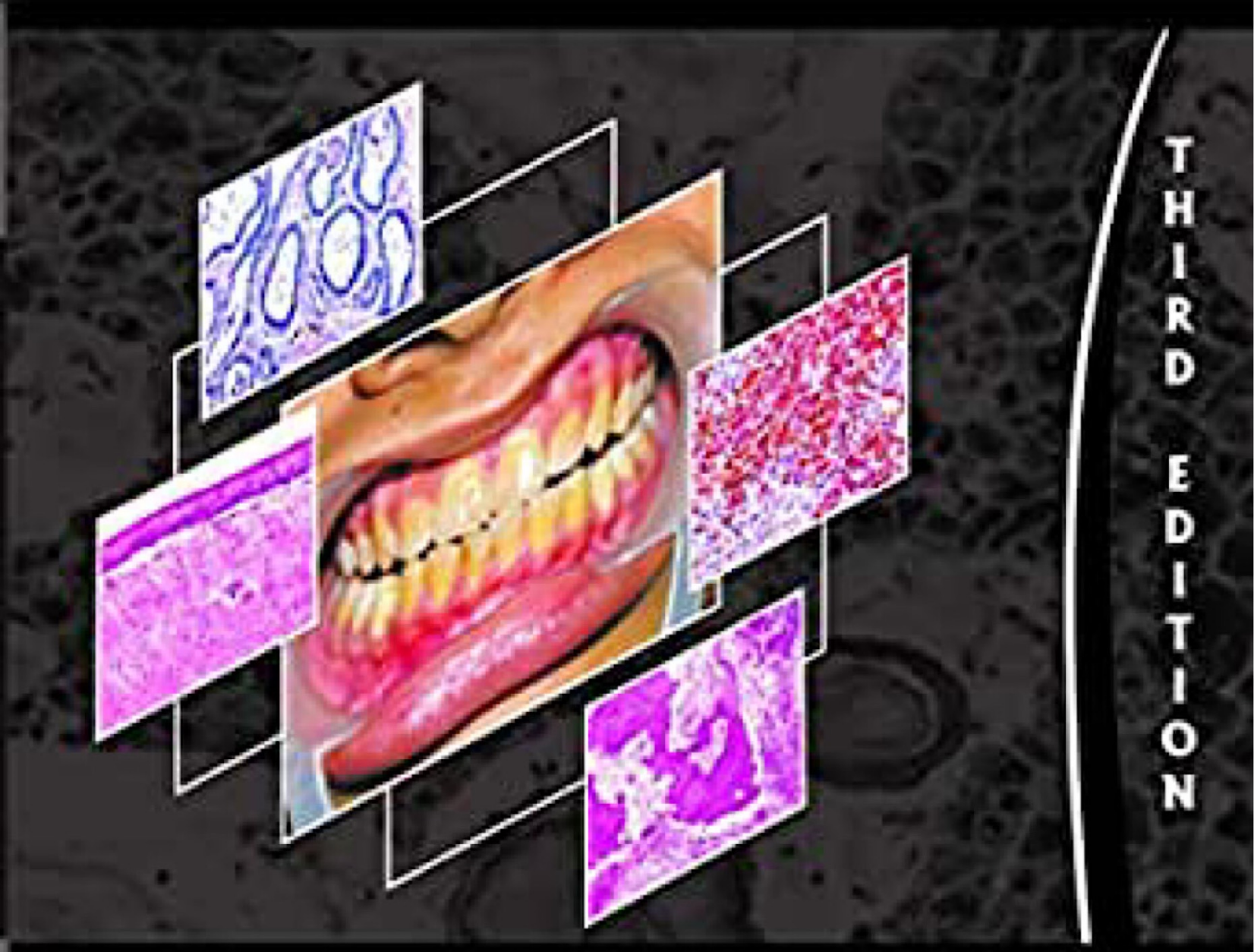

THIRD EDITION

Essentials of ORAL PATHOLOGY

Swapan Kumar Purkait

Forewords
RR Paul
Jay Gopal Roy
Tamal Kanti Pal

JAYPEE

Essentials of
Oral Pathology

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Essentials of Oral Pathology

THIRD EDITION

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Essentials of Oral Pathology

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https://t.me/RoyalDentistryLibrary

To

My children Prithu and Pubali

and my wife Maitreyee

https://t.me/RoyalDentistryLibrary

Foreword .....

Today our society needs not just a dental surgeon, but a medically competent dental surgeon. Oral pathology is undoubtedly the most integral subject of teaching in dental curriculum which bridges the gap between the medical and dental sciences. But the available textbooks in this field of oral pathology are so voluminous that it becomes virtually impossible for any dental student to gather comprehensive knowledge out of those textbooks during their BDS course of studies. In view of this, the textbook titled *Essentials of Oral Pathology* written by Dr Swapan Kumar Purkait seems to fill this lacuna admirably. I am sure this book will be of immense importance to the general dental practitioners too.

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https://t.me/RoyalDentistryLibrary

Foreword .....

It gives me immense pleasure to introduce the third edition of the book on oral pathology titled *Essentials of Oral Pathology* by Dr Swapan Kumar Purkait to the budding graduates of dentistry. Oral and maxillofacial pathology is a specialty of dentistry and a very fundamental subject for all the students contemplating to practice clinical dentistry at large.

The purpose of the latest edition of this book remains the same, i.e. to provide the reader with a comprehensive discussion of a wide variety of diseases that affects the maxillofacial region. The previous editions have been well accepted and so far thousands of students were benefitted by reading the same.

The immense effort put in by the author in bringing out this edition is highly commendable. We all trust in the basic philosophy that education brings in knowledge with consistent effort and knowledge when properly nurtured brings in wisdom. Similarly, this book has also grown qualitatively and refined with every new edition.

This book has twenty-three chapters, illustrations and photographs arranged systematically to fit in with the course and curriculum for undergraduate teaching; though much emphasis is not given on in-depth detail of molecular and biochemical aspects of modern diagnostic pathology, since this book has been written keeping in mind the need of undergraduate students only.

Finally, I wish Dr Purkait all success in life and my deepest regards to him for sharing his knowledge with the students. I conclude by saying "Man is not immortal but remains immortal through his work". I am sure all of us will be benefitted by this book.

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Foreword to the Second Edition

There is an ongoing search for an improved approach to deliver oral healthcare to ail human across the globe. The gap between the reality and expectations in oral healthcare system has become wider and this disparity, however, lies with the failure of transforming fundamental biological science into own clinical practice.

Oral pathology is one of the basic sciences in dentistry, the thorough understanding of which can certainly bring about qualitative changes in our clinical approaches towards amelioration of disease entity, providing both early intervention with better therapeutics and preventions. With this mission in mind, Dr Swapan Kumar Purkait, an eminent oral pathologist, has strived for new second edition of his book *Essentials of Oral Pathology*.

It is with great pleasure and profound satisfaction, I have gone through the entire edition and found it to be very informative and useful for persuing undergraduate studies. This is a wonderful piece of work with simple language and lucid presentation also, easy for students to assimilate and reproduce. About 150 pages have been added to this new edition to incorporate current contents and references and other chapters are thoroughly updated throughout. New chapters like Syndromes Related to Oral Diseases, Classification of Oral Diseases, and Diseases of TM Joint, will certainly enrich the readers.

The breakneck increase in information and indecent speed of expanding knowledge have paved the way for the second edition to come out. I am sure that this book will find its own place in dental profession and the readers shall have ready access to a comprehensive reference that enables rapid retrieval of integrated and relevant information on the subject.

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Preface to the Third Edition ..

The second edition of *Essentials of Oral Pathology* was published seven years back in the year 2003. I am grateful to the students and teachers of oral pathology for their acceptance and appreciation of the book. The purpose of the third edition is primarily to make qualititative upliftment of the book and to provide the students with more elaborate discussions on oral and orofacial diseases. Moreover, some new topics have also been added in this version. The highlighting features of this edition are the introduction of some special aspects of various oral lesions and the addition of several tables to pinpoint the key features of many important diseases. This edition is also coming in multicolor version, which I hope will be beneficial to the students in understanding the subject better.

I sincerely request the teachers and students of oral pathology to express their views and kindly provide me with constructive suggestions as to how this book can be further improved.

Swapan Kumar Purkait

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Preface to the First Edition....

Oral Pathology is an important branch of dentistry and although, there are few good textbooks available in the subject, *Essentials of Oral Pathology* has been written with a view to present the subject to the students in a more simplified but comprehensive manner.

I hope the book will fulfill the need of the students by giving them relevant guidance in their day-to-day learning process as well as during their preparation for examination and above all, with the book in hand, students will find the subject easy to handle.

As no one is perfect in absolute sense, I also humbly accept my limitations regarding shortcomings in the book and therefore, I sincerely welcome the valuable suggestions from my senior colleagues and students regarding what further should be done to improve this book.

Swapan Kumar Purkait

Acknowledgments .....

This book has been accomplished with the help of many people from all over the country and I am indebted to all of them. I wish to thank and express my sincere regards to my teachers Dr RR Pal, Dr Amit Roy, Dr (Mrs) Kabita Chatterjee, and Dr Tamal Kanti Pal for their constant encouragement and inspirations.

Special thanks to Dr Jay Gopal Ray for his continuous encouragement and whole hearted support.

Heartiest thanks are extended to Dr Alok Banerjee, Dr (Mrs) Mousumi Pal, Dr KP Das and Dr Madhumita Bhattacharjee for providing me with some brilliant clinical photographs for this book.

Deepest thanks to my wife Maitreyee , my daughter Pubali and Mr Suman Guha who have done a great job in making the computer generated graphic illustrations and designing of the tables used in the book.

I am thankful to my student Dr Sumanta Kumar Kolay (now an oral pathologist too) for his continuous support and encouragement extended as always during the course of writing the book.

Heartiest thanks to my seniors, friends and colleagues Dr Tushar Deb, Dr Bijoy Das, Dr Sanjib Mitra, Dr Anjana Majumder, Dr S R Karmakar, Dr Arup Ghosh, Dr Neeta Singh, Dr Shila Dey, Dr Narendra Singh, Dr Jayanta Chatterjee, Dr Sumit Majumder, Dr A Mamud and Dr Sourav Bhattacharjee for their whole hearted support and encouragement.

I am fortunate to have the constant encouragement and trust of Shri Jitendar P Vij, the Chairman and Managing Director of Jaypee Brothers Medical Publishers (P) Ltd along with his editorial and production staff.

Last but not least, I sincerely thank the students and teachers of Oral and Maxillofacial Pathology, who have made the 1st and 2nd edition of my book successful and this 3rd edition would not have been possible without their acceptance and appreciation.

If someone's name is inadvertently not included in this column of acknowledgment, I sincerely apologize for that.

Contents .....

CHAPTER 1

Developmental Anomalies of Oral and Paraoral Structures

INTRODUCTION

Malformations or defects resulting from disturbance of growth and development are known as developmental anomalies. A large number of such developmental anomalies, which involve the body in general and oral structures in particular can occur during the embryonic life. Manifestations of such defects are evident either at birth or sometimes after birth. These anomalies often have some serious implications on the further growth and development of the involved organ during the later stages of life.

Moreover, developmental anomalies affecting the teeth are seen more often then any other defects in the oral cavity.

Disorders of development of teeth may be due to abnormalities in the differentiation of the dental lamina and tooth germs (abnormal morphodifferentiation), which results in various defects in the number, size and form of teeth.

Besides this, abnormalities in histodifferentiation may cause defective formation of dental hard tissues, resulting in the disturbance of tooth structure.

Disturbance in histodifferentiation often occurs at a later stage of tooth development as compared to the disturbance of morphodifferentiation.

DEVELOPMENTAL ANOMALIES OF ORAL SOFT TISSUES

ANOMALIES OF LIPS AND PALATE

LIP PITS AND FISTULAS

DEFINITION

Lip pits are congenital invaginations, which can involve either the paramedial portion of vermilion border of lower and upper lips or the labial commissural area.

Types of developmental anomalies

Congenital anomalies	The defects, which are present at birth or before birth during the intrauterine life, are known as congenital anomalies.
Hereditary developmental anomalies	When certain defects are inherited by the offspring from either of the parents, it is called hereditary anomaly. Such types of anomalies are always transmitted through genes.
Acquired anomalies	Acquired anomalies develop during intrauterine life due to some pathological environmental conditions. They are not transmitted through genes.
Hamartomatous anomalies	A hamartoma can be defined as an excessive, focal overgrowth of mature, normal calls and tissues, which are native to that particular anatomic location. Developmental abnormalities occurring due to such hamartomatous change in the tissue are known as hamartomatous developmental anomalies.
Idiopathic anomalies	Developmental abnormalities of unknown cause are called idiopathic anomalies.

ORIGIN

The condition arises probably due to notching of the lip at the early stage of labial development, which causes fixation of tissue at the base of the notch. The condition may also arise due to failure of a complete union of the embryonic lateral sulci of the lip, which persist in the later life**.** Both lip pits and the commissural pits are developmental malformations, which appear to be inherited as autosomal dominant traits.

CLINICAL FEATURES

Lip Pits

- The lip pit is a **small depression over the lip**, which can be either unilateral or bilateral and are more commonly seen on the lower lip.
- These pits can be up to 3 to 4 mm in diameter and may have a depth of up to 2 cm.
- Lip pit occur more commonly among females and their frequency ranges from 1: 75000 to 1: 100000 among Caucasians.
- Congenital lip pits may occur either as an isolated condition or they may be associated with cleft lip and/or cleft palate (Van der Woude's syndrome).
- The opening of a lip pit on the labial surface often appears as a **circular or transverse slit**, moreover a lip pit opening may be located at the apex of a nipple like elevation.
- Mucous secretion is visible at the opening of those pits, which communicate with an underlying minor underlying salivary gland.
- Since the salivary gland orifices open into these pits, as a result saliva often exudates from them. However, exudation of mucus from lip pits onto the lower labial skin may cause embracement to the patient.

Commissural Pits

- The commissural pits measure from 1 to 4 mm in diameter, are found either bilaterally or unilaterally and often they have a familial tendency.
- Commissural pits can occur in association with multiple preauricular pits.
- Unlike lip pits, the commissural pits are more frequent among males and black people are affected more often than whites.
- In both lip and commissural pits, there are no signs of inflammation or ulceration and both conditions are harmless.

TREATMENT

While commissural pits require no treatment, the lip pits are sometimes surgically excised for cosmetic reason.

DOUBLE LIP

Double lip is a developmental anomaly characterized by a horizontal fold of excess or redundant tissue, on the mucosal side of the lip. It is usually located on the inner aspect of upper lip, although the lower lip can also be occasionally involved.

CLINICAL FEATURES

- Double lip is an oral anomaly, which can be either a congenital or an acquired one, the aquired type occurs mostly due to trauma.
- The condition clinically appears as a **"cupid's bow"** when the lip is tense but it is not visible when the lip is at rest.
- The defect can occur either alone or in association with other anomalies.
- Double lip in association with blepharochalasis (dropping of the upper eye lid) and nontoxic thyroid enlargement are known as **Ascher's Syndrome**.
- Clinically a double vermillion border is apparent with a transverse furrow between the two borders, when the patient smiles.

TREATMENT

Although, it is excised sometimes for cosmetic reasons, double lip mostly requires no treatment.

FRENAL TAG

DEFINITION

Frenal tag is a redundant piece of mucosal tissue, which projects from the maxillary labial frenum.

CLINICAL FEATURES

- It is a familial condition and seems to be inherited as autosomal dominant trait.

- The shape and size of frenal tag varies from patient to patient and is clinically asymptomatic.
- Sometimes, the condition is mistaken for a fibrous hyperplasia caused by local injury or irritation.

HISTOPATHOLOGY

Histologically, frenal tag consists of normal oral epithelium and connective tissue.

TREATMENT

No treatment is required.

HEREDITARY INTESTINAL POLYPOSIS (PEUTZ-JEGHERS) SYNDROME

DEFINITION

Peutz-Jegher's syndrome is a hereditary condition characterized by gastrointestinal hamartomatous polyposis in association with mucocutaneous pigmentations.

The disease is transmitted either through an autosomal dominant gene or it can occur spontaneously. It is a developmental condition and although pigmentation is an important feature of this disease, the primary disorder is actually not of the melanocyte system.

Incidence rate: Approximately, one case per 60,000 to 300,000 populations.

CLINICAL FEATURES

- Peutz-Jegher's syndrome begins in infancy (2nd and 3rd decade of life) and there is no sex predilection.
- Patients almost always have a positive history of the disease in the family.
- There is multifocal melanin pigmentations in the perioral locations, which often manifest as discrete, **brown to bluish-black or purpleblack macules** on the skin.
- The size of the macule varies from 1 to 5 mm in diameter and these macules often group around the oral, nasal and orbital orifices.
- The **pigmentation** is **most intense at the vermilion border** of the lower lip and it often extends both to the facial skin as well as into the oral mucosa (crosses vermillion border in about 94 percent cases).
- **Buccal mucosa** is the most frequently involved intraoral site, followed by palate, gingiva, tongue and floor of the mouth, etc. Sometimes these macules can be seen over the hands and feet as well.
- The skin pigmentations tend to fade away in adult life, while the mucosal pigmentations continue to persist.
- **Intestinal polyposis** is the other very important feature of Peutz-Jegher's syndrome besides the melanotic pigmentations. Although the polyps occur throughout the small intestine, colon and stomach are more commonly affected.
- Presence of these polyps can cause **recurrent abdominal pain** (in patients younger than 25 years of age), unexplained **rectal bleeding** and **prolapse** of tissue from rectum with diarrhea.
- Occasionally intussusceptions and intestinal obstruction may cause even death.
- The syndrome can also cause precocious puberty, menstrual disturbances in females, gynecomastia in males and development of testicular mass, etc.
- The polyps occur either as a hamartomatous growth or as an inflammatory lesion and they may have a very limited neoplastic potential.
- There can be growth acceleration in few patients due to concomitant occurrence of sertoli cell tumor.

Key points of Peutz-Jegher's syndrome

- Melanin pigmentations of the vermillion border
- Multiple intestinal polyps
- Recurrent abdominal pain and obstruction
- Precocious puberty in some cases.

HISTOPATHOLOGY

Histologic examination of the oral macular lesions exhibits excessive accumulation of melanin granules in the basal cell layer.

DIFFERENTIAL DIAGNOSIS

- Albright syndrome
- Addison's disease
- Oral melanotic macule.

DIAGNOSTIC ASSESSMENT

- Pigmentation in the perioral region is unique and often diagnostic for Peutz-Jegher's syndrome.
- Radiographic examinations can be useful for detection of intestinal polyps.
- Genetic counseling.
- Familial history of the diseases also helps in making diagnosis.

TREATMENT

No treatment is required for the oral and perioral melanotic macules. However, surgical intervention may be required for the intestinal polyps causing intussusceptions.

ORAL MELANOTIC MACULE (EPHELIS)

DEFINITION

Oral melanotic macule is an idiopathic benign pigmented lesion of oral cavity; characterized by increased focal melanin pigmentations in the oral mucosa.

CLINICAL FEATURES

- Oral melanotic macules present small, flat, well circumscribed, asymptomatic areas in the oral mucosa.
- These are seen commonly on the vermilion border of the lip (mostly lower lip) near the midline. Intraorally, the gingiva, buccal mucosa and the palate are the most frequently involved sites.
- Most of the lesions are less than one centimeter in diameter or sometimes little more and their color ranges from brown or black or bluish green, etc.
- There is no specific age group for this condition, however middle aged females are most often affected.
- The oral lesions are painless, firm in consistency and elliptical in shape.
- Solitary lesion of oral melanotic macule on the lip is called **labial melanotic macule.**
- The conditions are asymptomatic and have no malignant potential.

HISTOPATHOLOGY

- Microscopically, oral melanotic macule presents diffuse accumulations of melanin granules in the basal keratinocytes and the lamina propria.
- The lesions do not evolve from proliferation of melanocytes and there is no risk of malignant transformation in them .
- Occasionally, melanin incontinence is observed with pigmented granules being seen in subepithelial melanophages.
- Melanophagocytosis can also be seen.

DIFFERENTIAL DIAGNOSIS

- Superficial melanoma
- Blue nevi
- Amalgam tattoo
- Addison's disease
- Peutz-Jegher's syndrome.

TREATMENT

The persistent, innocuous looking lesions do not require any treatment, however biopsy is mandatory for a definitive diagnosis of the condition as well as to rule out any possibility of malignant melanoma.

UVULA ELONGATA

DEFINITION

Uvula enlongata is a developmental anomaly characterized by abnormally long uvula, which touches or hangs lower than the base of the tongue.

CLINICAL FEATURES

- The condition is usually seen at birth and sometimes it has a familial tendency for occurrence.
- It is seen more frequently among females than males.
- Although it is mostly asymptomatic, some sensitive patients may **cough or gag** when the elongated uvula touches the epiglottis or the base of the tongue.
- Acquired cases of uvula elongata, may occur as a result of chronic pharyngitis due to cola nut chewing.

DIFFERENTIAL DIAGNOSIS

Neoplasms of the uvula.

TREATMENT

In most of the cases, no treatment is required. However, in symptomatic cases, astringents can be used which will contract the uvula. In more severe cases, amputation is recommended.

CHEILITIS GLANDULARIS

DEFINITION

Cheilitis Glandularis is an uncommon, fundamentally benign, developmental anomaly of the lips characterized by **chronic, progressive enlargement of the labial salivary glands**.

Von Volkmann first introduced the term in 1870 and described it as a clinically distinct, deep suppurative, chronic inflammatory condition of the lower lip with mucopurulent discharge.

ETIOLOGY

- Chronic exposure to sun (actinic damage), wind and dust
- Factitial injury
- Infection, e.g. HIV
- Neoplasm especially squamous cell carcinoma
- Use of tobacco
- Emotional stress
- Heredity.

Recent investigations indicate that overexposure to sun with superimposed bacterial infection is the more likely cause of this condition.

CLINICAL FEATURES

- Cheilitis glandularis commonly occurs among middle aged or elderly adults and often there is a male predilection.
- Inflammatory enlargement of the superficial or deep minor salivary glands of the lip often causes **progressive, multinodular swelling**.
- There may be **secretion of clear, viscous exudates** from the minor salivary duct openings on the labial mucosa.
- Enlargement of the labial salivary glands often cause **eversion and induration** of the lower lip.
- Lower lip is involved more often than the upper lip and the vermilion borders as well as the labial mucosa are of normal color.
- However in many cases, the lip shows **diffuse keratosis** with scaling of the surface.
- Patient sometimes complain of **burning** discomfort or a feeling of rawness in the lip.
- When the **lip is everted** due to swelling of the glands, its surface often reveals multiple pits or fistulas representing dilated and inflamed minor salivary duct openings.
- Externalization and chronic exposure of the delicate labial mucosa often result in **erosion, ulceration, crusting and infection**, etc.
- Few cases of cheilitis glandularis may undergo **malignant transformation** and produce carcinoma of the lip.

Key points of cheilitis glandularis

- Swelling of the lip due to enlargement of the minor salivary glands.
- Lower lip involved more frequently.
- Lip is everted with multiple fistulas found on the surface.
- Exudation on the lip surface with occasional erosion, ulceration and crusting.
- It is predominantly caused by sun and dust exposure, stress and tobacco use.
- Increased risk of malignant transformation.

TYPES

Clinically cheilitis glandularis can be of three basic types:

A. The simple type
B. The superficial suppurative type and
C. The deep suppurative type.

The simple type is the most common variant of the disease and it presents multiple, painless, pinhead size swellings on the lip with central depression.

The superficial suppurative type of cheilitis glandularis presents painless swelling of the lip with induration, areas of shallow ulcerations and crusting.

The deep suppurative type is characterized by deep seated inflammation, abscess formation in the lip with development of fistulas tracts. The disease often heals by scarring.

Many believe these subtypes probably represent a continuation of the same disease process, i.e. if

the simple type of cheilitis glandularis is not properly treated, it becomes secondarily infected and progresses to the next type and then to the next.

DIFFERENTIAL DIAGNOSIS

- Cheilitis granulomatosa
- Crohn's disease
- Bacterial infection (Elephantiasis nostras verrucosa)
- Actinic cheilitis
- Squamous cell carcinoma
- Eczematous cheilitis
- Chronic factitial injury.

HISTOPATHOLOGY

- The surface epithelium can be either normal or hyperkeratotic.
- The underlying salivary gland tissue shows hypertrophy and inflammation with distention of acini.
- Squamous metaplasia of the ductal epithelium may be seen.
- Dysplastic changes can be noted in some cases especially in type II and type III cases with increased risk of malignant transformation.
- Frank evidences of squamous cell carcinoma are reported in about 18 to 25 percent cases in relation to this disease.

TREATMENT

Biopsy is mandatory especially in suspected cases, where the lip shows excessive keratosis or ulcerations.

Lesions with premalignant changes should be treated by surgical stripping of the lip without involving the vermillion border to save the esthetics.

CHEILITIS GRANULOMATOSA

Cheilitis granulomatosa is an atypical granulomatous disease of the lip, the origin of which is not clearly understood.

PATHOGENESIS

As mentioned above the exact cause of cheilitis granulomatosa is not known. Some investigators believe it as a regional form of sarcoidosis or Crohn's disease, while others suggest it as a granulomatous lesion of allergic origin.

The disease may also occur due to hypersensitivity to bacterial toxins from a chronic focus of infection in another nearby location.

CLINICAL FEATURES

- Children and young adults commonly develop this disease (median age 25 years) and usually there is a female predominance.
- Either lower or upper or both lips show **a sudden diffuse, nontendered, nodular enlargement,** which involves the entire lip.
- Generally, the lower lip is enlarged on a more regular basis.
- In some rare cases, patients exhibit lip swelling along with swelling of cheeks, eyelids and scalp, etc.
- The swelling is usually **painless, firm** and exhibits no pitting upon pressure.
- There is no sign of inflammation or ulceration on the surface of involved lips in the initial stage.
- During the early stage, the disease is sometimes accompanied by **fever, malaise and visual disturbance**, etc. Regional lymph nodes are enlarged in about 50 percent cases.
- The initial swelling **subsides within few hours or days**, however with more and more attacks of the disease, the swelling tends to become larger in size and **persists longer**, and eventually become permanent. Some lesions can even regress very slowly over the years.
- Enlarged lips often create some **cosmetic problems** due to the presence of **several cracks** and **fissures** on the surface along with a reddish-brown discoloration.
- Patient may also have difficulties during eating, drinking or talking.
- Few lesions may exhibit **scaling, fissuring and vesicle or pustule formation** at the vermilion border. The fissured lip is often painful and is firm, rubbery in consistency.
- Patients sometime complain of **decreased salivary secretion** and loss of **taste sensation**.
- Cheilitis granulomatosa in association with facial paralysis and fissured tongue constitutes the " **Melkersson-Rosenthal Syndrome**".

- The facial paralysis is intermittent at first but later on it becomes permanent in nature, the paralysis may be unilateral or bilateral, complete or incomplete.
- Besides lip lesions, few other oral lesions can possibly occur in association with cheilitis granulomatosa, these include nodular or papillary tumor on the tongue, some multinodular lesions and a reddish or bluish plaque on the buccal mucosa or palate.

Key points of cheilitis granulomatosa

- Diffuse, firm painless swelling of the lip with difficulty in eating, drinking and talking.
- Granulomatous inflammation or allergy is the suspected underlying cause.
- Cheilitis granulomatosa, facial paralysis and scrotal tongue constitute Melkersson-Rosenthal syndrome.

HISTOPATHOLOGICAL FEATURES

- Microscopically, cheilitis granulomatosa (Fig. 1.1) shows granulomatous inflammation of the lip with infiltration by chronic inflammatory cells, chiefly lymphocytes, plasma cells and histiocytes.
- The multinodular, noncaseating granulomas are often located close to the blood vessels and these are composed of epitheloid cells and swirled collagen fascicles with interspersed Langhans type of multinucleated giant cells.
- These noncaseating granulomas often simulate sarcoidosis and these lesions may replace the minor salivary glands of the lip.
- Generalized edema and dilated blood vessels are present throughout the connective tissue.

DIFFERENTIAL DIAGNOSIS

- Sarcoidosis
- Cheilitis glandularis.
- Angioneurotic edema
- Leprosy
- Crohn's disease
- Traumatic injury
- Lymphoma
- Edema and cheilitis subsequent to odontogenic infections.

TREATMENT

- Intralesional injection of steroid (Triamcinolone) may result in reduction in the size of the lesion.
- Surgical excision of the granulomas may be effective but often there is recurrence.
- Elimination of odontogenic and periodontal infections in the vicinity may produce reduction in the signs and symptoms of the disease.

ANOMALIES OF THE ORAL MUCOSA

FORDYCE'S GRANULES

DEFINITION

Fordyce's granules are **ectopic collections of numerous sebaceous glands**, generally unassociated with hair follicles and are found in various locations within the oral cavity (Fig. 1.2).

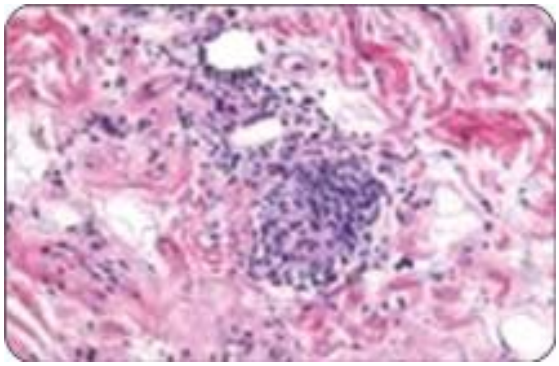

Fig. 1.1: Photomicrograph of cheilitis granulomatosa

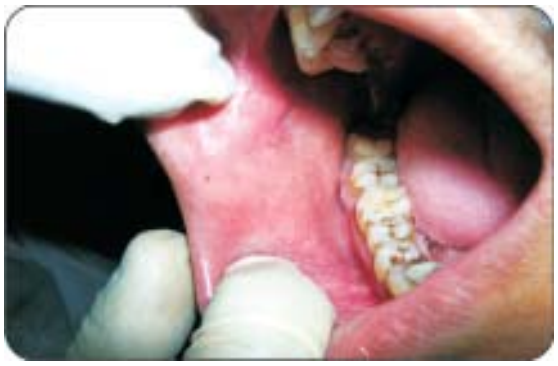

Fig. 1.2: Fordyce's granules

CLINICAL FEATURES

- Fordyce's granules are mostly seen in **adult life** and there is often a male predilection. These are rarely found in children before puberty.
- They commonly occur in a **bilaterally symmetrical pattern** over the upper lip, buccal mucosa, gingiva, anterior pillars of fauces and occasionally over the tongue. Fordyce's granules are seen rarely in the lower lip.
- Fordyce's granules can also be present in many extraoral locations such as the esophagus, genitalia, nipples, palms and the parotid glands, etc.
- Normally these glands are present in the 60 to 70% of adult population but their number varies widely between individuals.
- The number of Fordyce's granules in the upper lip increases during puberty while there is an increase in the number of these glands in the buccal mucosa in the later stages of life.
- Fordyce's granules clinically appear as **multiple, small, discrete, rice-like or milia-like yellowish-white bodies** beneath the surface mucosa. They measure about 1 to 2 mm in diameter.
- Those are completely asymptomatic conditions and in most of the cases patients are not aware of their presence in the mouth.
- On occasions, clusters of numerous sebaceous glands may form slightly raised confluent plaques with a creamy appearance.

HISTOPATHOLOGY

- Histologically, Fordyce's granules of the oral mucosa are identical to those of sebaceous glands, which are normally found in the skin, except the fact that they are not associated with hair follicles (Fig. 1.3).

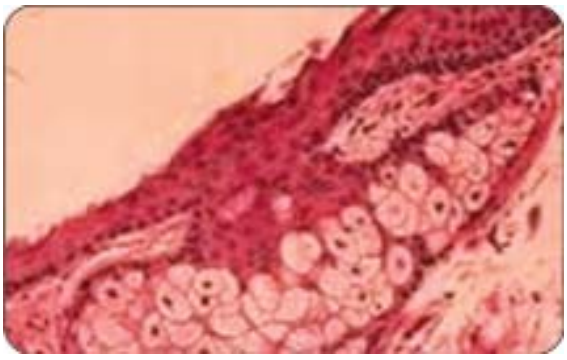

Fig. 1.3: Photomicrograph of Fordyce's granules

- These glands are located superficially, quite close to the surface epithelium and are composed of 1 to 5 lobules.
- They empty into a duct, which opens directly onto the mucosal surface. The duct may show keratin plugging.
- The **peripheral cells** of the Fordyce's granules are **flat and darkly stained**, whereas the inner cells are lipid rich and **pale** in appearance.

Key points of Fordyce's granules

- These are ectopic collections of sebaceous glands in the oral cavity (normal location is skin).
- Appear as multiple, yellowish, milia-like discrete granules on the buccal mucosa (bilaterally).
- Sebaceous cyst may develop from them.

DIFFERENTIAL DIAGNOSIS

The smaller size, multiplicity and typical yellow color are characteristic of the Fordyce's granules and are unlikely to be confused with any other mucosal lesions.

TREATMENT

No treatment is required for this condition. However, on rare occasions, sebaceous cysts or adenomas may develop from the preexisting Fordyce's granules.

FOCAL EPITHELIAL HYPERPLASIA

DEFINITION

Focal epithelial hyperplasia (commonly known as **Heck's disease**) is a condition characterized by multiple papillary or sessile hyperplastic areas in the oral mucosa.

ETIOLOGY AND PATHOGENESIS

- The disease is specifically found among American Indians, Northern native people and other ethnic groups in Europe and Africa.
- The exact etiology of Heck's disease is not known but it is probably caused by the Human Papilloma Virus (HIV) type 13 and 32.
- Similar appearing lesions may also be encountered among HIV seropositive homosexual males.

CLINICAL FEATURES

- The disease commonly occurs among children between the ages of 3 to 18 years and there is no sex predilection.

- Clinically, focal epithelial hyperplasia presents **multiple, small, pedunculated, polypoid or nodular soft tissue growths** in the oral cavity.
- They also can appear as well demarcated, slightly raised **plaques**.
- Sometimes several hyperplastic lesions may cluster together to produce a typical **"Cobblestone"** appearance.
- Labial and buccal mucosa are the most common sites and lower lip is more frequently affected than the upper. However, the disease can also involve the tongue, gingiva and anterior faucial pillars, etc.
- Individual lesions measure about 1 to 5 mm in diameter and are either white or pink in color.
- Most of the lesions regress spontaneously after about 4 to 6 months and occasionally few lesions can recur.

DIFFERENTIAL DIAGNOSIS

- Leukoplakia
- Psoriasis
- Keratoacanthoma
- Veruciform Xanthoma.

HISTOPATHOLOGY

- Focal epithelial hyperplasia histologically shows hyperparakeratosis of the covering epithelium with extensive acanthosis (increased thickening of the spinus cell layer).
- The epithelial cells of the upper spinus layer show enlarged nuclei and vacuolated clear cytoplasms (koilocytes).
- Deeper layer of epithelium reveals thickening, elongation and even fusion of the retepegs.
- Basal cell layer of the epithelium exhibit increased mitotic activity.
- Occasionally focal areas of liquefaction degeneration of the basal layer may be found.
- The underlying connective tissue is loose, well vascularized and exhibit variable infiltrates of lymphocytes.

TREATMENT

Since focal epithelial hyperplasia is a harmless, self-regressing condition, it usually requires no treatment.

WHITE SPONGE NEVUS

DEFINITION

White sponge nevus or Cannon's disease is a congenital mucosal abnormality, which appears to follow an autosomal dominant hereditary pattern and manifests as a white lesion of the oral mucosa.

PATHOGENESIS

- This condition is transmitted as an autosomal dominant trait with incomplete penetrance and variable expressivities.
- Mutations in the genes coding for keratins 4 and 13 (the pair of keratins expressed by epithelial cells in the mucosa affected by the disorder) have been identified, suggesting the disorder as a hereditary keratin defect.
- The heaping up of cells on the surface of the epithelium also suggests the possibility of an impaired normal desquamation process of the superficial strata of cells.

CLINICAL FEATURES

- White sponge nevus has its onset mostly **during childhood**. Some lesions are congenital and are present at birth and few lesions may even initiate during the adolescent period.
- There is no sex predilection, **several members of the same family** are often affected.
- The intraoral lesions are **almost always bilateral** and are mostly found over the buccal **mucosa** and tongue. Occasionally, the vestibular mucosa, palate, gingiva and floor of the mouth, etc. are also affected.
- Besides the oral mucosa, white sponge nevus can be seen on the conjuctivital, esophageal, nasal and anogenital mucosa as well.
- Clinically, white sponge nevus presents a **thick, bilateral, asymptomatic, deeply folded or corrugated white or gray lesion on the oral mucosa**.
- The surface of the lesion is **soft, uneven** and has a **shaggy** appearance with a **spongy** consistency.
- The lesions can be either diffuse or patchy and have a **translucent opalescence** similar to that of leukodema.

- The disease can sometimes present **ragged white areas**, which can be **peeled off by gentle rubbing** without any ensuing bleeding.
- It is a perfectly **benign condition** but is often mistaken for leukoplakia.

HISTOPATHOLOGY

- White sponge nevus histologically shows **marked thickening of the epithelium** with mild to moderate hyperparakeratinization, acanthosis and spongiosis.
- Marked intracellular edema of the spinus and parakeratinized cell layer of the epithelium is an important characteristic feature of the disease.
- The cells with intracellular edema show vacuolated cytoplasms and shrunken (pyknotic) nuclei.
- Intrestingly under microscope only the cell walls and the pyknotic nuclei at the centers of the cells are visible, which often gives rise to a so called **"basket weave"** appearance.
- Parakeratin plugging is another important finding in white sponge nevus, which runs from the surface and extends deep into the spinus layer.
- Individual cell keratinization may be seen in spinus cell layer.
- The basal cells are intact and the lamina propria shows no inflammatory changes.
- There is no evidence that this lesion undergoes malignant transformation.

ELECTRON MICROSCOPIC STUDY

Ultra structural studies of white sponge nevus reveal that some cells of the spinus layer differentiate early and become enriched with tonofilaments.

DIFFERENTIAL DIAGNOSIS

Thick, corrugated, diffuse white lesion in the mouth, with history of involvement of several members of the same family is usually suggestive of white sponge nevus.

However the following diseases are to be considered in the differential diagnosis of white sponge nevus.

- Leukoplakia
- Hereditary intraepithelial dyskeratosis
- Lichen planus
- Candidiasis
- Leukodema.

TREATMENT

No treatment is required for this disease.

DEVELOPMENTAL DEFECTS OF THE GINGIVAE

FIBROMATOSIS GINGIVAE

DEFINITION

Fibromatosis gingivae are rare, benign, diffuse, noninflammatory hyperplasia of the gingival tissue, which sometimes cover the entire teeth.

It is a hereditary condition, which is transmitted as an autosomal dominant trait. The disease is probably the result of a diffuse infiltrative hyperplasic proliferation of the fibroblast cells and mature collagen fibers of the gingival tissue.

CLINICAL FEATURES

- Clinically the disease is characterized by **dense, diffuse, smooth or nodular overgrowth** of the gingival tissue.
- Fibromatosis gingivae can be either **generalized** or **localized** in nature and it is similar in appearance to the dilantin hyperplasia of gingiva.
- The gingival enlargement **mostly appears in young children** or it may be present even at birth, however in some cases the swelling may not be noticed until the adult life.
- Both sexes are equally affected in gingival fibromatosis.
- The gingiva shows **multinodular enlargements especially in the interdental papilla regions**.
- The gingival tissue changes become obvious soon after the eruption of the deciduous teeth.
- The hyperplastic tissue is **firm, painless** and retains the normal **coral pink color** of gingiva.
- Sometimes the **markedly enlarged gingiva may cover the entire crown of the erupted teeth**. The eruption process of teeth is however normal.

- Elimination of dental plaque **does not** make any significant reduction in the severity of the disease.
- Occasionally, the condition is associated with **hypertrichosis, epilepsy and mental retardation**, etc.
- Gingival fibromatosis can also be associated with other syndromes, e.g. **Cowden's syndrome** and **Rutherford's Syndrome** (features of individual syndrome are given in the relevant chapter dealing with syndromes).
- Moreover, gingival fibromatosis can be a feature of "Laband Syndrome", which is characterized by splenomegaly, enlarged nasal and external ear soft tissue, shortened terminal phalanges, hypermobility of joints and hypoplasia of nails.
- Sometimes symmetrical fibrous overgrowths may occur bilaterally in the maxillary tuberosity region and few of such cases are possibly related to gingival fibromatosis.

HISTOPATHOLOGY

Histopathologically gingival fibromatosis presents the following features:

- The covering epithelium is hyperplastic and often exhibits thin elongated retepegs.
- The fibrous connective tissue consists mainly of course bundles of collagen fibers with scattered mature spindle shaped fibroblasts few of which are multinucleated.
- Mucoid changes in the gingival connective tissue may occur due to the accumulation of excessive amount of ground substances.
- There are significant numbers of mast cells often associated with the fibroblastic proliferation.
- Histologically, hereditary gingival fibromatosis is indistinguishable from other forms of gingival enlargements including those which are drug-induced.

DIFFERENTIAL DIAGNOSIS

- Phenytonin (Dilatin) sodium induced gingival hyperplasia.
- Generalized hyperplastic gingivitis.
- Leukemic infiltration of the gingiva.

History of familial involvement is extremely important in making the diagnosis of the disease.

TREATMENT

Periodic gingivectomy with placement of gingival acrylic splints for cosmetic and functional reasons.

RETROCUSPID PAPILLA

Retrocuspid papilla is a slightly raised area of mandibular alveolar mucosa, which as the name implies, is commonly located lingual to the cuspids.

- This structure measures about 2 to 4 mm and is often present bilaterally between the marginal gingiva and the mucogingival junctions.
- Retrocuspid papilla is more common among children and it has structural resemblance to the incisive papilla.
- Histologically, the papilla represents a focus of fibrovascular tissue with an orthokeratinized or parakeratinized surface and it usually covers an osseous foramen of a nutrient blood vessel.

DEVELOPMENTAL ANOMALIES INVOLVING THE JAWBONE

AGNATHIA

Agnathia refers to the complete failure of development of jawbone, involving either maxilla or mandible or even both the jaws. It is an extremely rare condition, however, often a portion of the jawbone, e.g. premaxilla, condyle, or ramus, etc. can be developmentally missing.

MICROGNATHIA

Micrognathia is an orofacial anomaly characterized by development of jaws, which are unusually smaller than normal (Figs 1.4 to 1.8).

CAUSES

- Pierre-Robin syndrome
- Hallerman-Steriff syndrome
- Trisomy 13
- Trisomy 18
- Turner syndrome
- Marfan syndrome
- Progeria

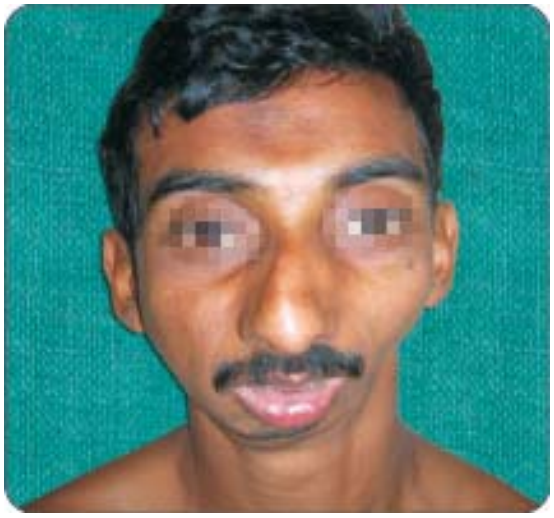

Fig. 1.4: Micrognathia (seen from front)-I

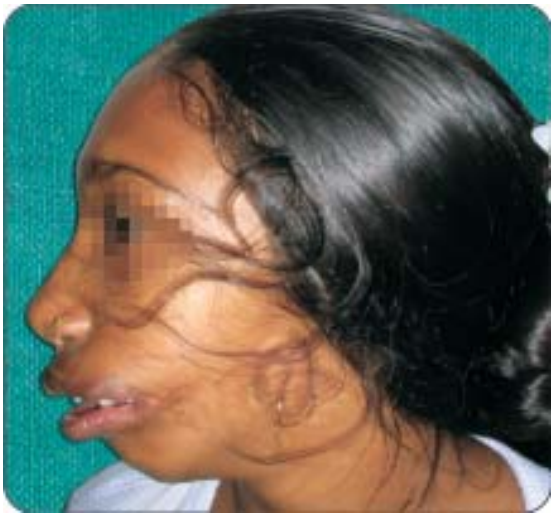

Fig. 1.6: Hemifacial microstomia (seen from side)-I

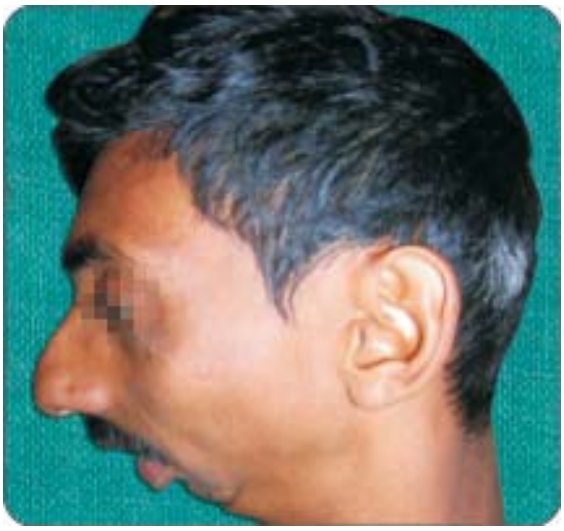

Fig. 1.5: Micrognathia (seen from side)-II

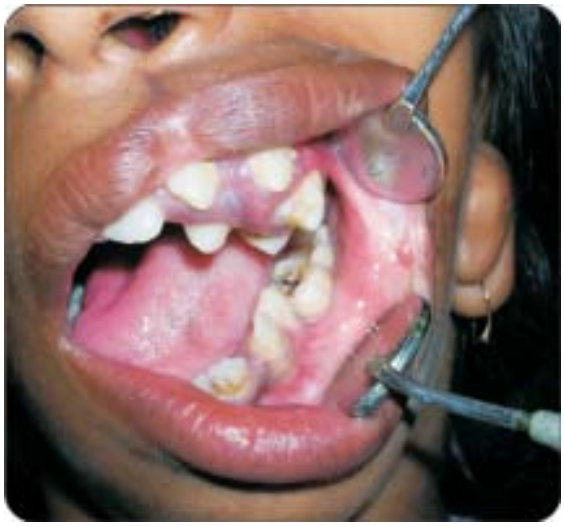

Fig. 1.7: Hemifacial microstomia (seen from front)-II

TYPES OF MICROGNATHIA

Micrognathia can be of two types:
A. Pseudomicrognathia
B. True micrognathia

Pseudomicrognathia: It is a condition where normal sized jawbone appears to look smaller when compared with the opposing jaw. A jawbone of standard size may appear smaller, if the opposite jaw is larger than normal or if it is positioned more posteriorly in relation to the skull.

True micrognathia: It is the condition, where the jawbone is actually smaller than normal and it can be either a congenital or an acquired problem.

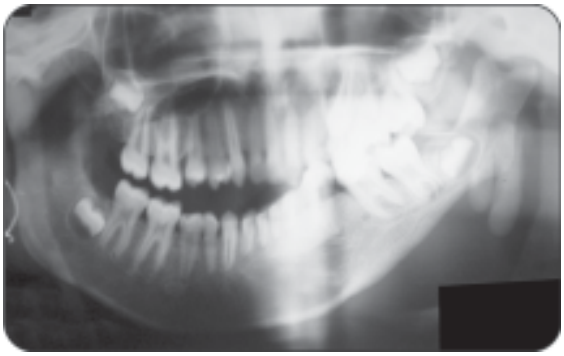

Fig. 1.8: Radiograph of hemifacial microstomia

The **congenital micrognathia** may follow a hereditary pattern and it often occurs in association with other congenital diseases such as Pierre-Robin Syndrome or congenital heart disease, etc.

Congenitally missing premaxilla often leads to maxillary micrognathia and patients with this anomaly show retracted middle third of the face.

Congenital mandibular micrognathia may occur due to posterior positioning of the condyle in relation to the skull.

Acquired micrognathia mostly occurs due to trauma or severe infections in the orofacial region especially in younger age. It may cause difficulty in feeding the child. Ankylosis of the temporomandibular joint in young individuals often leads to mandibular micrognathia with retruded chin.

CLINICAL FEATURES OF MICROGNATHIA

- Micrognathia often results in defective alignment of teeth, crowding and malocclusion, etc.
- Retruded chin with small face.
- Difficulty in feeding the children.
- Difficulty in proper articulation and speech.

MACROGNATHIA

Macrognathia is a developmental anomaly characterized by an abnormally large jaw. The condition can affect both the jaws at a time but more often it involves either maxilla or mandible.

TYPES OF MACROGNATHIA

True macrognathia: When the jawbone is abnormally large in size in true sense, it is called true macrognathia.

Pseudomacrognathia: *A* normal sized jaw may look larger when the opposing jaw is smaller than normal in size. This condition is known as pseudomacrognathia.

COMMON CAUSES OF TRUE MACROGNATHIA

- ***Pituitary gigantism:*** It is often associated with abnormally large jawbones. Both jaws are affected in gigantism and the bony overgrowth is proportionate to the generalized increase in the size of the skeleton.
- ***Paget's disease of bone:*** Paget's disease often causes increase in the size of maxilla, which is directly related to the generalized overgrowth of the cranium.
- ***Acromegaly:*** Progressive increase in the size of mandible occurs in cases of acromegally.
- ***Leontasis ossea:*** It is a form of fibrous dysplasia of bone and the disease is often associated with enlargement of maxilla.
- ***Hereditary causes:*** Mandibular prognathism often occurs hereditarily.

Mandibular prognathism may occur due to anterior positioning of the lower jaw in relation to the cranium, even though the exact size of the jaw is normal.

However, there are certain factors, which cause mandibular prognathism and thereby create an appearance of mandibular macrognathia.

These factors are as follows:

- Increased height of the ramus.
- Increased length of the body of mandible.
- Increased gonian angle.
- Decreased maxillary length.
- Posterior positioning of the maxilla in relation to the cranium.
- Prominent chin button.
- Varying soft tissue contours.

CLINICAL FEATURES OF MACROGNATHIA

- Mandibular protrusion (when manduibular bone is affected).
- Gummy smile (mostly maxillary).
- Ramus of mandible forms a less steep angle with body of the mandible.
- Excessive condylar growth.
- Prominent chin.

TREATMENT

In case of macrognathia, surgical correction (osteotomy) of the abnormally large jaw is often performed for both functional and esthetic reasons.

FACIAL HEMIHYPERTROPHY

DEFINITION (Figs 1.9 and 1.10)

Facial hemihypertrophy is a developmental condition characterized by disproportionate

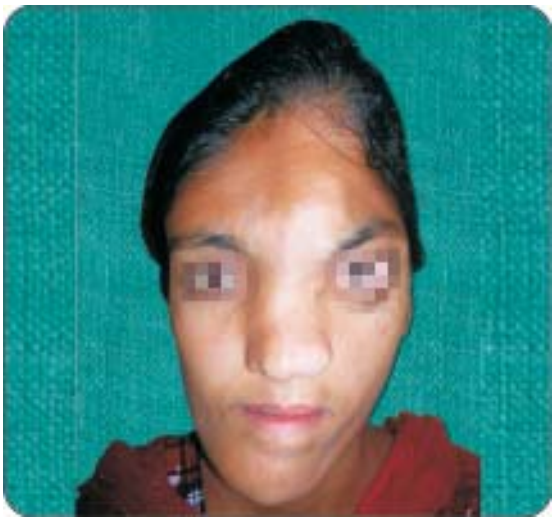

Fig. 1.9: Facial hemihypertrophy (seen from front)-I

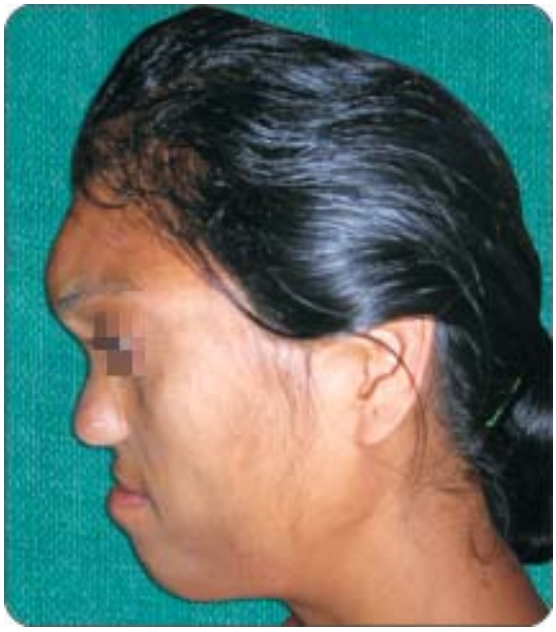

Fig. 1.10: Facial hemihypertrophy (seen from side)-II

unilateral enlargement of the face (Figs 1.9 and 1.10). Though the name is hemihypertrophy the actual underlying condition is a hyperplasia.

Although most humans exhibit some degrees of facial asymmetry only few individuals actually develop clinically significant facial hemihypertrophy.

ETIOLOGY

Although, a number of factors have been proposed to explain this condition, the most important ones appear to be vascular and neurogenic disturbances that cause an increased neurovascular supply to the affected side of the face resulting in its overgrowth. Other possible factors include the following:

- Hormonal imbalance
- Incomplete twining
- Chromosomal abnormality
- Defective intrauterine development (due to asymmetric intrauterine pressure)
- Lymphatic abnormalities.

CLINICAL FEATURES (FIGS 1.11 AND 1.12)

Facial hemihypertrophy clinically exhibits the following features:

- Unilateral enlargement of the facial soft tissues, bones and teeth.
- A positive family history is reported in many of these cases.
- Either side of the face can be affected and there is a slight female predilection for this condition.
- The asymmetry is more specifically noticed in the frontal bone, maxilla, palate, mandible, alveolar process, condyles and the associated soft tissues.
- The skin is thick and coarse on the affected side and also there is presence of thick and abundant hair (hypertrichosis).

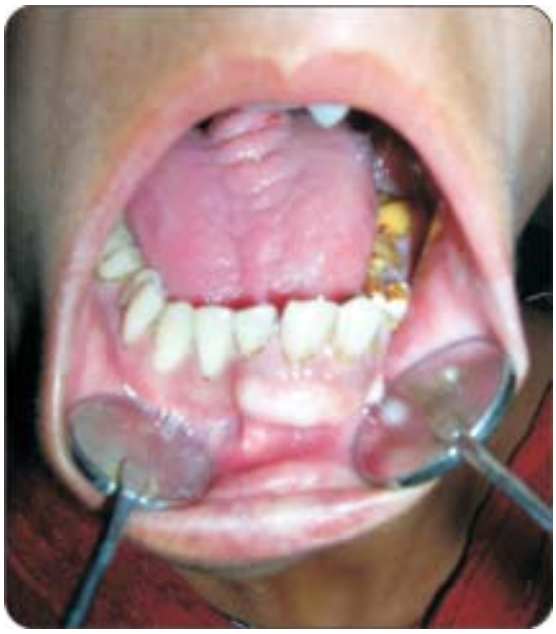

Fig. 1.11: Facial hemihypertrophy-III

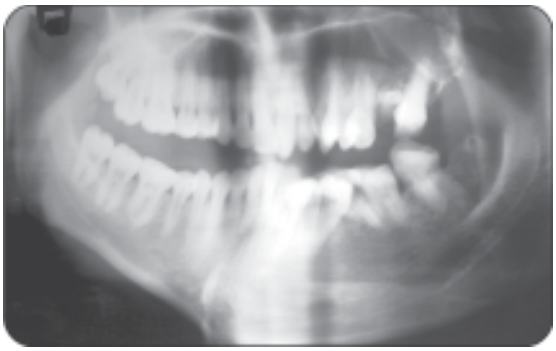

Fig. 1.12: Radiograph of facial hemihypertrophy

- The sebaceous and sweat glands on the affected side show excessive secretions.
- The ear and eye on the affected side may also be enlarged.
- Unilateral enlargement of the cerebral hemisphere may cause mental retardation and seizure in about 15 to 20% cases.
- There can be an increased incidence of certain systemic conditions in facial hemihypertrophy such as Wilms, tumor of kidney, adrenocortical tumor and hepatoblastoma, etc.
- On rare occasions, the hypertrophy may extend beyond the face and include the limbs or even the entire one side of the body.

ORAL MANIFESTATIONS

- Unilateral macroglossia with an increase in the size of the fungiform papilla is often seen.
- Crowns and roots of teeth, especially of the permanent teeth are often enlarged on the affected side.
- The teeth on the affected side may also erupt prematurely.
- There is often early shedding of deciduous teeth on the affected side.
- The jawbone proper is larger and thicker on the affected side.
- Because of the osseous and dental asymmetries in facial hemihypertrophy malocclusion often develops.
- Because of the overgrowth of soft tissue, buccal mucosa on the affected side appears pendulus and velvety, and folds of tissue may hang from there in the oral cavity.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of facial hemihypertrophy includes the following:

- Neurofibromatosis
- Fibrous dysplasia is of bone
- Arteriovenous malformations of jaws.

Key points of facial hemihypertrophy

- Unilateral enlargement of face including jaws, teeth, alveolar bone and soft tissues.
- Crown size of tooth and roots are larger on the affected side.
- Teeth on the affected side erupt earlier, tongue is larger and malocclusion is common.
- It's a developmental defect but hormonal imbalance and lymphatic abnormality, etc. are also important predisposing factors.

TREATMENT

No treatment is usually required for facial hemihypertrophy. However, selective surgical treatments may be performed to improve functional and cosmetic status wherever necessary.

FACIAL HEMIATROPHY

DEFINITION

Facial hemiatrophy also known as Parry-Romberg syndrome, is a developmental anomaly characterized by progressive decrease in the size of one side of the face due to atrophy of the facial structures.

ETIOLOGY

The exact etiology of the disease is not known however certain possible factors have been identified which can precipitate the condition. These factors include the following:

- Peripheral nerve dysfunction
- Trauma
- Heredity
- Peripheral trigeminal neuritis
- Infection
- Regional systematic sclerosis.

CLINICAL FEATURES

- The condition usually begins in the first or second decade of life. Many cases may be present since birth.

- Initially a slightly depressed vertical furrow or line is noticed at the midline of the forehead and eyebrow.
- As the condition progresses, facial tissues on the affected side including the skin, subcutaneous tissue, muscle and bone, etc. become atrophic, resulting in facial deformity.
- Usually the left side of the face is involved more often than the right side.
- Affected side of the face shows hyperpigmentation of skin with loss of hair.
- Severe cases may often result in hollowing of the cheek and depressed eye in the orbit.
- Other features associated with facial hemiatrophy include trigeminal neuralgia, contralateral jacksonian epilepsy and ocular and hair changes.
- The cartilage of the ear, nose and larynx, etc. may be affected.
- Occasionally the disease may affect other parts of the body.

ORAL MANIFESTATIONS

- Intraoral tissues on the affected side exhibit an overall atrophy.
- Delayed development of the jawbone.
- Tooth eruption on the affected side may also be retarded.
- Teeth on the affected side often have shorter crowns and roots.
- Development of the roots of teeth on the affected side is also delayed.

TREATMENT

There is no effective treatment for facial hemiatrophy. Progression of the condition ceases after certain age and it remains static thereafter for the remaining part of life.

CLEFT LIP AND CLEFT PALATE

Cleft lip and palate are the most common developmental defects in the head and neck region.

DEFINITION

Cleft lip: It is a developmental anomaly characterized by a **wedge-shaped** defect in the lip, which results from failure of two parts of the lip to fuse together at the time of development. This defect is more commonly seen in relation to the upper lip.

Cleft palate: It is a developmental defect of palate characterized by lack of complete fusion of two lateral halves of the palate resulting in a cleft. Cleft in the palate leads to communication between oral and the nasal cavity.

Cleft of the maxillofacial skeleton are quiet common entities and these can involve many structures of the orofacial region.

Congenital malformations causing clefts in the orofacial region

- Cleft lip
- Clefts of the primary palate
- Cleft of the secondary palate
- Mandibular cleft
- Oblique facial cleft
- Submucosal cleft palate
- Bifid uvula
- Pits of the lip.

These developmental defects often have very serious impacts on the growth, development and functions of the involved facial organ. Moreover, such defects can jeopardize the appearance of the face and badly affect the personality of the patient as well.

ETIOLOGY

The etiology of cleft lip and cleft palate covers both hereditary and environmental factors.

Hereditary Factors

Heredity is the most important single factor in the development of cleft lip and cleft palate. Different studies indicate that nearly 40 percent of cleft lip cases with or without cleft palate are hereditary in origin. Heredity also plays role in the development of about 20 percent cases of isolated cleft palate.

Moreover research also indicates that cleft lip or cleft palate of hereditary origin can occur either due to polygenic influence or monogenic influence.

Polygenic inheritance of cleft lip or cleft palate: If the origin of the disease is influenced by several different genes acting together, it is known as

polygenic inheritance. It is presumed that every individual carries some genetic liability for clefting and only if the combined liabilities of both the parents exceed a minimum threshold level, then clefting occurs in their offspring.

Monogenic inheritance of cleft lip and cleft palate: When clefting is influenced by only a single gene, it is called monogenic defect. Moreover the cleft lip and cleft palate of monogenic origin can be associated with numerous other syndromes.

Environmental Factors

Several environmental factors have been identified which probably play an accessory role in the development of cleft lip and cleft palate.

The factors include the following:

- Nutritional factors such as deficiency of or excess of vitamin A and deficiency of riboflavin.
- Maternal smoking (during pregnancy) is a very high risk factor.
- Psychogenic, emotional or traumatic stress in pregnant mothers.
- Relative ischemia to the area due to defective vascular supply.
- Mechanical obstruction by enlarged tongue.
- High dose of steroid therapy during pregnancy.
- Localized mucopolysaccharide metabolism defect in the area.
- Infections.
- Substances such as alcohol, drugs or toxins in the circulation.
- Pathological conditions like Streeter's fetal dysplasia.
- Lack of inherent developmental force.

PATHOGENESIS OF CLEFT LIP AND CLEFT PALATE

Cleft lip and cleft palate usually develop due to **incomplete obliteration** and maturation of different embryonic processes, which are associated with the formation of normal lip and palate.

- Mandibular cleft (lower lip and/or mandibular bone) usually occurs either due to **failure of the copula to form the mandibular arch** or **due to persistence of the central groove** of the mandibular process. Mandibular clefts are mostly midline defects.
- Cleft of the upper lip and premaxilla occur due to failure of mesodermal penetration and subsequent obliteration of the ectodermal grooves between the **median nasal process**, **lateral nasal process** and **the maxillary process**, which occurs during the seventh week of intrauterine life.
- The tongue occupies the space between two palatal halves during the initial phase of development. However, ninth and tenth week of intrauterine life are associated with mandibular enlargement and gradual downward movement of the tongue.
- If the tongue does not move downwards sufficiently, the palatal shelves remain separated and do not rotate to their horizontal position, this causes lack of fusion between the palatal shelves resulting in clefts.
- Palatal fusion occurs anteroposteriorly and is completed in between 11th and 12th week of the intrauterine life.
- Isolated cleft of the palate develops due to the failure of fusion between two palatal shelves in the midline.

A number of both genetic and environmental disturbances have been isolated, which can cause breakdown of the normal series of interdependent events or steps during the development of facial structures and result ultimately in cleft formation.

- ***Disturbed mesenchymal cell migration and/or proliferation:*** Failure of fusion of facial growth centers or palatal processes due to impaired mosenchymal cell replacement after palatal fusion.
- ***Suppressed cell division in associated structures:*** Reduced growth of cranial and/or Meckel's cartilages.
- ***Impaired intrinsic tissue function:*** Reduced tongue mobility and delayed ability or inability of palatal processes to elevate.
- ***Disturbance in inductive tissue interactions:*** Aberrant message leading to failure of palatal fusion.
- ***Suppressed programmed epithelial cell death following fusion:*** Incomplete palatal fusion or reopening of fused processes.

Classification of cleft lip and cleft palate

Davis and Ritchie classification	• **Group I:** Clefts anterior to the alveolus(unilateral, median, or bilateral CL). • **Group II:** Postalveolar clefts (CP alone, soft palate alone,soft palate and hard palate, or submucous cleft).
Veau classification	• **Group I (A):** Defects of the soft palate only. • **Group II (B):** Defects involving the hard palate and soft palate. • **Group III(C):** Defects involving the soft palate to the alveolus, usually involving the lip. • **Group IV (D):** Complete bilateral clefts.
Kernahan and Stark symbolic classification	• **Areas 1 and 4:** Lip. • **Areas 2 and 5:** Alveolus. • **Areas 3 and 6:** Palate between alveolus and the incisive foramen. • **Areas 7 and 8:** Hard palate. • **Area 9:** Soft palate.
International confederation of plastic and reconstructive surgery classification	• **Group I:** Defects of the lip or alveolus. • **Group II:** Clefts of the secondary palate (hard palate, soft palate, or both). • **Group III:** Any combination of clefts involving the primary and secondary palates.

INCIDENCE OF CLEFT LIP AND CLEFT PALATE

Incidence varies with racial and geographic background. Incidence of cleft lip and/or cleft palate is about 1 in 800 child births (range in 1:500–1:2500). It is interesting to note that when a couple have their first baby born with the defect of either cleft lip or cleft palate or both, their second baby will carry a 1% risk of having the same defect. The incidence of cleft lip and cleft palate are on the rise among modern population because the modern maxillofacial and plastic surgery can provide hugely improved and almost perfect esthetic rehabilitation to those patients who had cleft lip or cleft palate.

After the perfect surgical repair, the grown up people do not have any problem in free social mixing. Moreover, marriages between such people, who are genetically harboring the defect may give birth to children with even higher risk of developing cleft lip and cleft palate.

COMMON SYNDROMES ASSOCIATED WITH CLEFT PALATE

- Pierre-Robin syndrome
- Goldenhar syndrome
- Median cleft face syndrome
- Oral facial digital syndrome
- Apert's syndrome
- Cleidocranial dysplasia
- Schenthaner-Marie-Sainton syndrome
- Nagar syndrome
- Elashy-Waters syndrome
- Crouzon syndrome
- Larsen syndrome.
- Treacher-Collins syndrome
- Marfan syndrome
- Otopalatodigital syndrome
- Down syndrome
- Edward's syndrome.

CLINICAL FEATURES OF CLEFT LIP AND CLEFT PALATE

- These defects occur more commonly among male people.

- Most common type of cleft in both sexes combined is cleft lip and palate (Fig. 1.13).
- Most common type of isolated cleft lip only is unilateral complete type.
- The mildest form of cleft palate is the cleft uvula.
- Clefting involves left side of the face more often than the right side.
- As cleft palate creates a communication between the oral and the nasal cavities, patients often feel difficulty in taking foods and drinks due to nasal reflux or regurgitation.
- Breastfeeding is impossible to babies having cleft lip or cleft palate, as they cannot generate sufficient suction.
- In case of cleft palate, upper anterior teeth may be misplaced, deformed or impacted.
- Bony deficiency of upper jaw may cause retrusion of maxilla with narrow arched palate.
- Maxillary canine or premolars on the affected side may contact in lingual occlusion to the corresponding mandibular teeth due to retrusion of the maxillary bone.
- Deflection of nasal tip towards the non-cleft side and larger naris on the clefted side.
- Bilateral complete cleft is the worst situation, where complete separation of the anterior palate occurs (Fig. 1.14), which projects towards the mid portion of the lip and is attached only by the nasal septum.

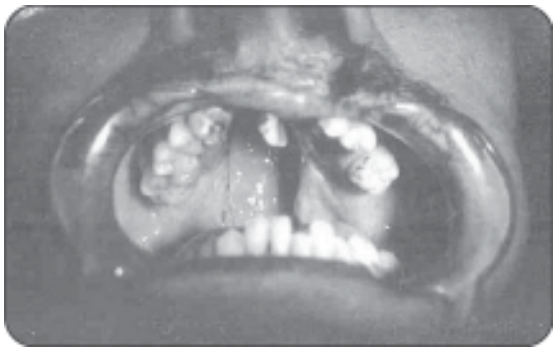

Fig. 1.14: Bilateral complete cleft palate

- Increased susceptibility to middle ear infections via the auditory tube.
- Difficulty is correct phonation and articulation of speech.
- There may be associated major congenital defects in the body including heart defects, spina bifida and mental deficiency, etc.
- Mental trauma to the child due to the unusual appearance as well as due to the speech problems, which often prevents them from mixing with other children freely.
- Improper or untimely surgical correction of these defects may also cause persistence of some ugly appearance and defective speech; moreover improper surgical correction may also result in an unbalanced growth of the mid face region in future.

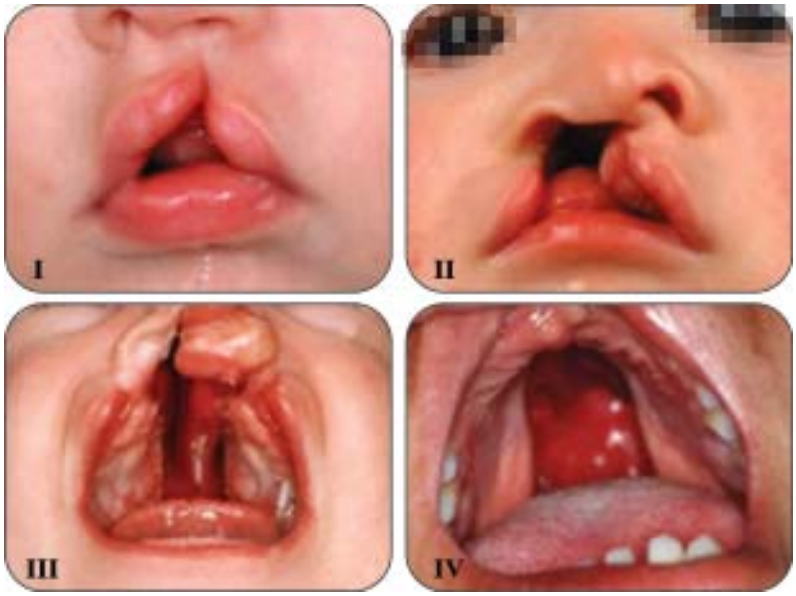

Fig. 1.13: Cleft lip and palate

Key points of cleft lip and cleft palate

- Important developmental anomaly occurring due to failure of fusion between various embryonic processes associated with development of normal lips and palate.
- Genetic abnormality is the single most important cause.
- More common in maxillary arch than mandibular arch.
- Maxillary cleft lip along with cleft palate occurs due to failure of fusion between median nasal, lateral nasal and maxillary processes in varying combinations and extents.
- Two palatal halves may also fail to fuse.
- Cleft lip and palate may be unilateral or bilateral; may be complete or incomplete types.
- Clinically, difficulties in food intake, speech, nasal regurgitation of milk in children, malocclusion and poor look, etc. are the important features.
- Timely surgical intervention is required.

TREATMENT

Treatment should be aimed at achieving the following goals:

A. Restoration of feeding to the children.
B. Proper development of speech.
C. Prevention of maxillary arch collapse.
D. Cosmetic repair of the face and lips.

- Cleft lip is treated surgically in the **first week after birth**, when the blood hemoglobin level is high and the kid is protected by the maternal antibodies.
- Sometimes, the surgery may be deferred until the baby attains 2 to 3 months of age, as by this time, the infant becomes adapted to its independent existence.
- Generally, cleft palates are corrected surgically at the **age of 18 months** or immediately after that. This particular time is selected since after this age there will be development of speech and any further delayed in treatment will cause abnormal speech development.
- Familial, social and psychological support is necessary during the protracted management.
- **Obturators** may be given in untreated adult patients with palatal clefts. The appliance helps in keeping the palatal clefts closed and thereby helps in speech and taking food.

DEVELOPMENTAL ANOMALIES OF THE TONGUE

AGLOSSIA

Aglossia is an extremely rare congenital defect characterized **complete absence of the tongue**. This condition is usually associated with other serious developmental defects in the body. Sometimes it occurs in association with aglossia-adactylia syndrome characterized by congenital absence or severe hypoplasia of tongue with absence of the digits.

MICROGLOSSIA

Microglossia is a rare congenital anomaly in which only a **tiny or rudimentary** tongue develops in the oral cavity. Although microglossia may develop as an isolated case but in most cases it occurs in association with other congenital anomalies, e.g. oromandibular limb hypogenesis syndrome or hypoglossia-hypodactylia syndrome, etc.

- Microglossia without limb deformity can occur but they are also associated with some other birth defects such as partial anodontia, sublingual gland hypertrophy and dextrocardia, etc.
- However, patients with microglossia don't have severe speech difficulties or difficulty in taking food.
- Small children often have problem in sucking milk.
- Since the size of the tongue often determines the growth and size of the mandibular arch, in case of microglossia the length of the mandibular arch is often smaller.
- Moreover, the smaller mandibular arch length often leads to development of severe malocclusion.

MACROGLOSSIA

Macroglossia is a relatively common condition characterized by an abnormally large tongue in the oral cavity.

TYPES

Macroglossia can be either congenital or acquired (secondary) in nature.

Causes of macroglossia

A. CAUSES OF CONGENITAL MACROGLOSSIA

- Idiopathic muscle hypertrophy causing over-development of the tongue musculature.
- Lysosomal storage diseases:
  - Hurler syndrome
  - Hunter syndrome
  - MaroteauxLamy syndrome.
- Down syndrome
- Beckwith's hypoglycemic syndrome.
- Multiple endocrine neoplasia syndrome.
- Lingual thyroid nodule.
- Gargolysm.
- Trisomy 22.
- Neonatal diabetes mellitus.

B. CAUSES OF ACQUIRED (SECONDARY) MACROGLOSSIA

Tumors in the tongue

- Lymphangioma
- Neurofibromatosis
- Plasmacytoma
- Hemangioma
- Carcinoma
- Metastatic tumors

Infiltrative diseases

- Amyloidosis
- Sarcoidosis

Systemic conditions

- Uremia
- Iatrogenic macroglossia

Traumatic conditions

- Surgery
- Tongue biting
- Radiation injury
- Hemorrhage
- Intubation injury

Endocrine disorders

- Acromegaly
- Hypothyroidism
- Myxedema
- Cretinism
- Diabetes

Obstructive lesions in the tongue

- Lymphatic obstruction of the tongue by any malignant tumor.

Inflammatory conditions of tongue

- Syphilis
- Pemphigus
- Small pox
- Actinomycosis
- Pellagra
- Ludwig's angina
- Tuberculosis
- Scurvy
- Typhoid

Cystic lesions in the tongue

- Dermoid cyst
- Epidermoid cyst

Relative Macroglossia

Relative macroglossia is a condition in which a normal sized tongue appears abnormally large if it is particularly enclosed within a small oral cavity. It happens mostly in cases of maxillary retrusion or in cases of restricated growth of nasopharynx.

Lymphangioma restricted to the tongue or in continuity with a cystic hygroma of the neck is the **most common cause of macroglossia**.

Relative macroglossia can also occur in conditions like enlarged tonsils or adenoids , habitual posturing of tongue, low palate with reduced volume of oral cavity and mandibular retrognathism, etc.

Apparent Macroglossia

Apparent macroglossia is a condition, where the tongue appears abnormally large due to poor muscular control of the tongue, although there is no real increase in the bulk of the tongue tissue. Apparent macroglossia is often seen in cretinism and in "Happy puppet" syndrome.

CLINICAL FEATURES OF MACROGLOSSIA

- Macroglossia causes displacement of teeth and malocclusion as the enlarged tongue creates continuous pressure or thrust on the teeth.
- It may disturb the process of speech and food intake to some extent.
- Some macroglossias may cause cosmetic deformity.
- The lateral margin of the tongue exhibits scalloping or indentations as the tongue is always pressed against the teeth.
- Children with macroglossia often develop tongue-thrusting habits, which may lead to malocclusion, open bite and diestema formation, etc.
- Macroglossia developing in adult people (as in acromegaly or in tumors, etc.) may produce spacing of teeth and distortion of the mandibular arch.
- Blockage of the pharyngeal airway due to macroglossia may result in a condition called "**obstruction sleep apnea**", which is characterized by intermittent cessation of respiration during sleep.

- Macroglossia can also be an important component of "Beckwith's hypoglycemic syndrome, which features—neonatal hypoglycemia, mild microcephaly, umbilical hernia, high birth weight and postnatal somatic gigantism.

It is important to note that CT scans can be helpful in determining, if the tongue size is normal or there is any deviation.

TREATMENT

- Removal of the primary cause whenever possible.
- Surgical reduction or trimming may be required when macroglossia disturbs the oropharyngeal function or is causing some major cosmetic problems.

ANKYLOGLOSSIA

DEFINITION

Ankyloglossia can be defined as a congenital developmental condition characterized by **fixation of the tongue to the floor of the mouth**; causing restricted tongue mobility. During functional movements, the tip of the normal tongue should touch the anterior palate but in case of ankyloglossia, it fails to reach up to that limit.

Complete ankyloglossia is an extremely rare condition, however partial ankyloglossia, which is otherwise known as "**tongue-tie**" is a relatively common developmental anomaly of the tongue. The tonguetie occurs either due to a short and thick lingual frenulum (a membrane connecting the undersurface of the tongue to the floor of the mouth) or due to a frenulum, which attaches too near to the tip of the tongue.

Ankyloglossia is almost always a congenital disorder and its prevalence rate ranges from 0.04 to 6.8 percent. According to few investigators this condition may sometimes develop as a result of trauma. Recent study of Harris EF et al indicate that incidence of tongue tie may increase with maternal use of cocaine during pregnancy.

CLINICAL FEATURES

- Ankyloglossia affects the males more frequently than females (2.6:1)
- Although most affected individuals can perform tongue functions almost normally, the restricted tongue mobility in ankyloglossia may sometimes cause the following problems:
  - Speech disorders—patient cannot properly pronounciate certain consonants and diphthongs such as L, R, T, D, N, TH, SH, Z, etc.
  - Patient pronounciates the word "lemonade" as wemonade.
  - Infants feel difficulty in sucking breast milk.
  - Deformities in dental occlusion especially development of open bite and mandibular prognathism, etc.
  - Difficulty in swallowing food and maintaining oral hygiene.
  - Tension in the anterior lingual gingiva in tongue-tie may initiate some localized gingival or periodontal diseases near the site of frenal attachment (e.g. gingival recession and persistent gap between lower incisors).
  - Difficulty in kissing, licking one's lips, eating icecream cones and performing tongue tricks.

Ankyloglossia may occur sometimes in association with the following syndromes:

- Ankyloglossum spurious syndrome
- Vander Woudes syndrome
- Fraser's syndrome
- Rainbow's syndrome
- Orofacial digital syndrome, etc.

TREATMENT

Partial ankyloglossia in most of the cases does not require any treatment, however in severe cases of ankyloglossia, surgical correction (frenulctomy) of the lingual frenulum is done to free the tongue. Sometimes, the offending frenulum may tear spontaneously resulting in freeing of tongue.

CLEFT TONGUE

Developmental disturbance may sometimes cause partial or complete cleft in the tongue. Although a complete cleft or bifid tongue is a rare congenital anomaly, however a partially cleft tongue is more frequently encountered.

Cleft tongue usually develops due to partial or complete failure of union between the two lateral lingual swellings during embryogenesis. Incomplete cleft in the tongue develops due to failure of mesenchymal tissue proliferation that obliterates the groove.

Partial cleft tongue clinically exhibits a deep groove in the midline, while the bifid tongue shows a complete cleft along its long axis. Cleft tongue in most of the cases is an asymptomatic condition although sometimes irritation can be felt due to accumulation of food debri or microorganisms at the bottom of the cleft.

Sometimes, cleft tongue may occur as a feature of the orofacial digital syndrome, other features of this syndrome include frontal bossing, short upper lip with cleft, presence of thick fibrous brands in the lower anterior mucobuccal fold eliminating the sulcus and cleft of the mandibular alveolar process, etc.

FISSURED TONGUE (SCROTAL TONGUE)

Fissured tongue is a congenital developmental malformation; characterized by presence of **numerous shallow or deep groves (fissures) on the dorsal and lateral surface of the tongue.**

ETIOLOGY

The exact etiology for this condition is not known, however the following factors are often suspected:

- Genetic defect (polygenic or autosomal mode of inheritance).
- Vitamin deficiency
- Trauma
- It may be a normal variation of tongue architecture.

CLINICAL FEATURES

- The overall worldwide prevalence rate of fissured tongue is about 7 percent (may be as high as 21 percent), prevalence in USA is about 2 to 5 percent.
- Slightly more common among males.
- Usually there is no clinical symptom in fissured tongue but collection of food debris and microorganisms in the fissures or groves may sometimes cause discomfort.
- Similar discomfort may also be felt when fissured tongue occurs in association with geographic tongue.
- The fissures or groves often radiate from a central groove on the dorsal surface in an oblique direction.
- The large and deep fissures may be inter-connected and they separate the dorsum of the tongue into multiple lobules.
- The average depth of individual fissure is about 6 millimeter.
- The disease often occurs in association with Melkersson-Rosenthal syndrome and some investigators believe that fissured tongue can be a feature of benign migratory glossitis.

HISTOPATHOLOGY

Histopathologically fissured tongue produces the following features:

- There will be loss of filliform papilla from the surface mucosa.
- Neutrophilic microabscess formation within the epithelium.
- Hyperplasia of the rete-pegs and increased thickness of the lamina propria.
- Mixed inflammatory cell infiltration in the connective tissue stroma.

TREATMENT

No treatment is required for fissured tongue except brushing of the tongue to eliminate the debris that irritates.

MEDIAN RHOMBOID GLOSSITIS

DEFINITION

Median rhomboid glossitis is an asymptomatic, elongated, erythematous patch of atrophic mucosa on the middorsal surface of the tongue.

ETIOPATHOGENESIS

In the past median rhomboid glossitis was thought to represent a developmental defect of the tongue, presumably arising as a result of persistence of the 'tuberculum impar'on the surface of dorsum of the tongue.

During normal embryognesis, however the tuberculum impar should retrude and is overgrown by the lateral lingual swellings.

In recent times, however several investigators believe that median rhomboid glossitis occurs due to chronic infection by *Candida albicans*.

CLINICAL FEATURES

Incidence: The average frequency of median rhomboid glossitis is about 0.2 percent among the general population.

Age: The condition is mostly seen among adults (30–50 years) and is rarely found among children.

Sex: Median rhomboid glossitis is seen more frequently among males (M : F-3 : 1).

Site: The lesion is located immediately anterior to the foramen cecum and the circumvallate papillae, in the midline on the dorsurm of tongue (at the junction of the anterior two-third and posterior one-third areas).

PRESENTATION (FIGS 1.15A AND B)

- The median rhomboid glossitis starts as a narrow, mildly erythematous area located along the median fissure on the dorsum of the tongue just anterior to the circumvalate papilla.
- The lesion finally appears as a **diamond or lozenge shaped** area devoid papilla.
- Clinically, the lesion is asymptomatic and it often remains unnoticed by the patient for many years.
- It enlarges slowly and the fully developed lesion of median rhomboid glossitis reaches to a size of little less than 2 cm in diameter.
- The color of the lesion varies from **pale pink to bright red** and occasionally there is presence of a white halo.
- The surface is usually smooth, flat or slightly raised and is sometimes fissured or lobulated.
- In many cases, the lesion exhibits an erythematous and nodular hyperplasia characteristic of chronic **hyperplastic candidiasis**.
- Some patients even develop a similar lesion on the midline of the palate just opposite to the tongue lesion and it occurs due to repeated contact with the infected tongue surface to the palate (kissing lesion).
- Median rhomboid glossitis is usually asymptomatic but occasionally it may cause slight soreness or burning sensation.
- The lesion is clinically suspicious and it is often mistaken for carcinoma of the tongue. Although dorsum of the tongue, where median rhomboid

Key points of median rhomboid glossitis

- Diamond or lozenge shaped depappilated area on the mid dorsum of the tongue, anterior to the circumvalate papilla.
- Color is erythematous and surface is generally smooth.
- Condition is asymptomatic with occasional irritations.
- Superficial candidiasis may be present
- Often mistaken for carcinoma, but it's an innocent developmental anomaly.

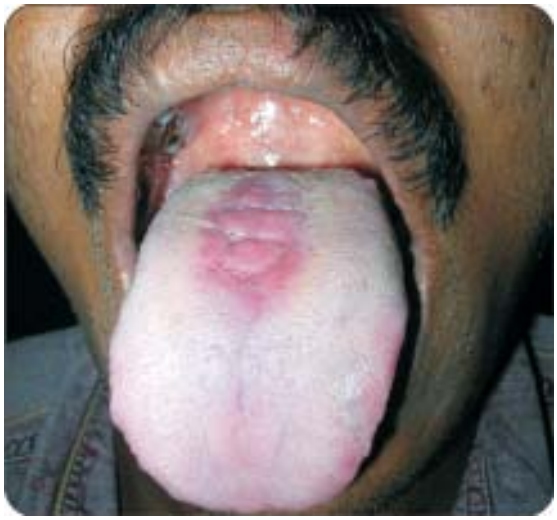

Fig. 1.15A: Median rhomboid glossitis-I

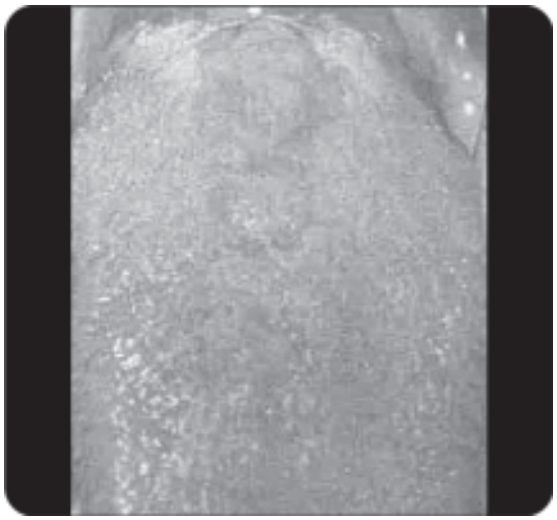

Fig. 1.15B: Median rhomboid glossitis-II

glossitis is located is not a frequent site for carcinoma of the tongue.
- In some cases the disease may regress spontaneously.

DIFFERENTIAL DIAGNOSIS

- Squamous cell carcinoma
- 'Gumma' of tertiary syphilis
- Granular cell myoblastoma
- Lingual thyroid nodule
- Tuberculous granuloma
- Deep fungal infection.

HISTOPATHOLOGY

Microscopically, median rhomboid glossitis presents the following features:
- Mild to severe parakeratosis of the surface epithelium.
- Loss of both filliform and fungiform papilla.
- Thinning of the supra-papillary epithelium.
- There may be presence of acanthosis with elongation of rete-ridges.
- The rete-ridges may either divide or anastomose.
- Superficial layer of the epithelium often shows neutrophilic infiltration, and often there is presence of numerous candidal hyphae.
- The underlying connective tissue is usually very vascular and is infiltrated by chronic inflammatory cells.
- Areas of irregular hyperplasia may be seen in the epithelium as a result of chronic inflammation in the underlying connective tissue.
- On occasions, the epithelium may show features of dysplasia or individual cell keratinization due to the chronic fungal infection.

TREATMENT

No treatment is basically required for this lesion. Antifungal agents and antiseptic gurgles are used to relieve the erythema and irritation in the area.

LINGUAL VARICES

DEFINITION

A varix is a dilated, tortuous vein which is often subjected to increased hydrostatic pressure but is poorly supported by the surrounding tissue.

CLINICAL FEATURES

- Varicosities can be observed in many oral locations like ventral surface of tongue, floor of the mouth, lips, buccal mucosa and the commissure, etc.
- Among all these intraoral locations, ventral surface of tongue and floor of the mouth are the most common sites for oral varices.
- Clinically lingual varices appear as small, round, purplish nodules, lateral to the sublingual vein, which is usually also deflected.
- Lingual varices are common among people over the age of 50 years and the varices tend to become more conspicuous with advancing age.
- Thrombosis can occur occasionally in these varicose veins, however only rarely there are any clinical symptoms.
- In case of lingual varices, there is absence of any similar lesion in the skin and other mucosal locations.
- The lesion interestingly has no bleeding tendency either.
- Presence of lingual varices before the ages of 50 indicates premature ageing.
- Lingual varices may occur in association with leg varicosities, however there is no relationship established between cardiopulmonary disorder and lingual varices.
- Sometimes, lingual varices can be indistinguishable from hereditary hemorrhagic telangiectasia.

TREATMENT

No treatment is required for lingual varices.

GEOGRAPHIC TONGUE

DEFINITION

Geographic tongue is the multifocal, patchy irregular areas of depapillation of tongue characterized by frequent remissions and recurrences.

ETIOLOGY

The exact etiology of geographic tongue is not known, however patients often have a positive family history of the similar problem for

generations. However, many investigators believe that emotional stress, asthma, eczema and allergy may also precipitate this condition.

CLINICAL FEATURES (FIGS 1.16 TO 1.18)

- The condition occurs in about 1 to 2 percent of the population.
- It can be seen among children as well as adults and there is a slight female predilection
- Geographic tongue clinically presents **multiple, irregular, well-demarcated, smooth patchy erythematous areas on the dorsum of the tongue with desquamation of the filliform papilla.**
- At the periphery, these lesions are often surrounded by a well-defined, slightly raised, yellowish-white, serpigenous line on the dorsum of the tongue.
- Although, the filliform papillae are absent in the desquamated zone, the fungiform papillae remain present, which appear as **few red dots**, projecting from the surface.
- The lesions **heal centrally and spread centrifugally**, and they may even sometimes involve the ventral surface of the tongue.
- Remission of the initial lesion is always followed by fresh recurrent lesion at a new location over the tongue. Because of this tendency for migration of the lesion from one area to the other, it is often called "**migratory glossitis**" (Fig. 1.19).
- Moreover, the benign migratory glossitis lesion mimics the continental outlines on the globe and this also makes frequent use of the term "geographic tongue" for the condition.
- The condition is mostly painless and asymptomatic, however on few occasions, it may produce soreness or burning sensation

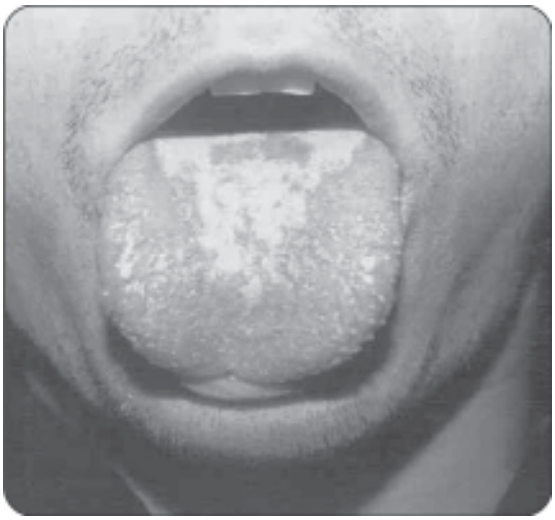

Fig. 1.16: Geographic tongue-I

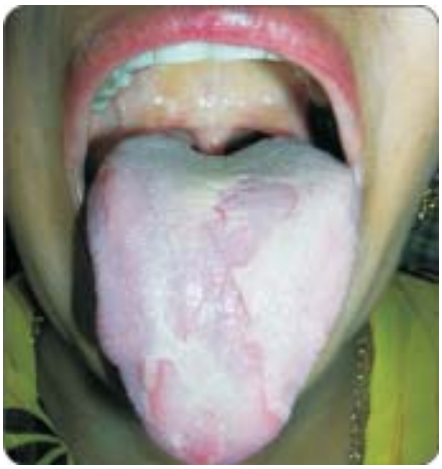

Fig. 1.17: Geographic tongue-II

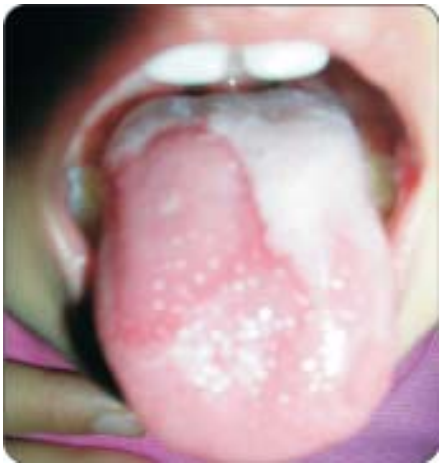

Fig. 1.18: Geographic tongue-III

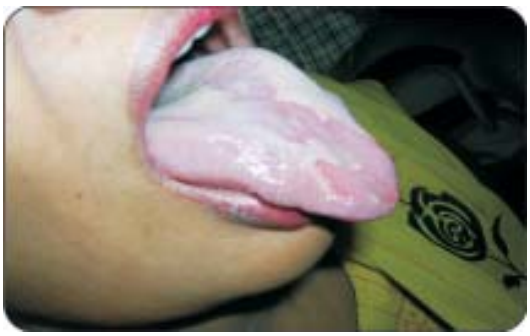

Fig. 1.19: Benign migratory glossitis (Geographic tongue-IV)

(glossodynia) particularly during taking spicy or citrus foods.
- Soreness of the tongue may be aggravated due to use of chemicals, e.g. chlorhexidine mouth-washes or tooth whiteners, etc.
- The abnormal clinical appearance and the persisting nature of the lesion along with the associated soreness often makes the patient cancerophoveik.
- Sometimes several lesions may coalesce together to produce a typical "**scalloped pattern**".
- Occasionally these lesions may occur in association with scrotal tongue or psoriasis.

Key points of geographic tongue

- Developmental anomaly characterized by multiple, irregular, patchy, depapillated areas on the dorsum of the tongue.
- The patch heals up at one location only to reappear at a newer location; apparently exhibiting a sense of 'migration'.
- The lesions have irregular border and are often surrounded by a white line at the periphery.
- Patches exhibit loss of filliform papilla but fungiform papilla are retained which appear as elevated, red rods.
- Mostly asymptomatic but occasional burning sensations; no treatment required.

HISTOPATHOLOGY

- Geographic tongue microscopically shows hyperparakeratinization of the covering epithelium of tongue with loss of filliform papilla.
- Intercellular edema and accumulation of neutrophil polymorphs (so called spongiotic abscess) is often seen in the superficial layers of the epithelium.
- Mild inflammatory cell infiltration is present in the underlying connective tissue.
- The condition is histologically similar to hyperplastic candidiasis, however candidal hyphae are absent.

DIFFERENTIAL DIAGNOSIS

- Psoriasis
- Lichenoid reactions
- Reiter's syndrome
- Chronic hyperplastic candidosis
- Familiar dysautonomia.

TREATMENT

There is no specific treatment for geographic tongue. Heavy doses of vitamins may produce some results in few cases. Sometimes antihistaminic and local steroidal antinflammatory drugs are also used.

HAIRY TONGUE

DEFINITION

Hairy tongue is an unusual condition, which occurs due to **hypertrophy of the filliform papilla of tongue along with loss of normal desquamation process**. The abnormal **hair–like** growth of the papilla eventually leads to formation of a **pigmented, thick, matted layer** on the tongue surface often heavily coated with bacteria and fungi.

Etiology of hairy tongue

- Poor oral hygiene
- Fungal infections
- Prolonged use of antibiotics
- Heavy smoking
- Excessive use of antiseptic mouth washes
- Chronic illness
- Lack of tooth brushing and consumption of soft foods with little or no roughage.

PATHOGENESIS

- Normally the keratinized surface layers of the tongue papillae are continuously desquamated through friction of the tongue with food, rough surface of the palate and the upper anterior teeth. Following desquamation, tongue papillae are replaced by newer epithelial cells from below.
- Lack of tongue movements due to local or systematic disease disturbs the regular desquamation process of the tongue papilla; especially the filliform papilla, which lengthens considerably and produces a **hairy appearance** on the tongue surface.
- Such hypertrophied papillae are often coated with microorganisms and become discolored

by retaining pigments from foods, medicines and chromogenic bacteria, etc.

CLINICAL FEATURES

- Hairy tongue commonly affects the mid dorsum of the tongue.
- Hypertrophy of the filliform papilla produces a thick matted layer on the dorsal surface.
- Hairy tongue in extreme cases may produce a thick, leathery coating on the tongue surface and this condition is often known as "**earthy** or **encrusted tongue**".
- Hypertrophied filliform papilla may **grow up to half a centimeter long**, which often brushes the soft palate and produces **gagging** sensations.
- Hairy tongue in many cases produces halitosis.
- There can be irritation to the tongue due to accumulation of food debris and microorganisms.
- Hairy tongue is often considered as the mirror of general health status since it is often associated with various systemic diseases.

DIFFERENTIAL DIAGNOSIS

- Candidiasis
- Leukoplakia
- Lichen planas
- Oral hairy leukoplakia.

TREATMENT

- Cleaning and scraping of the tongue.
- Application of topical keratolytic agents.
- Consumption of yoghurt.
- The affected tongue papilla often rapidly returns to normal when long-term antibiotics or other drugs are discontinued.

LINGUAL THYROID NODULE

DEFINITION

Accessory accumulation of functional **thyroid gland tissue within the body of the tongue** is called lingual thyroid nodule.

PATHOGENESIS

Embryologically thyroid gland develops as an endodermal downgrowth at the site of the foramen caecum. It then migrates inferiorly along the thyroglossal tract to its ultimate destination in the anterolateral surface of the trachea of the anterior neck. If all or part of the thyroid analogue fails to migrate, then lingual thyroid nodule develops, which is characterized by a mass of thyroid tissue on the midposterior dorsum of the tongue. Lingual thyroid nodule therefore represents a thyroid remnant in the site of the thyroid gland's origin.

CLINICAL FEATURES

- Lingual thyroid nodule is predominantly seen in females and it becomes clinically apparent usually during puberty or adolescence.
- In the tongue, thyroid tissue appears as a deep seated, nodular, exophytic mass, measuring about 2 to 3 cm in diameter and is located posterior to the foramen caecum mostly in the midline.
- Sometimes, it can also be present as a smooth cystic or a vascular swelling.
- Symptoms may vary, which include change of voice (dysphonia) bleeding, pain, difficulty in swallowing (dysphagia), respiratory obstruction (dyspnea) and a feeling of tightness in the throat.

HISTOPATHOLOGY

- Histologically, most cases of lingual thyroid nodules are composed of normal mature thyroid tissue, although embryonic or fetal thyroid gland tissues may also be seen.
- Occasionally, thyroid nodules may exhibit colloid degeneration or goiter.
- Microscopic examination of human tongues removed at autopsy reveals remnants of the thyroid tissue within the tongue in as many as 10% cases, although there was no clinically evident thyroid nodule among them.

DIFFERENTIAL DIAGNOSIS

- Thyroglossal tract cyst
- Neoplasms.

DIAGNOSIS

Diagnostic procedures include:

- Iodine-131 and technetium scans.
- Preoperative biopsy from the thyroid nodule.

TREATMENT

Surgical Excision

Before excision of a lingual thyroid nodule is planned, it must be determined if the patient has a normal functioning thyroid gland in the anterior neck with sufficient secretion to support the daily requirements.

Lingual thyroid nodules can be excised only if a normal thyroid gland is present in the neck. If the secretion from the thyroid gland in the neck is subnormal, then thyroid replacement therapy may be required.

THYROGLOSSAL TRACT CYST

DEFINITION

The thyroglossal tract cyst is an uncommon developmental **cystic lesion arising from the embryonic remnants of the thyroglossal tract**. It develops on the midline of the neck, anywhere between the base of the tongue above and the thyroid gland below.

ORIGIN

- The thyroglossal tract cyst arises from the remnants of the embryonic thyroglossal tract, which had not become obliterated.
- Initiation of the process of cyst development is triggered by infection of the lymphoid tissue in the area of the remnants, through drainage from upper respiratory tract infection.
- The cyst can arise anywhere along the length of the thyroglossal tract, which extends from the foramen caecum of tongue to the thyroid gland; however most of the cysts (70 to 80% cases) **develop below the hyoid bone on the midline of the neck**, where the tract makes two distinct turns on its way to the thyroid gland.

CLINICAL FEATURES

- The cyst occurs primarily in children and young adults.
- It presents a slow enlarging, asymptomatic mobile swelling involving the midline of the anterior neck above the thyroid gland.
- The firm cystic mass may vary in size from a few millimeters to several centimeters.
- When seen in the region of the tongue, it appears as a dome-shaped compressible lesion.
- The cyst moves during swallowing.
- A small percentage of these cysts can occur within the tongue and these lesions may produce dysphagia.
- If infected or inflamed a draining fistula may develop, which communicates between the cyst and the overlying skin surface.
- Neoplasms including carcinomas have been reported to develop from these cysts.

HISTOPATHOLOGY

- The cyst is usually lined by stratified squamous epithelium or ciliated columnar epithelium or transitional epithelium or a mixture of any of these epithelial types.
- The lining epithelium of the cyst often occurs in association with follicles of the glandular thyroid epithelium.
- Lymphoid aggregates, thyroid tissue, mucous glands and sebaceous glands, etc. are often present within the capsule of thyroglossal tract cyst.
- In some cases the lining epithelium of the cyst or the remnants of the thyroglossal tract may undergo malignant transformation and results in the development of carcinoma.

DIFFERENTIAL DIAGNOSIS

- Lingual thyroid nodule
- Mesenchymal neoplasms
- Dermoid cysts
- Epidermoid cyst.

TREATMENT

Thyroglossal tract cyst should be surgically excised along with the tract. Rate of recurrence is very high. To minimize the recurrence of the cyst involving the hyoid area, it is sometimes recommended that the central portion of the hyoid bone and its associated remnants of thyroglossal tract be removed.

ANOMALIES OF ORAL LYMPHOID TISSUE

REACTIVE LYMPHOID AGGREGATES

The oropharyngeal lymphoid tissue is primarily distributed in a circular arrangement called the "**Waldeyer ring**" in the posterior region of the mouth. It consist of three main masses of lymphoid tissue namely the paired palatine tonsils, the pharyngeal tonsils (adenoids) and the lingual tonsils.

Besides this, lymphoid tissues may also be found in a variety of intraoral locations like the buccal mucosa, soft palate, floor of the mouth and gingiva, etc.

Reactive hyperplasias may occur in lymphoid tissue in any of these locations. Lingual tonsil is one of the largest oral lymphoid aggregates and its common location is the posterior part of the tongue. It may extend anteriorly up to the region of the foliate papilla and reactive lymphoid hyperplasia of the lingual tonsil in this location is sometimes termed as 'foliate papillitis'.

When inflamed, the lingual tonsils produce swelling, erythema of the overlying mucosa and pain or discomfort, etc. especially during swallowing. There can be diagnostic confusion if the involvement is unilateral rather than bilateral.

Sometimes, children and adolescents may have islands of extra pharyngeal lymphoid tissue called 'oral tonsils' on either side of the lingual frenum and they appear as discrete, slightly elevated, reddish plaques in the floor of the mouth.

Oral tonsils consist of lymphoid aggregates, which exhibit germinal centers surfaced by nonkeratinized squamous epithelium with or without occasional crypts. It must be remembered that lymphoma the malignant neoplasm of the lymphoid tissue origin, can develop from any of the lymphoid tissue aggregates found in the oral cavity.

LYMPHOEPITHELIAL CYST (BRANCHIAL CYST)

DEFINITION

Lymphoepithelial cyst is the term used to describe cystic lesion previously classified as branchial cyst. It is a developmental cyst with an uncertain pathogenesis.

CLINICAL FEATURES

Age: Lymphoepithelial cysts occur during late childhood or early adulthood.

Sex: It occurs more frequently among males than females.

Site: The most common location is the lateral aspect of the neck, anterior to the sternomastoid muscle.

Intraoral lymphoepithelial cysts are uncommon lesions but whenever they occur, these lesions involve floor of the mouth in 50% cases and ventral and posterolateral surface of tongue in 40% cases. Other sites involved may be the soft palate, mucobuccal fold and anterior faucial pillars.

CLINICAL PRESENTATION

- Lymphoepithelial cyst generally presents as an **asymptomatic, circumscribed, movable swelling on the lateral aspect of the neck anterior to the sternomastoid muscle**.
- Intraorally it commonly appears as a small, slow enlarging, elevated, yellowish-pink nodule.
- The cysts may be unilateral or bilateral and may be tendered on palpation.
- A draining fistula may develop, which communicates between the cyst and the overlying skin surface.
- The size of the cyst ranges from few millimeters to 1.5 to 2 cm in diameter.
- Recent reports indicate that there is a marked increase in the incidence of lymphoepithelial cyst of the major salivary glands, among patients those, who are tested positive for HIV.

HISTOPATHOLOGY

- Histologically the lesion consists of a cystic cavity lined by thin stratified squamous epithelium.
- The cyst is generally embedded in a circumscribed mass of lymphoid tissue, which typically exhibits discrete follicles of the lymph node pattern.

- The capsule of the cyst also presents variable amount of connective tissue, being infiltrated by lymphocytes, plasma cells, macrophages and occasional multinucleated giants cells.
- Cystic lumen is filled up with either a thin watery fluid or a thick gelatinous material containing desquamated orthokeratin, sloughed epithelial cells and lymphocytes, etc.

PATHOGENESIS

- Lymphoepithelial cyst is probably derived from epithelium entrapped within lymphoid tissues of the neck during embryologic development of the cervical sinuses or second branchial clefts or pouches.
- An alternate theory suggests that the epithelium in lymphoepithelial cyst might be derived from the ductal epithelium of salivary glands, which remained entrapped within the cervical lymph nodes during embryogenesis.

DIFFERENTIAL DIAGNOSIS

- Inflammatory lesions
- Teratoma
- Warthins tumor
- Dermoid cyst
- Neoplasms of the minor salivary gland
- Salivary lymphoma.

TREATMENT

The intraoral counterpart of lymphoepithelial cyst is treated by conservative surgery. Recurrence is usually rare.

ANGIOLYMPHOID HYPERPLASIA WITH EOSINOPHILIA (ALHE)

DEFINITION

This is a benign condition characterized by subcutaneous nodular aggregates of lymphocytes and eosinophils, regional lymphadenopathy and peripheral blood eosinophilia.

Similar findings were also noted under the heading of Kimura's disease, characterized by eosinophilic granuloma of soft tissue and eosinophilic lymphofolliculosis. However, unlike angiolymphoid hyperplasia with eosinophilia, Kimura's disease has a distinct male predilection and is not associated with regional lymphadenopathy.

ETIOLOGY

- A vascular proliferation along with intense inflammatory cell infiltration in the lesion suggests a reactive etiology for this condition.
- A reactive immunologic cause has also been suggested as the disease shows increased serum IgE levels and deposition of IgE within the lymphoid follicles.
- According to some investigators, candida albicans might be having some role in the initiation of this disease. Since, anti-candida albicans antibody can be demonstrated within the lesion and moreover, the condition improves after hyposensitization to these allergens.

CLINICAL FEATURES

Age: Mean age of occurrence is about 35 years.

Sex: More common among males.

Site: Although 85% of the lesions usually occur in the head and neck area, oral lesions one rare.

Lower lip is the commonest site.

PRESENTATION

- The lesion clinically presents a slow enlarging, painless submucosal nodule.
- It measures about 1.5 cm in diameter and is movable.
- In about 40% cases eosinophilia is detected in peripheral blood examination.
- Some of the patients may exhibit multiple lesions in the oral cavity.

HISTOPATHOLOGY

- Microscopically angiolymphoid hyperplasia with eosinophilia reveals a circumscribed lesion, which is grossly separable from the surrounding tissue.
- A nodular mass of hyperplastic lymphoid tissue is seen with well-defined lymphoid follicles.

- Patchy areas of inflammatory infiltrates comprising of lymphocytes, eosinophils and macrophages are seen.
- Proliferating blood capillaries with plump endothelial cells are often noticed within the inflammatory zone.

DIFFERENTIAL DIAGNOSIS

- Minor salivary gland neoplasm
- Mucocele
- Lipoma
- Schwannoma
- Eosinophilic granuloma.

TREATMENT

- Surgical excision
- Intralesional steroid therapy may produce some response.
  Recurrence is rare.

ANOMALIES OF THE SALIVARY GLAND

See Chapter 4.

DEVELOPMENTAL ANOMALIES INVOLVING ORAL HARD TISSUES

ABNORMALITIES OF TEETH

Teeth develop from the cooperative interaction of two germ layers: a) ectoderm and b) ectomesenchyme. The tooth development begins at about the sixth week of the intrauterine life when few cells of the oral ectoderm undergo proliferation and eventually result in the formation of the dental lamina. The odontogenic cells (tooth forming cells) emerge from dental lamina and the later event constitutes the beginning of tooth development. The enamel develops from the ectoderm while the dentin, pulp, cementum, periodontal ligament and alveolar bone develop from the ectomesenchyme. The development of tooth occurs in several stages, namely the

i. The stage of initiation (bud stage).
ii. The stage of proliferation (cap stage).
iii. The stage of histodifferentiation (bell stage).
iv. The stage of morphodifferentiation.
v. The stage of apposition.
vi. The stage of calcification and
vii. The stage of eruption.

Developmental anomalies may occur during any of these developmental stages of tooth formation, which are, manifested clinically in the later life once the tooth is fully formed. These anomalies of tooth can occur either due to genetic factors or due to some environmental factors, however in few instances, even both of these factors could be involved together to cause some defects in the teeth. Developmental disturbances can results in the formation of some peculiar or strange looking teeth which exhibit mild to extreme variations from the normal teeth .

DISTURBANCE IN SIZE OF TEETH

MICRODONTIA

DEFINITIONS

Microdontia is the condition in which one or more teeth are smaller than normal in size. When all teeth are involved, it is called generalized microdontia and when only a few teeth are involved it is called localized or focal microdontia.

It is important to note that size of both teeth and the jaws are almost always genetically determined. However, wide variations are often seen in the ratio of tooth size and jaw size. Therefore alterations in the size of tooth are often proportionately variable to the size of the jaw.

Causes of microdontia

- Genetic factor—microdontia is predominantly a genetic disorder, which is caused by a faulty gene and occurs more often in the children of relative parents
- Dens-invaginatus
- Cleft lip and cleft palate
- Hereditary ectodermal dysplasia
- Radiotherapy during pregnancy
- Congenital syphilis
- Hypopituitarism
- Peg-shaped laterals
- Supernumerary teeth
- Idiopathic.

TYPES OF MICRODONTIA

True Generalized Microdontia

- When all the teeth in both arches are uniformly and measurably smaller than normal the condition is known as true generalized microdontia.
- This is an extremely uncommon condition and can be seen in pituitary dwarfism.
- True generalized microdontia can also be associated with other congenital defects like down syndrome and congenital heart disease, etc.

Relative Generalized Microdontia

- Relative generalized microdontia is the condition in which teeth of normal size may look smaller, if they are placed in an abnormally large maxilla or mandible.
- In such cases larger size of the jaws give an illusion of microdontia although the teeth are not really small.
- Relative microdontia often exhibits spacing in between the teeth.

Focal Microdontia

- When one or two teeth in the jaw are measurably smaller in size while rest of the teeth are normal, the condition is called focal microdontia.
- Microdontia involving one or two teeth in the dental arch is far more common than the generalized types.
- The affected teeth are often present symmetrically in the jaw and in addition to being miniature in size, these teeth often exhibit alteration in their shape as well.
- Maxillary lateral incisors and maxillary third molars are the most frequently involved teeth in focal microdontia.
- When maxillary lateral incisors are involved, the teeth often appear 'cone' or 'peg' shaped and are often designated as peg laterals. These teeth often give a peculiar facial expression of the patient.
- These peg laterals carry an autosomal dominant type of inheritance pattern and tend to be familial.
- Maxillary and mandibular second premolars may sometimes exhibit microdontia.
- Supernumerary teeth are almost always smaller than the normal teeth and are often conical in shape.
- There are certain situations in which smaller teeth can be found in the mouth, although these conditions may not be truly developmental in nature.

Examples:

- Smaller teeth can be seen in the affected side of the jaw in facial hemiatrophy.
- In case of gemination or twinning one single tooth germ splits into two, during development and gives rise to two separate teeth, which are always smaller than normal.
- Small, conical teeth are often seen in hereditary ectodermal dysplasia.
- Multiple miniature teeth can be found in compound odontomes and in teratoma.
- A retained deciduous tooth within the permanent dentition may give an illusion of focal microdontia.

CLINICAL SIGNIFICANCE OF MICRODONTIA

- In microdontia, teeth are often spaced which may be disturbing cosmetically.
- There may be difficulty in speech and taking food.
- When shapes of these teeth are also altered along with microdontia (e.g. peg laterals), it will require immediate correction.
- Crown and bridge prosthetic work may be required for esthetic rehabilitation of such teeth.

MACRODONTIA

DEFINITION

Macrodontia is a condition in which teeth in the jaws are measurably larger than normal in size. This is a far less common anomaly of tooth than microdontia.

Causes of macrodontia

- Pituitary gigantism
- Fusion of teeth
- Facial hemihypertrophy
- Idiopathic

TYPES OF MACRODONTIA

Macrodontia can be of three types, which are as follows:

A. ***True generalized macrodontia:*** When all the teeth in both arches are measurably larger than normal, the condition is termed as true generalized macrodontia. It can be seen infrequently in case of pituitary gigantism.

B. ***Relative generalized macrodontia:*** Relative generalized macrodontia is used to designate a condition in which the normal sized teeth appear somewhat larger because of the smaller jaw size. In such cases the dental arches often exhibit crowding of teeth.

C. ***Focal or localized macrodontia:*** Localized macrodontia is occasionally seen on the affected side of the mouth with hemifacial hypertrophy. Macrodontia of individual tooth is a rare entity and it mostly affects the incisors (Fig 1.20). However focal macrodontia should not be confused with 'fusion' of teeth, (in which two adjacent teeth unite together to form a single large tooth).

DISTURBANCE IN NUMBER OF TEETH

ANODONTIA

DEFINITION

Anodontia can be defined as a condition in which there is congenital absence of teeth in the oral cavity.

TYPES

Anodontia can be of two types:

A. ***Complete or total anodontia:*** Congenital absence of all teeth.

Fig. 1.20: Macrodontia of upper central incisor

B. ***Partial anodontia or oligodontia or hypodontia:*** Congenital absence of one or few teeth.

Anodontia can further be divided into the following types:

True anodontia: True anodontia occurs due to failure of development or formation of tooth in the jawbone.

Pseudoanodontia: Refers to the condition in which the teeth are actually present within the jawbone but are not clinically visible in the mouth, as they have not erupted. Examples of pseudoanodontia can be impacted teeth or submerged teeth, etc.

False anodontia: False anodontia is the condition in which the teeth are missing in the oral cavity because of their previous extraction or exfoliation.

Etiology of anodontia

- Idiopathic anodontia
- Hereditary anodontia
- Environmental factor
- Ectodermal dysplasia
- Incontinentia pigmenti
- Hyalinosis cutis mucosae
- Mandibulo-oculofacial dyscephaly
- Chondroectodermal dysplasia
- Book's syndrome
- Rieger's syndrome
- Down's syndrome
- Syndrome associated anodontia
- Radiation injury to the developing tooth germs
- Cleft lip and cleft palate.

Complete or Total Anodontia

Total anodontia is a rare condition in which there is neither any deciduous tooth nor any permanent tooth present in the oral cavity.

- It is usually seen in association with hereditary ectodermal dysplasia. This condition is usually inherited as an x-linked recessive trait and although it primarily affects males but an autosomal dominant form can occur, which affects females.
- There will be inherited defects in the ectodermally derived structures of the body

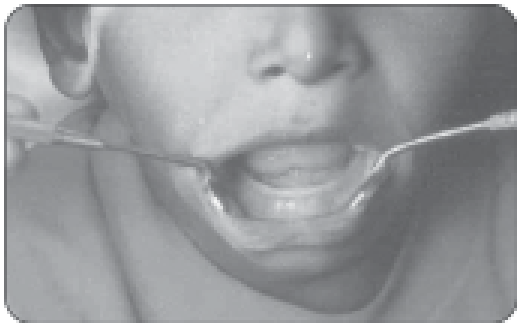

Fig. 1.21: Complete (total) anodontia

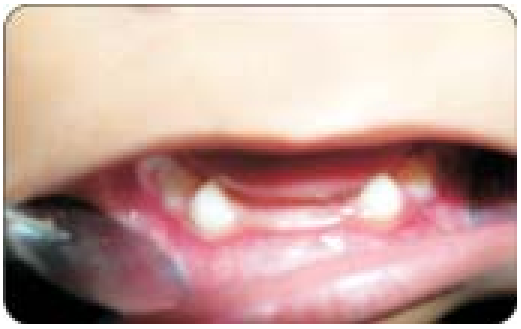

Fig. 1.22: Partial anodontia

such as hair, sweat gland, teeth and salivary gland, etc. with a typical inability to regulate body temperature.

- Although complete anodontia is a common feature of hereditary ectodermal dysphasia, however in many cases the cuspids are present in the mouth and the teeth are often malformed with conical crowns.
- Complete anodontia sometimes occur among children those who have received high doses of radiation to the jaws as infants for therapeutic reasons (Fig. 1.21).

High doses of radiation cause destruction of tooth germs resulting in complete failure of tooth formation in future, moreover even a very lower dose may cause cessation of odontogenesis.

Partial Anodontia

Partial anodontia is a much more common phenomenon and is characterized by congenial absence of one or few teeth (Fig. 1.22). This condition is also known as hypodontia or oligodontia. The condition is more commonly seen in permanent dentition.

In partial anodontia, when a deciduous tooth is congenitally absent it is very much likely that its permanent successor will also be missing thereby suggesting some genetic influence.

Incidence Rate

Incidence rate of partial anodontia varies in different population groups but near about 35% of the general population will have at least one congenitally missing tooth.

A familial tendency for congenitally absent teeth is a well-recognized phenomenon.

Commonly Missing Teeth in Partial Anodontia

- In partial anodontia, any tooth can be congenitally missing, however it is often noticed that certain teeth tend to be absent more often than others.
- The third molars (any one or all four of them) are the most frequently observed congenitally missing teeth.
- Maxillary lateral incisors and mandibular premolars are the next most common group of teeth, which are often congenitally absent.
- When deciduous teeth are involved it partial anodontia, the maxillary lateral incisors are most likely to be affected.
- It should be noted that mandibular first molars and mandibular lateral incisors are the teeth, which are least likely to be missing during anodontia.

Diseases or Clinical Conditions to be Commonly Associated with Partial Anodontia

Incontinentia pigmenti: This hereditary disorder is characterized by diffuse slate-gray macules of the skin, white lesions of the oral mucosa, skeletal, ocular and neuralgic disturbances; and partial anodontia with delayed eruption of tooth.

Hyalinosis cutis mucosae: This disease is characterized by pathologic accumulation of glycoprotein in the body and it often manifests with the following features: Hoarseness of voice, vesicular skin lesions, nodular or papillary lesions of the oral mucosa, intracranial calcifications and hypodontia.

Mandibulo-Oculo-Facial dyscephaly: This disease is also known as Hallermann-Steriff syndrome and is characterized by brachycephaly, frontal bossing, microstomia, TM joint disturbance, blue sclera, hypotrichosis and hypodontia with retention of deciduous teeth.

Chondroectodermal dysplasia: This hereditary disorder is characterized by developmental abnormalities in both ectodermal and mesodermal tissues. Although it shares few features with hereditary ectodermal dysplasia but both are different pathologic entities.

Chondroectodermal dysplasia clinically manifest with the features like—defective nails and hair, normal sweat glands, congenital absence of numerous teeth, fusion of the upper lip to the anterior maxillary alveolar ridge, short limbs with polydactyly and congenital heart defects, etc.

Book's syndrome: This syndrome is commonly associated with localized hypodontia and its other features include—premature whitening of hairs and hyperhydrosis of the palms and soles.

Rieger's syndrome: It is an autosomal dominant hereditary disorder and it shows oligodontia or hypodontia with serious ophthalmic defects.

SUPERNUMERARY TEETH

DEFINITION

Presence of any extra tooth or teeth in the dental arch, in addition to the normal series of teeth is known as **supernumerary teeth**. The condition is also known as hyperdontia or polydontia. Supernumerary teeth occur less frequently than the anodontia. These teeth may erupt spontaneously in the oral cavity or they may be impacted and are detected incidentally during routine radiographic examinations.

ETIOLOGY OF SUPERNUMERARY TEETH

- Heredity, these are more commonly seen among the family members of the affected individual as compared to the general population.
- Dichotomy (division into two) of the tooth bud.
- Localized conditioned hyperactivity of the dental lamina.
- Fragmentation of the dental lamina during development of cleft lip and cleft palate.

MODE OF FORMATION

- A supernumerary tooth may develop either from an accessory tooth bud in the dental lamina and can be seen in any part of the dental arch.
- It may develop due to spitting of a regular normal tooth bud during the initial phase of odontogenesis.
- The supernumerary tooth can occur in both males as well as in females.
- A supernumerary tooth may resemble the corresponding tooth (i.e. where they are located) but in many cases it may have a conical shape. Therefore, morphologically sometimes these teeth may look like molars, premolar or like incisors, etc. depending upon their location or sometimes they may have an altogether different morphologic appearance. However in most of the cases these extra teeth are much more smaller in size (miniature form) than their normal counterparts.

COMMON LOCATIONS

- Supernumerary teeth can occur in any location but they often have a predilection for certain sites.
- These are far more common in maxilla (90%) as compared to mandible.
- Supernumerary teeth are more often seen in maxillary permanent dentition and are rarely seen in deciduous dentition.

TYPES OF SUPERNUMERARY TEETH

According to the Site

Supernumerary tooth developing or erupting at certain sites may be known by certain special terms and these are as follows:

Mesiodens

Mesiodens are the most common of all supernumerary teeth and these are located in the midline, on the palatal aspect, between the roots of two upper central incisors. These teeth can be either impacted or inverted or may be horizontal in orientation. Mesiodens develop before or at the time of development of the upper central incisor teeth.

Distomolars

Distomolars are supernumerary molars, which are usually located on the distal aspect of the regular molar teeth in the dental arch.

Paramolars

These are also extra molar teeth, which are usually located either in the buccal or in the lingual aspect of the normal molars. Both distomolars and paramolars are often known as the **fourth molars**.

Extra lateral incisors

Although rare, extra lateral incisor teeth can be present and they are more common in the maxillary arch.

Most of the supernumerary teeth exhibit conical crowns; they may be either single or multiple in numbers and are either erupted or impacted.

According to Morphology

According to their morphological characteristics supernumerary teeth can be classified into the following types:

Conical type: These supernumerary teeth are small, often peg-shaped and mostly seen in the permanent dentition, i.e. mesiodens.

Tuberculate type: These supernumerary teeth posses more than one cusp or tubercle, are often barrel-shaped and may be invaginated. These are more commonly seen in the incisor area, on the palatal aspect of upper incisors and the teeth are often impacted.

Supplemental type: This type of supernumerary tooth shows duplication (similarity in appearance) of any normal tooth in the dental arch. Most common example is the one which resembles permanent maxillary lateral incisor.

Odontome associated: These supernumerary teeth occur in association with compound odontome as multiple miniature teeth inside the tumor.

Types of supernumerary teeth

According to the site:
• Mesiodens
• Distomolars
• Paramolars
• Extra lateral incisors
According to morphology:
• Conical type
• Tuberculate type
• Supplemental type
• Odontome associated

INCIDENCE RATE OF SUPERNUMERARY TEETH

- 2.1 percent in permanent dentition.
- 0.8 percent in deciduous dentition.

CLINICAL FEATURES

- In many cases, the supernumerary teeth remain clinically asymptomatic.
- The supernumerary tooth may develop as a single one or they may be multiple in numbers, moreover these teeth can be either unilateral or bilateral.
- The extra tooth may be either erupted or impacted in the oral cavity and both upper and lower jaw can be affected.
- Supernumerary teeth may sometimes produce crowding or malocclusion and they often cause cosmetic problems.
- They may cause rotation, protrusion or displacement of the normal teeth.
- In many instances, these teeth are responsible for either failure of eruption or delayed eruption of other normal teeth.
- In many cases these extra teeth may be either directly or indirectly responsible for increased caries incidence and periodontal problems.
- Multiple supernumerary teeth (most of them are impacted), may occur in association with conditions like cleidocranial dysplaisa or Gardener's syndrome etc.
- Supernumerary teeth can occur in the deciduous dentition and whenever they occur, the most common one is the maxillary lateral incisor.
- Supernumerary teeth may initiate the development of some pathological conditions in the jaw, e.g. dentigerous cyst may develop in relation to an impacted supernumerary tooth.
- Supernumerary teeth may sometimes occur in association with cleft palate; moreover presence of these extra teeth often creates problem in the surgical correction of cleft palate itself.

- Presence of supernumerary teeth may create problems in orthodontic correction of teeth and also in the placement of implants in the jaw.
- These extra teeth often cause root resorption of the neighboring normal teeth in the jaw.
- In mandible the most common supernumerary teeth are the extra premolars, although fourth molars or additional incisors are also occasionally found.

TREATMENT

- Supernumerary teeth are mostly nonfunctional and they should be extracted especially if they are causing displacement or delayed eruption of the normal teeth.
- Impacted supernumerary teeth should also be removed surgically since they can interfere with normal tooth alignment or can develop some pathology.

DISTURBANCES IN ERUPTION OF TEETH

Eruption is the process in which the developing teeth move from their area of formation inside the jaw into the oral cavity to become a part of the dental arch.

The eruption time for both deciduous and permanent teeth often vary among different persons. Therefore, it is sometimes difficult to assess the exact eruption time for a particular tooth in any given individual. However, when the eruption of tooth occurs in the mouth either much before or long after the expected normal time, then we can consider that an eruption abnormally exists.

TYPES OF ERUPTION ABNORMALITIES

- Premature eruption
- Delayed eruption
- Impacted tooth
- Embedded tooth
- Eruption sequestrum.

PREMATURE ERUPTION

DEFINITION

Premature eruption can be defined as a situation when a tooth erupts into the oral cavity much before its normal time of eruption.

TYPES

- ***Natal teeth:*** These are erupted deciduous teeth present at birth.
- ***Neonatal teeth:*** These are deciduous teeth, which erupt during the first 30 days of life.

ETIOLOGY

The exact etiology of premature eruption is not known, however a familial pattern is sometimes noticed.

COMMONLY INVOLVED TEETH

- Premature eruption usually involves only one or two teeth, most commonly the deciduous mandibular central incisors.
- Natal or neonatal teeth are not supernumerary teeth, in fact they are part of the normal component of deciduous dentition and therefore these teeth should be preserved in the mouth if possible.
- Premature eruption of permanent teeth may occur as a result of loss of preceding deciduous teeth at a much earlier time. It is often seen that when a single deciduous tooth exfoliates prematurely, its permanent counterpart erupts much before its normal time of eruption.
- However, in hyperthyroidism the entire permanent dentition may erupt prematurely.

DELAYED ERUPTION

DEFINITION

Delayed eruption refers to the first appearance of the teeth in the oral cavity at a much later time than what is normally expected.

This is a relatively uncommon phenomenon and can involve both deciduous as well as the permanent dentition.

IDIOPATHIC DELAYED ERUPTION

In many cases however the exact cause for the delayed eruption is not clearly known. Delayed eruption of permanent teeth may occur due to the same local or systematic factors, which are responsible for the delayed eruption of deciduous teeth.

Factors causing delayed eruption of tooth

Systemic Factors	*Local Factors*
• Decreased secretion of growth hormone in early life, resulting in a small jaw with insufficient space for eruption of all teeth. • Rickets. • Failure of timely resorption of deciduous teeth with delayed eruption of the permanent successors. • Cleidocranial dysplasia. • Cretinism • Ionizing radiation in the jaw in early life. • Fetal alcohol syndrome—occurs due to maternal alcoholism and it causes delayed eruption of teeth and mottled opacity of enamel at the incisal margin.	• Obstruction from an impacted tooth or a supernumerary tooth. • Obstruction from a tumor or cyst in the jaw. • Abnormal position of the crypt. • Retained deciduous teeth. • Gingival fibromatosis. • Cleft lip and cleft palate. • Premature loss of primary teeth. • Fracture of jaw during the time of eruption of teeth. • Crowding of teeth.

IMPACTED TEETH

DEFINITION

Impaction is defined as the cessation of eruption of tooth caused by a clinically and radiographically detectable physical barrier in the eruption path or by an ectopic position of the tooth.

FACTORS CAUSING IMPACTION OF TOOTH

- ***Micrognathia:*** A smaller jaw cannot afford to accommodate all the teeth supposed to be present in the arch, hence few of them may become impacted.
- ***Malocclusion:*** Abnormal orientation of some teeth, which have erupted at an earlier age may sometime block the normal pathway for the eruption of few other teeth which are due to erupt later.
- ***Rotation of teeth:*** Rotation results in eruption of a tooth at a different angulation in the jaw, which results in impaction of such tooth.
- ***Premature exfoliation of deciduous teeth:*** It causes partial closure of space in the alveolar ridge.
- ***Retained deciduous tooth:*** An abnormally retained deciduous tooth may resist the eruption of its permanent counterpart and the later may sometimes become impacted.
- ***Supernumerary tooth:*** A supernumerary tooth may sometimes obstruct the pathway for eruption of other teeth resulting in their impaction. On the other hand, in many instances a supernumerary tooth itself may remain impacted due to lack of space for eruption.
- ***Odontogenic cyst (e.g. keratocyst):*** It may act as a physical barrier and result in the impaction of tooth in the region.
- ***Odontogenic tumor (e.g. odontome):*** It also may results in impaction of a tooth by acting as physical barrier in the path of eruption.
- ***Cleft palate:*** In many cases, teeth may be impacted in the area of cleft palate.
- ***Nonodontogenic tumors or cysts:*** These lesions may sometimes cause impaction of tooth as they obstruct the path of eruption of a tooth.
- ***Cleidocranial dyplasia:*** This disease entity is often associated with multiple impactions.
- ***Gardner's syndrome:*** It is also associated with multiple impacted teeth.
- ***Amelogenesis imperfecta:*** Impacted teeth are also seen in various forms of amelogenesis imperfecta.
- ***Syndrome associated with enamel defects:*** Impacted teeth can also be seen in case of syndrome associated enamel defects such as Ameloonychohypohydrotic syndrome and Trichodento-osseous syndrome, etc.

Key points of impaction of tooth

It is the failure of eruption of tooth due to any physical barrier in the path of the erupting tooth.

Causes: Premature exfoliation of deciduous tooth, retained deciduous tooth, small sized jaw, crowding or malocclusion, and any cyst or tumor in the path of eruption.

Common teeth affected: Mandibular and maxillary third molars, maxillary canines.

Different types of impactions: Mesioangular impaction (impacted tooth is inclined towards midline), distoangular impaction (tooth is inclined away from midline), horizontal impaction, vertical impaction, partial impaction, complete impaction, bony impaction and soft tissue impaction, etc.

Clinical features: Recurrent pain, swelling, trismus, lymphadenopathy. difficulty in closing mouth, difficulty in swallowing, fever, etc.

Complications of impactions: Cellulitis, space infection, osteomyelitis, ludwig's angina.

Investigations: X-rays (IOPA, OPG)

Treatment: Surgical removal of the impacted tooth

TEETH WHICH MAY BE COMMONLY IMPACTED

- Although, virtually any tooth can be impacted, the commonest impacted teeth are the mandibular and maxillary third molars.
- The next common teeth are the mandibular second premolars and maxillary canines.
- The supernumerary teeth can be impacted in many cases.

CLASSIFICATION OF IMPACTION

Impactions are commonly classified in the following manner:

Mesioangular impaction: This is a common type and in this case the long axis of the impacted tooth is inclined mesially (towards midline of dental arch) as compared to the remaining teeth in the jaw.

Distoangular impaction: In this type the long axis of the impacted tooth is distally inclined (away from the midline of dental arch).

Horizontal impaction: Horizontally impacted teeth lies parallel to the long axis of the jawbone.

Vertical impaction: In this case the impacted tooth stands vertically but it occlusal plane is far below the occlusal plane of other erupted teeth.

Completely impacted tooth: When an impacted tooth is totally enclosed by bone, it is called a completely impacted tooth.

A completely impacted tooth does not communicate with the oral cavity and is therefore not susceptible to caries or infection.

Submerged tooth: when there is cessation of eruption of a deciduous tooth after gingival emergence, it is called a submerged tooth. The occlusal surface of the tooth lies above the gingiva but below the occlusal plane of the remaining teeth.

Embedded tooth: When an individual tooth fails to erupt for no apparent cause, it is called an embedded tooth. The tooth lies below the gum line and there is no physical barrier present as may be seen in case of impaction.

Partially impacted tooth: When an impacted tooth is partly surrounded by bone and partly by soft tissue, it is considered as a partially impacted tooth.

Partially impacted teeth often communicate with the oral cavity via an inconspicuous periodontal pocket and therefore make the tooth vulnerable to caries or infections.

RADIOGRAPHIC FEATURES OF IMPACTED TEETH

Radiographs are very much essential for determining the various aspects of an impacted tooth:

- Radiograph helps in determining the types of impaction (mesioangular or distoangular or vertical types, etc.)
- It also helps to determine the position of the root apex of the impacted tooth in relation to the mandibular canal in case of lower teeth.

Types of X-rays used in impactions

- Intraoral periapical radiographs (IOPA).
- Panoramic radiograph (Orthopantomogram).
- Right and left oblique lateral radiograph of the jaw.
- Standard occlusal radiograph.
- Paranasal sinus view radiographs.

- It can reveal the curvature of the root of the impacted tooth.
- Presence of resorptions (either root or crown) of the impacted tooth as well as dental caries, etc. may be detected by radiographs.
- Radiographs can help to detect any pathology, e.g. abscess, tumor or cyst, etc. which are associated with an impacted tooth.

CLINICAL FEATURES OF IMPACTION

Impacted teeth may sometimes remain innocent for the entire life but in many cases they can produce some clinical symptoms, which are as follows:

- Infection with associated pain and swelling.
- Trismus and extraoral sinus formation.
- Malocclusion and crowding in the dental arch.
- Root resorption of the adjacent erupted teeth.
- Predisposition to dentigerous cyst development.
- May precipitate the development of tumor in the jaw.
- Increases the possibility of periodontal problems.
- Impacted teeth often favor food impaction and therefore can result in development of caries in the adjacent teeth.
- External resorption of the impacted tooth.
- Sometimes, impacted tooth can be found within the maxillary antrum.
- In many cases root of the impacted tooth may be present at a close proximity to the mandibular canal and in such cases possibility of damage to the neurovascular bundle is very high at the time of removal of such teeth.
- Presence of impacted tooth may weaken the jawbone in some cases and there is an increased possibility of fracture of this bone when subjected to trauma.
- Impacted teeth may predispose to the development of osteomyelitis, cellulites and space infections, etc.

TREATMENT

Treatment modalities vary depending upon the individual impacted tooth and the specific circumstances.

- Most impacted molars are surgically extracted. However special efforts are made to save the impacted maxillary canines since these are cornerstones of the upper dental arch.
- If the impaction is caused by any physical factor such as a cyst, tumor or any supernumerary teeth, the treatment procedure must include elimination or removal of those lesions.

ERUPTION SEQUESTRUM

It is a small fragment of necrosed bone, which is sometimes seen overlying an erupting tooth. This type of bone fragment is probably detached from the alveolar ridge during the emergence of the erupting tooth outside gingiva. Lack of complete resorption of the overlying alveolar bone during tooth eruption is the cause of formation of eruption sequestrum. Clinically it may cause pain, soreness and difficulty in taking food, etc.

DISTURBANCES IN THE SHAPE OF TEETH

GEMINATION (TWINNING)

DEFINITION

Gemination is a developmental anomaly characterized by **a partial cleavage in a single tooth germ resulting in the formation of an anomalous tooth with two partially separated crowns and one root**. It is therefore an abortive attempt at division of one tooth into two.

The term **twinning** refers to the complete and equal division of a single tooth germ that result in the formation of one normal and one supernumerary tooth.

- Gemination affects both deciduous as well as the permanent dentition.
- There is no sex predilection.
- Geminated tooth often shows doubling of both the crown as well as the root.
- Gemination mostly affects the deciduous mandibular incisors and permanent maxillary incisors.
- Clinically the geminated tooth reveals either an extremely widened crown or their can actually be an indentation or groove delineating the two crown forms.

PATHOGENESIS

Gemination is the result of either "schizodontism"—the splitting of a tooth germ during development or it can result from "synodontism", the fusion of a regular tooth bud with one supernumerary tooth bud.

Gemination often clinically resembles another developmental anomaly called 'fusion'. Gemination can be distinguished from fusion by the fact that full complement (number) of teeth are present in the dental arch in case of gemination (one extra tooth is present in case of twinning) where as in case of fusion one regular tooth is missing from the dental arch.

Problems in gemination: The following problems can occur due to gemination of tooth:

- Tooth malposition
- Spacing of teeth
- Dental arch asymmetry
- Cosmetic problems
- Periodontal problems
- Increased caries susceptibility
- Disturbance in the eruption of adjacent teeth.

TREATMENT

Since gemination produces some cosmetic disturbance, construction of esthetic crown or bridge may be necessary for cosmetic rehabilitation.

FUSION

DEFINITION

Fusion can be defined as the **union of two adjacent normally separated tooth germs at the level of dentin during development (Figs 1.23 and 1.24)**. It results in union of two teeth by dentin and enamel, pulp chambers are often shared or they may be separate.

Fusion results in one anomalous large tooth formation in place of two normal regular sized teeth and the tooth have either a single enlarged root or two roots. One of the most important criteria for fusion is that the fused tooth must exhibit confluent dentin.

CAUSES OF FUSION

- Hereditary cause.
- Trauma during development of teeth.

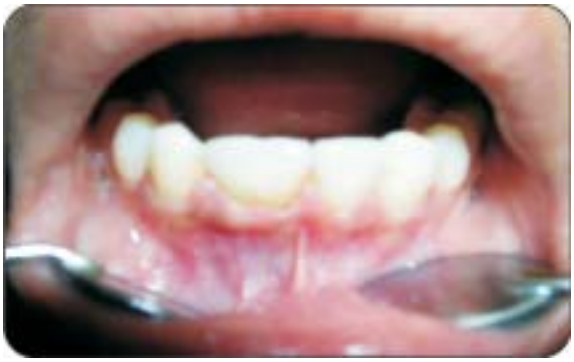

Fig. 1.23: Fusion of teeth-I

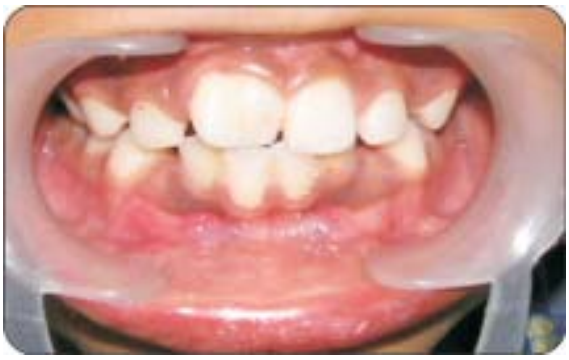

Fig. 1.24: Fusion of teeth-II

- Physical force or pressure causing contact between two adjacent tooth germs.

CLINICAL FEATURES

- Both deciduous as well as permanent teeth can be affected in case of fusion, although it is more common in deciduous teeth.
- Fusion can occur between two normal teeth or between one normal and one supernumerary tooth.
- Fusion can occur bilaterally in the jaw.
- In both dentitions, the incisor teeth are more frequently affected.
- There is no sex prediliction in case of fusion.
- Fusion can be complete or incomplete and its extent will depend on the stage of odontogenesis at which the fusion took place.
- In case of fusion between two adjacent deciduous teeth, the resultant fused tooth may not exfoliate normally and thus may interfere with the eruption of the permanent successor.

COMPLETE FUSION

If fusion begins before the calcification of the tooth has occurred, then the fusion will be complete and the fused tooth crown will incorporate all components of both the participating teeth including their enamel, dentin, cementum and the pulp.

INCOMPLETE FUSION

If fusion begins in the later stages of tooth development, then the fused tooth may exhibit separate crowns and the fusion process may be limited to the roots only, with pulp canals either fused or separate. This condition is called incomplete fusion.

RADIOGRAPHIC FEATURES (FIG. 1.25)

Radiographs can be immensely helpful in determining the complete or incomplete fusion. Complete fusion gives rise to the development of a single large tooth with single root canal.

CLINICAL COMPLICATIONS

Fusion often Creates the Following Problems:

- There can be spacing or diastema formation between the teeth.

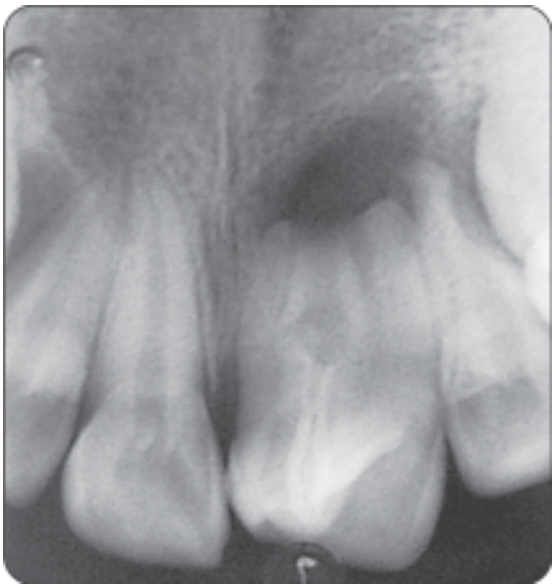

Fig. 1.25: Radiograph of fusion of teeth

- There can be crowding of teeth in the arch, especially when fusion occurs between one normal and one supernumerary tooth.
- Esthetic problems.
- Periodontal complication.
- **Fusion can be differentiated from gemination by counting the number of teeth** in the arch, since in case of fusion there will be one tooth less in the dental arch. However, in case of twining there will be one extra tooth in the dental arch.

TREATMENT

Depending upon the extent of clinical problem, fabrication of cosmetic crowns or bridges may be necessary for esthetic recovery in case of fusion.

CONCRESCENCE

DEFINITION

Union of the roots of two or more adjoining completely formed teeth **along the line of cementum** is known as concrescence.

This is a type of fusion, which is limited only to the roots of the teeth and it occurs due to deposition of cementum after the root formation of the involved teeth have been completed.

ETIOLOGY

- Traumatic injury
- Crowding of teeth
- Hypercementosis associated with chronic inflammation.

PATHOGENESIS

The condition is thought to occur as a result of traumatic injury to the jaw, which causes loss of interdental bone and brings the roots of the neighboring teeth in close proximity to one another. Finally such fusion occurs between the roots of two or more such separate teeth due to deposition of cementum between them.

IMPORTANT FEATURES

- Concrescence represents an acquired defect and it can occur in both erupted and unerupted teeth.

- There is no sex predilection.
- In case of concrescence, union never takes place between the enamel, dentin or the pulp of the involved teeth except cementum.
- In concrescence, the union mostly occurs between two teeth, however there may be cases where union occurs between multiple teeth.
- Permanent maxillary molars are more often affected than any other teeth.

Key points of concrescence

- Union between roots of two or more adjacent teeth (radicular version of fusion).
- Occurs due to deposition of cementum causing obliteration of periodontal ligament space with subsequent union between adjacent teeth.
- It develops only after the root completion of teeth has occurred.
- Trauma is believed to be the single most important underlying cause.
- X-ray helps in confirming the diagnosis.
- May cause difficulty in extraction of the affected teeth in undiagnosed cases.

- Concrescence also frequently occurs between one normal tooth and one supernumerary tooth.
- Concrescence rarely involves the deciduous dentition.
- Concrescence frequently occurs in those areas of the dental arch where the roots of the neighboring teeth are anatomically placed close to one another (e.g. between maxillary second and third molars).
- Concrescence can be more complicated if the union occurs between one erupted tooth with an impacted tooth.
- Clinically, the condition can not be detected since the union takes place in the root areas of tooth; the crowns of the involved teeth look normal and unsuspecting.

RADIOGRAPHIC FEATURES

Radiographs reveal obliteration of periodontal ligament space in the interradicular areas of teeth.

CLINICAL SIGNIFICANCE

- The clinical significance of concrescence relates primarily to its radiographic diagnosis before planning a tooth extraction. Because in undiagnosed cases attempted extraction of the affected tooth may cause trauma to the jaw or may result in removal of many teeth instead of one.

DILACERATION

DEFINITION

Dilaceration is a developmental disturbance in the shape of tooth, it refers to a **severe angulation or a sharp bend or curve in the root or crown of a formed tooth.**

The bend is mostly located at the junction between the crown and the root of the tooth; in other cases it may be located at the mid portion of the root or sometimes even near the root apex.

In dilacerations the bend in the tooth sometimes can be as stiff as 90 degree. When the bend is restricted only to the root portion of the tooth the condition is known as 'flexion'.

PATHOGENESIS

The condition probably occurs subsequent to trauma or due to any other defect of development, which alters the angulation of the tooth germ during the root formation.

- It is generally believed that trauma to a partially calcified tooth may cause displacement of the hard calcified portion of the tooth away from its normal axis and later on, the unclassified portion develops with an unusual angulation.
- In dilacerations, the location of the curve or bend on the tooth depends on the extent to which the permanent tooth was formed at the time of injury.
- Injury to a deciduous tooth may push a partly formed permanent tooth further down apically into the jaw and as a result a bend in the permanent tooth develops.

Key points of dilacerations

- Developmental anomaly of tooth characterized by a sharp bend or curve along the length of the tooth.
- Injury to the deciduous tooth with subsequent pressure on the developing permanent tooth is the most likely cause.
- The affected often looks 'hook shaped due to curving of the root.
- X-ray is very useful for diagnosis.
- They may get broken during removal.

- Some investigators believe that trauma is not always an essential factor for the development of dilacerations and according to them the anomaly occurs as a result of continued root formation during a curved or tortuous path of eruption.
- In some cases the cause of the defect is idiopathic.

CLINICAL FEATURES

- Dilaceration may involve any tooth belonging to either the deciduous as well as the permanent dentition.
- There is no sex predilection.
- Sometimes dilaceration at the coronal portion of the tooth is observed.
- The tooth typically looks "**hook-shaped**" due to the bending in the root.

Dilaceration in a tooth can easily be detected by radiographs and care should be taken during extraction of such teeth. Since these teeth are more prone to fracture during removal.

TAURODONTISM

DEFINITION

Taurodontism or **'bull-like' tooth** is a peculiar developmental condition in which, the **crown portion of the tooth is enlarged at the expanse of its roots.**

PATHOGENESIS

The condition probably occurs due to failure of the Hertwig's root sheath to invaginate at the proper horizontal level during tooth development.

CLINICAL FEATURES

- The affected tooth in taurodontism exhibits large crown with elongated pulp chamber and short rudimentary root.
- The affected tooth is usually rectangular in shape with minimum constriction at the cervical area; moreover the furcation area of the tooth is more apically placed than normal.
- The tooth often has a greater apico-occlusal height and the level of furcation of the roots is situated much below the cervical area.
- In taurodontism the affected tooth generally exhibit certain morphologic changes.
- This defect can involve both sexes equally.
- Taurodontism commonly affects the multi-rooted permanent molars and sometimes the premolars. It is rarely seen in the primary dentition.
- This dental anomaly may sometimes be associated with some craniofacial deformities, e.g. Down syndrome, Klinefelter syndrome, amelogenesis imperfecta and Poly-X syndrome, etc.
- Patients with hypodontia may have taurodontism in about 30% cases.
- Anthropologic studies indicate that taurodontism was relatively common among Neanderthal men.

TREATMENT

No treatment is required for taurodontism; however this anomaly can pose some difficulty during root canal treatments.

DENS-IN-DENTE (DENS-INVAGINATUS)

DEFINITION

Dens-in-dente refers to a folding or invagination on the surface of the tooth towards the pulp; which begins before the calcification of the tooth and eventually after calcification the defect produces a typical appearance of a **"tooth within a tooth"**.

- The defect in generally localized to a single tooth and interestingly maxillary lateral incisors are more often affected than any other tooth in the dental arch.
- Bilateral involvement (of the same tooth on either side of jaw) is often seen and sometimes the defect can involve multiple teeth including the supernumeraries.

TYPES

Dens-in-dente is often broadly divided into two types—coronal type and radicular type.

Coronal type: Coronal type of dens in dente occurs when the invagination or folding occurs on the crown portion of the tooth. The coronal type is further divided into three subtypes, which are as follows:

Type I—The invagination within the crown of the tooth.

Type II—The invagination extends below the cemento enamel junction (CEJ) of tooth but it may or may not communicate with the pulp.

Type III—The invagination extends through the root and perforates in the apical or lateral radicular area.

Radicular type: In case of dens-in-dente if the invagination occurs in the root portion of the tooth it is called the radicular type and the condition presumably occurs due to folding of the Hertwig's sheath during the development of root.

CLINICAL FORMS OF DENS-IN-DENTE

Depending upon the extent or depth of the invagination towards the pulp, the dens-in-dente presents several clinical forms and these are mostly determined by radiographs.

Mild form: This form of dens-in-dente is characterized by the presence of a deeply invaginated or accentuated lingual pit area. Such external pits can be clinically inconspicuous but are clearly visible with the periapical radiographs.

Intermediate form: Intermediate form of dens in dente radiographically reveals a small, pear shaped invagination of the enamel and dentine into the pulp chamber, this produces a typical appearance of "tooth with in a tooth".

Extreme form: In this form of dens-in-dente the invagination extends beyond the pulp chamber in the root of the affected tooth. This condition is sometimes known as "**dilated odontomes".**

Key points of dense-in-dente

- Focal area of invagination on the surface of the tooth, which produces a typical 'tooth within a tooth' appearance.
- Trauma probably causes the invagination in the developing tooth towards the pulp, before the tooth is calcified.
- Once the invaginated part becomes calcified along with the remaining tooth structure; it produces a 'tooth within a tooth' appearance.
- The anomaly may involve the crown of tooth (coronal type) or it may involve the root (radicular type).
- The defect increases caries susceptibility of the tooth with increased risk of pulpitis.

CLINICAL SIGNIFICANCE OF DENS-IN-DENTE

Since the base of the pit or the deep invagination in dens-in-dente is composed of a thin and often defective layer of enamel and dentine, this makes the tooth extremely vulnerable to caries soon after the tooth erupts into the oral cavity.

As a result most of the teeth with dens in dente frequently develop pulpitis, pulp necrosis, periapical cysts or periapical abscesses, etc.

TREATMENT

Early detection of the condition and restoration of the defect is the best treatment. In case of pulp involvement with or without apical pathology, endodontic treatment should be attempted. However in more severe form of the defect, extraction of the affected tooth should be done.

DENS-EVAGINATUS

DEFINITION

Dens-evaginatus is a rare developmental anomaly of tooth, in which a focal area of the crown projects outwards and gives rise to a "**globe shaped**" or "**nipple shaped**" protuberance on the occlusal surface. The projected portion often appears as an extra cusp or tubercle.

PATHOGENESIS

Dens-evaginatus probably develops as a result of excessive localized elongation and proliferation of the inner enamel epithelium as well as the odontogenic mesenchyme into the dental organ. The condition usually occurs during the early stage of tooth development.

CLINICAL FEATURES

- Dens-evaginatus **primarily affects the premolars** and the affected tooth exhibits a globe shaped **extra cusp or bump** on the occlusal surface, which is often centrally located between the buccal and lingual cusps.
- The condition can also affect the molars, canines or even the incisors. In such cases, the defect may occur either unilaterally or bilaterally.
- Dens-evaginatus is commonly seen among Chinese, Japanese, Filipino, American-Indians and occasionally Caucasians.

- Clinically, this defect may sometimes interfere with tooth eruption and in such cases there may be incomplete eruption of tooth or displacement of tooth with occlusal disharmony.
- Since the **extra cusp contains a vital pulp-horn**, its attrition, fracture or deliberate cutting may result in pulp exposure with pain, pulpitis and the other associated symptoms.
- Similar complications may also arise when reduction of the extra cusp is attempted intentionally by the dentist.

TREATMENT

The condition usually does not require any treatment as long as it is asymtomatic. In case of occusal disharmony, minor reduction should be attempted. However, in case of exposure or fracture of the extra cup, endodontic treatment of the tooth should be done.

TALON CUSP

DEFINITION

Talon cusp is an anomalous projection from the lingual aspect of the maxillary and mandibular permanent incisors. A 'talon' is the claw of a bird of prey and the name talon cusp has evolved since this anomalous structure often resembles an **"eagle's talon"**.

CLINICAL FEATURES

- This abnormal cusp arises from the cingulum area of incisor teeth, which extends up to the incisal edge **as a prominent T-shaped projection**.
- It is usually an asymptomatic condition however; in some cases it may cause problems like poor esthetics, increased susceptibility to trauma and caries and occlusal disharmony, etc.
- The projected structure in talon cusp usually consists of normal appearing enamel and dentin; moreover in few cases there can be presence of vital pulp tissue as well.
- Wearing or deliberate grinding of talon cusp may lead to pulp exposure and pain.
- Occasionally lingual pits develop on either side of the talon cusp.
- This anomaly is rare among general population; however it is often seen in patients suffering from Rubinstein-Taybi syndrome.

TREATMENT

- Whenever the lingual pits are present restorative treatments should be done to prevent caries.
- When talon cusp interferes with normal occlusion, preventive care should be taken by performing endodontic and restorative treatment.

ENAMEL PEARL

Enamel pearls are white**, dome shaped calcified projections** of enamel, usually located at the **furcation areas** of the molar teeth.

Maxillary molars are more frequently affected than any other teeth.

Enamel pearls are radiographically seen as 1 to 3 mm round radiopaque areas at the furcation region of tooth.

General causes of malformed crown of tooth

- Supernumerary tooth.
- Peg shaped laterals.
- Environmental enamel hypoplasia.
- Dens-invaginatus.
- Dens-evaginatus.
- Turner's tooth.
- Fusion of tooth.
- Gemination of tooth.
- Talon cusp.
- Ghost tooth.
- Congenital syphilis.
- Vitamin-D resistant rickets.
- Amelogenesis imperfecta.
- Dentinogenesis imperfecta.
- Renal osteodystrophy.
- Hypoparathyroidism.
- Epidermolysis bullosa.
- Radiotherapy during infancy.

Histologically, these are composed of normal appearing enamel, sometimes with a central core of dentin.

It is believed that the epithelial component of root sheath of Hertwig may sometimes retain its ameloblastic potential and therefore may synthesize enamel in some focal areas in place of cementum. This gives rise to the formation of enamel pearl.

DISTURBANCE IN THE STRUCTURE OF TEETH

DISTURBANCE IN THE STRUCTURE OF ENAMEL

Enamel is normally formed by the specialized odontogenic epithelial cells called ameloblasts and the entire process of formation of enamel takes place in three distinct stages, which are as follows:

Stage I: Enamel matrix formation (Secretory stage)
Stage II: Initial mineralization
Stage III: Enamel maturation

Enamel matrix formation: In the first stage or secretory stage the ameloblast cells cause synthesis and secretion of special proteins namely the amelogenins and enamelins. These two proteins constitute the basic structural elements of the enamel matrix.

Initial mineralization: Initial mineralization starts immediately after the secretion of enamel matrix proteins and during this the enamel microcrystals start to abut the plasma membrane of the ameloblast cells.

Maturation: The stage of maturation is characterized by simultaneous dual activity of withdrawal of protein and water from enamel with concomitant huge increase in its mineral content. All these three stages are completed before the eruption of the tooth in the oral cavity.

During the process of enamel formation, the ameloblast cells are susceptible to various external factors, which can damage the ameloblast cells and thus disturb the process of amelogenesis. The effect of disturbed amelogenesis is reflected on the surface enamel after the tooth erupts in the oral cavity.

Defect in the enamel due to disturbance during its formative process can be either qualitative or it can be quantitative.

- Quantitatively defective enamel having normal thickness is known as **enamel hypoplasia**.
- Qualitatively defective enamel having normal thickness is called **enamel hypocalcification**.

The type of developmental defect in enamel depends upon which factor was responsible for the defective amelogenesis and moreover the disturbance occurred during which stage of enamel synthesis.

Therefore depending upon the stages of formation of enamel; the defects arising in it under the influence of the external factors are as follows:

Defective amelogenesis

Responsible Factors	*Developmental Defects*
Matrix formation	Enamel hypoplasia
Initial mineralization	Enamel hypocalcification
Enamel maturation	Enamel hypomineralization

ACQUIRED DISTURBANCES OF ENAMEL

FOCAL ENAMEL HYPOPLASIA

When local infection or trauma causes damage to the ameloblast cells during odontogenesis, it may result in defects in enamel formation in isolated permanent tooth and this phenomenon is often known as **focal enamel hypoplasia**.

- This is probably the most common form of enamel hypoplasia among all the varieties.
- It occurs in permanent tooth due to periapical spread of infection from a carious deciduous tooth or from trauma to the deciduous tooth.
- In such cases the trauma or the infection in the existing deciduous tooth may cause damage to the ameloblast cells, which are supposed to form the enamel of the underlying permanent successor.
- The tooth affected in this process is commonly known as the **`Turner's tooth'.**
- Depending on the severity of the injury, the crown of the Turner's tooth may only have an area of enamel hypoplasia that is relatively smooth with some pitting on the surface.

- However, in very severe cases, the crown of the Turner's tooth is grossly deformed and exhibits severe pitting with a yellowish or brownish discoloration of the surface.

IDIOPATHIC ENAMEL OPACITIES

This condition is characterized by white opaque spots on the smooth surface enamel, which occur due to some unknown cause.

- Some of these spots may eventually turn brown after the tooth is erupted in the mouth.
- Enamel opacities may affect deciduous as well as permanent dentition and maxillary central incisor is the most frequently involved tooth.
- Histologically these opaque spots represent the area of hypomineralization.

GENERALIZED ENAMEL HYPOPLASIA

A short-term systemic or environmental disturbance in the functioning of ameloblasts at a specific period of time during odontogenesis often manifests clinically as a horizontal line of small pits or grooves on the enamel surface.

This line on the tooth surface indicates the zone of enamel hypoplasia and it corresponds to the time of development and the duration of the insult.

If the duration of the systemic or environmental insult is brief, the line of hypoplasia on the enamel surface will be narrow, whereas a prolonged insult may produce a wider zone of hypoplasia and also affect more number of teeth as well.

It has been observed from different clinical studies that generalized enamel hypolasia due to systemic or environmental disturbances usually involves those teeth, which develop in children during their first year of life. That is why the teeth like permanent incisors, cuspids and the first molars are often affected by generalized enamel hypoplasia.

Whereas the teeth like premolars, second molars and third molars are seldom affected by this defect since formation of the teeth begins usually 3 years after birth or even later.

EFFECT OF INDIVIDUAL SYSTEMIC CONDITIONS ON ENAMEL HYPOPLASIA

NUTRITIONAL DEFICIENCY

Since ameloblasts are amongst the most sensitive cells in the body in terms of metabolic requirements and any serious nutritional deficiency occurring during odontogenesis may result in generalized enamel hypoplasia of teeth.

- Deficiency of Vitamin A, C, and D often causes injury to the ameloblast cells and results in enamel hypoplasia.
- Hypoplasia of enamel due to nutritional deficiency commonly affects the central and lateral incisors, the cuspids and the first molars.
- The teeth exhibit variable degrees of pitting on the enamel surface.

CONGENITAL SYPHILIS

Enamel hypoplasia resulting from congenital syphilis is a well known phenomenon.

- The disease is contracted by the child in utero from a mother, who had active infection with *Treponema pallidum*.
- In syphilis, the infection is diffuse in nature and it can involve virtually any organ of the body. However, certain body tissues like the bone, nerves and the teeth are more susceptible to this infection as compared to other tissues of the body.
- The disease produces characteristic hypoplastic change in the enamel of permanent incisors and first molars due to infection to the developing tooth germ by Treponemal spirochetes.
- The organism causes inflammation of the tooth germ during the morphodifferentiation stage resulting in hyperplasia in the epithelium of the enamel organ.
- Because of the inflammation of the tooth germ and subsequent hyperplastic change in the enamel organ, enamel hypoplasia results often in association with some specific morphologic changes in the affected tooth.
- In congenital syphilis, the affected permanent incisors exhibit tapering of the mesial and

distal surfaces towards the incisal edge rather than toward the cervical margin and this gives a typical `**screwdriver**' appearance of these teeth.

- Moreover, these teeth also have a central notch at their incisal edge and hence are called `**Hutchinson's incisors**'. These changes are more pronounced in maxillary central incisors.
- The lateral incisors in congenital syphilis are usually "peg-shaped" and are called "**peg-laterals**".
- Congenital syphilis also produces some classic changes is molar teeth (usually the first molars), which are characterized by a crumpled and discolored occlusal surface and occlusal two third area of the crown.
- The affected teeth are often covered by a globular mass of enamel and such teeth are popularly known as '**Moon molars**' or '**Mulberry molars**'.
- It is important to note that not all the patients suffering from congenital syphilis will develop the hypoplastic enamel defects in their teeth as mentioned above.
- Moreover, few people with no history of congenital syphilis may exhibit similar dental changes.

HYPOCALCEMIA

Enamel hypoplasia may result from hypocalcemia secondary to Vitamin-D deficiency and the defect is usually pitting type.

EXANTHEMATOUS DISEASE

Exanthematous diseases are a group of diseases caused by a number of viruses but these have a prominent common feature of skin rash, e.g. smallpox, chickenpox, cowpox, measles, rubella.

- Severe form of these diseases in childhood often cause generalized enamel hypoplasia and it probably happens due to prolonged high fever associated with the infection, which may result in injury to the ameloblast cells.
- In such cases the enamel hypoplasia will usually occur in those portions of the teeth, which are undergoing development at the time of infection.
- Similar type of enamel hypoplasia can also occur in rickets and in congenital hypo-parathyroidism.

BIRTH INJURIES AND LOW BIRTH WEIGHT

- Enamel hypoplasia is a common developmental anomaly in case of birth injuries and it might result from a transient cessation of ameloblastic activity at the time of injury during labor.
- Children of low birth weight often exhibit enamel hypoplasia and it probably results from oxygen deprivation and mineral depletion to the ameloblast cells during perinatal management.
- Both deciduous as well as the permanent teeth develop hypoplastic enamel in these conditions.

Effects of raised fluoride levels on enamel and bone

Fluoride level	*Effects*	*Clinical appearance*
0.5 to 1.5 ppm	On the higher side, few people have very mild defects.	Not detectable
2.5 ppm	Mild defects in most and moderate defect in few people.	Noticeable white spots
4.4 ppm	Moderate to severe defects in nearly all patients.	Opaque and pitted
6 ppm	All patients affected.	Severe disfigurement of tooth
8 ppm	Osteosclerosis of bone.	Skeletal deformity with increased bone density seen in the X-rays

FLUORIDES AND MOTTLING

If fluoride levels in the drinking water exceeds 1 PPM (Parts per Million) it can cause **mottling of enamel**. Mottling is a type of enamel hypoplasia, which occurs as a result of damage to the ameloblast cells due to fluoride toxicity when the ion is absorbed in the body at a very high concentration. Besides causing damage to the enamel forming cells the excess fluorides also cause disturbance in the calcification process of enamel, and mottling actually results from this dual effect of fluoride toxicity.

CLINICAL FEATURES OF MOTTLING OF ENAMEL

- Excessive amount of fluoride in drinking water causes sclerosis of the skeleton, which is characterized by calcification of the muscles and ligaments (especially intervertebral muscles and ligaments) with stiffening of the body and pain. The bone changes include increased thickening and mineralization similar to that of Paget's disease of bone.
- Mottling is a generalized disturbance affecting all those teeth exposed to excess fluoride during odontogenesis or development of tooth (Fig. 1.26).
- The condition does not affect adults.
- Mostly the permanent dentition is affected and the involvement of deciduous teeth is rare.
- The mottled teeth often have chalky or typical 'paper white' opaque enamel with areas of flecking or pitting.
- The damage can be extensive in some teeth, which exhibit fracturing of enamel with an associated brown or black pigmentation.
- Mottled teeth are less susceptible to caries.

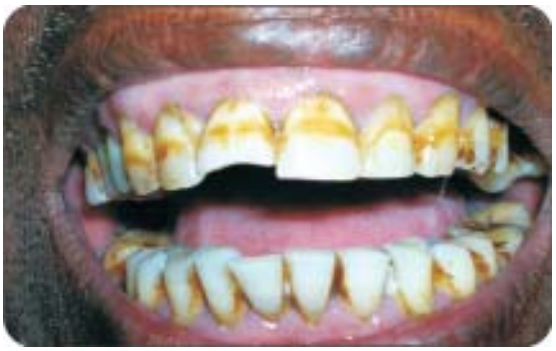

Fig. 1.26: Fluorosis

HEREDITARY DISTURBANCE OF ENAMEL FORMATION

AMELOGENESIS IMPERFECTA

DEFINITION

Amelogenesis imperfecta is a heterogenous group of hereditary disorders of enamel formation, affecting both deciduous and the permanent dentition.

The disease involves only the ectodermal component of the tooth (i.e. enamel) while the mesodermal structures of tooth, (e.g. dentin, cementum and pulp), etc. always remain normal.

TYPES

Normally, the process of enamel formation progresses through three stages:

A. Stage of enamel matrix formation.
B. Stage of early mineralization.
C. Stage of enamel maturation.

Amelogenesis imperfecta may set in during any stage of enamel formation. Four basic types of the disease have been identified, which corresponds with three developmental stages of enamel.

Type I	Hypoplastic type of amelogenesis imperfecta
Type II	Hypomaturation type of amelogenesis imperfecta
Type III	Hypocalcification type of amelogenesis imperfecta
Type IV	Hypomaturation Hypoplastic type with Taurodontism

Hypoplastic Type

The enamel thickness is usually far below normal in hypoplastic type of amelogenesis imperfecta since the disease affects the stage of matrix formation. The teeth exhibit either complete absence of enamel from the crown surface or there may be a very thin layer of enamel on some focal areas of crown.

Hypomaturation Type

This type occurs due to interruption in the process of maturation of enamel. Here the enamel is of normal thickness but it does not have the normal hardness and translucency (snow-capped tooth).

The enamel can be pierced with an explorer tip with firm pressure.

Hypocalcification Type

Hypocalcification type of amelogenesis imperfecta represents the disturbance in the process of early mineralization of the enamel.

In this type of amelogenesis imperfecta, the enamel is of normal thickness but is soft and can be easily removed with a blunt instrument.

Hypomaturation-Hypoplastic Type with Taurodontism

This is a rare condition where taurodontism is reported in association with amelogenesis imperfecta.

CLINICAL FEATURES OF AMELOGENESIS IMPERFECTA (FIGS 1.27 AND 1.28)

- Amelogenesis imperfecta affects both deciduous as well as the permanent dentition.
- Sex predilection varies according to the mode of inheritance.
- The color of the teeth is mostly chalky white but sometimes it can be yellow or even dark brown.
- Besides the discoloration, these teeth are sensitive and are prone to disintegration.
- The contact points in the proximal surfaces are mostly open either due to lack of formation or early loss of enamel.

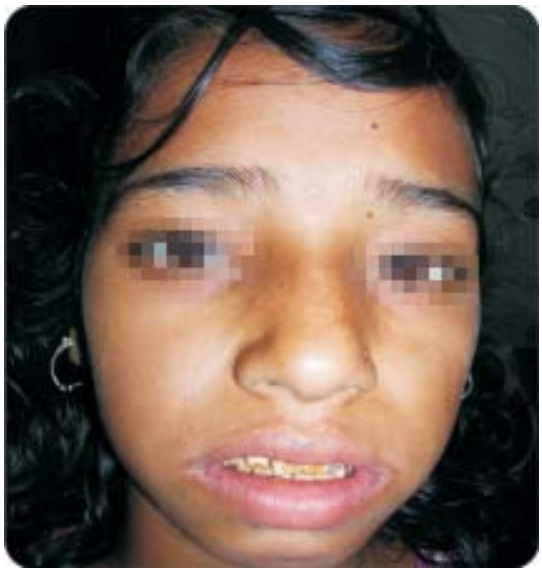

Fig. 1.27: Amelogenesis imperfecta-I

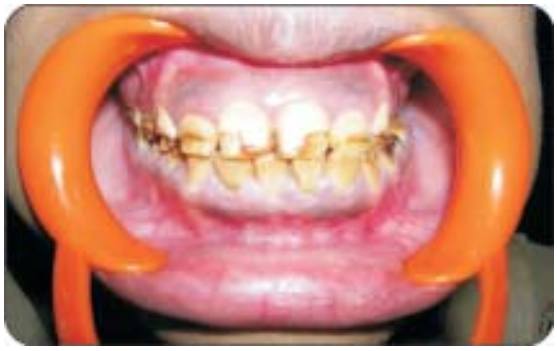

Fig. 1.28: Amelogenesis imperfecta-II

- The occlusal surfaces and the incisal edges of the teeth are often severely abraded.
- Sometimes, the tooth may be completely devoid of enamel and the patient which results in severe abrasion of the dentin.
- In some patients, the enamel may have a cheesy consistency which is easily removable from the tooth surface with dental explorers.
- Amelogenesis imperfecta can be associated with retained deciduous tooth and delayed eruption of permanent tooth.
- Alteration in the eruption pattern of teeth in amelogenesis imperfecta may further result in the development of anterior-open bite.
- On rare occasions, the enamel may look almost normal except the presence of few grooves and wrinkles on its surface.
- Amelogenesis imperfecta does not increase the susceptibility of the teeth to dental caries.
- In the mildest form of hypomaturation type, the enamel is of near normal hardness and the teeth exhibit some white opaque flecks at the incisal margins. These types of teeth are known as "**Snow-capped teeth**".
- Amelogenesis imperfecta may occur either as an isolated disease or it may develop as part of a syndrome which includes features like nephrocalcinosis and hypocalciurea, etc.

RADIOGRAPHIC FEATURES

In amelogenesis imperfecta, the thickness and radiodensity of enamel varies greatly. The tooth may be completely devoid of enamel and wherever the enamel is present, it is very thin and found mostly on the tip of the cusps and on the interproximal areas (Fig. 1.29).

Fig. 1.29: Radiographic of Amelogenesis imperfecta

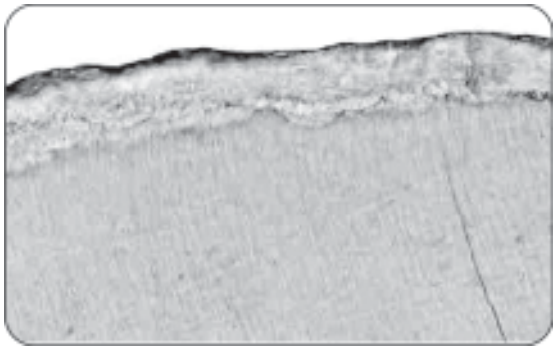

Fig. 1.30: Photomicrograph of amelogenesis imperfecta

- In hypoplastic type, the radiodensity of the enamel is usually greater than the adjacent dentin.
- The radiodensity of enamel in hypomaturation type is almost equal to that of the normal dentin.

Key points of amelogenesis imperfecta

- This is the hereditary enamel hypoplasia characterized by little or no formation of enamel.
- The disease has four types—hypoplasticty type, hypocalcification type and hypomaturation-hypoplastic type with Taurdontism.
- Thin layer of soft or cheesy enamel often present on the tooth surface; (predominantly on the cuspal and incisal areas), even the hard enamel whichever is present can be easily removed by dental explorers.
- The tooth often has a chalky discoloration.
- Lack of enamel results in severe abrasions of tooth.
- Besides enamel other structures of tooth, e.g. dentin, cementum and pulp are absolutely normal.

HISTOPATHOLOGY

Histologically, the enamel in hypoplastic type of amelogenesis imperfecta exhibits lack of differentiation of the ameloblast cells with little or no matrix formation (Fig. 1.30).

The enamel in hypocalcification type shows defective matrix structure and abnormal or subnormal mineral deposition.

The hypomaturation type reveals alteration in the enamel rod and rod-sheath structures.

TREATMENT

There is no definitive treatment for amelogenesis imperfecta, composite veneering can be done to improve overall aesthetics of teeth.

SYNDROME ASSOCIATED ENAMEL DEFECTS

A large number of syndromes and pathological conditions have been identified, which are often associated with hereditary enamel defects. In the following section few such syndromes or conditions have been discussed.

Epidermolysis bullosa: It is a bullous disease of the skin and mucous membrane. Dental defects associated with this condition include—enamel hypoplasia with random pitting.

Morquio's syndrome (Type-IV-Mucopolysaccharoidoses): Dental defects which occur in association with this syndrome include:

- Enamel hypoplasia with pointed peak-like cusp tips.
- Grey colored teeth with vertically oriented pits on the surface.

Sanfilippo's syndrome (Mucopolysaccharoidoses type-III): This syndrome presents features like-loss of enamel from the dentinal surfaces, defective formation of dentin and obliteration of pulp chambers.

Oculodento-osseous dysplasia: Dental defects in this syndrome include the following:

- Thick mandibular bone.
- Multifocal enamel hypoplasia of the tooth surface with pitting.

Classification of developmental defects in dentine

Local Causes	*General Causes*
Trauma in the deciduous tooth causing **'turner's tooth'**.	A. ***Dentinogenesis imperfecta:*** Type I—Dentinogenesis imperfecta associated with osteogenesis imperfecta. Type II—Dentinogenesis imperfecta not associated with osteogenesis imperfecta (only teeth are affected). Type III—Dentinogenesis imperfecta of Brandy wine type. B. ***Dentin dysplasia:*** Type I—Radicular dentin dysplasia (rootless teeth). Type II—Coronal dentin dysplasia. C. ***Environmental/systemic:*** Vitamin D—dependent rickets. Vitamin D—resistant rickets (hypophosphatemia). Hypophosphatasia. Juvenile hypoparathyroidism. Other mineral deficiencies. Drugs, e.g. chemotherapeutic agents.

- Moth-eaten radiographic appearance of the teeth.

***Amelo-onycho-hypohidrotic syndrome*:** This syndrome often shows severe hypoplastic-hypocalcified enamel.

Trichodentoosseous syndrome: Hypoplastic-hypocalcified enamel with pitting of the surface.

***Rieger syndrome*:** Enamel hypoplasia with abnormally shaped teeth.

DISTURBANCES IN STRUCTURE OF DENTIN

Dentin is the first formed dental hard tissue and it is produced by the specialized odontogenic mesenchymal cells called the odontoblasts. These dentin forming cells or odontoblasts are derived from the mesenchymal cells of the dental papilla under the influence of the internal enamel epithelium. In the initial stage of dentin formation a collagenous matrix is formed, which is embedded in a ground substance rich in glycosaminoglycans (gag). When sufficient thickness the dentin matrix is laid down the odontoblast cells migrate through it centripetally and their processes remain in the matrix, which begin to mineralize later. Mineralization of dentin is initiated by the formation of small crystallines, which subsequently grow and fuse together to form discrete calcific globules called calcospherites.

Most of the factors causing interference in the process of dentinogenesis are genetic in nature. However there are some environmental factors as well, which can also cause disturbance in the normal dentine formation.

DENTINOGENESIS IMPERFECTA (HEREDITARY OPALESCENT-DENTIN)

DEFINITION

Dentinogenesis imperfecta is an inherited disorder of dentin formation, characterized by excessive formation of defective dentin, which results in obliteration of pulp chambers and root canals of tooth. The condition affects both deciduous as well as the permanent dentition and it usually exhibits an autosomal dominant mode of transmission.

TYPES

The disorder has been classified into three types:

A. Type-I
B. Type-II
C. Type III

Type-I: Dentinogenesis imperfecta associated with Osteogenesis imperfecta (OI)

- This type is usually inherited as an autosomal dominant trait.
- It involves the deciduous teeth more often than the permanent teeth.
- Teeth will usually have an opalescent color (as seen in type II as well).
- Patients will exhibit features of osteogenesis imperfecta (since both conditions occur together), which include **bluish selera** of the eyes and several bony defects.
- It is important to note that not all cases of osteogenesis imperfecta will be associated with dentinogenesis imperfecta.
- Moreover, there is no correlation between dentinogenesis imperfecta and the severity of the osseous defects present in osteogenesis imperfecta.

Type-II: Dentinogenesis Imperfecta not Associated with Osteogenesis Imperfecta

- This type of dentinogenesis imperfecta is often known as "hereditary opalescent dentin" .
- It is the most common type among all the three forms of the disease, having incidence rate about 1 in 8000 people.
- The condition is inherited as an autosomal dominant trait.
- Involves deciduous and permanent teeth with equal frequency.

Type-III: Dentinogenesis Imperfecta Type III or the "Brandywine Type"

- Type III dentinogenesis imperfecta is a rare condition and is inherited as an autosomal dominant trait.
- It is commonly seen in a racial isolate area in the state of Maryland.
- It affects both dentitions and the disease is characterized by too little dentin formation in the tooth with presence of abnormally large pulp chambers.
- Clinically the disease is same as type I and type-II variants, however it often exhibits multiple pulp exposures and periapical lesions in deciduous teeth.
- Presence of little or no dentin in the tooth with large pulp chamber; results in a classic "**shell tooth**" appearance of the affected tooth.

CLINICAL FEATURES OF DENTINOGENESIS IMPERFECTA

- In all three types of dentinogenesis imperfecta both deciduous and permanent dentitions are affected with variable clinical presentations.
- The condition affects males and females with almost equal frequency.
- On eruption, the teeth exhibit a normal contour but they have an opalescent '**amber-like**' appearance.
- Few days after eruption, the teeth may achieve an almost normal color, following which they become translucent.
- Finally the teeth become either gray or yellowish-brown in color with a bluish reflection from the enamel.
- The teeth in dentinogenesis imperfecta often have '**tulip**' shape, which is characterized by a broad crown and a narrow constricted cervical area.
- The overlying enamel is structurally normal in most cases, however this enamel is lost rapidly from the dentin surface soon after the teeth erupt in the oral cavity.
- Enamel is lost early due to poor bonding between the enamel and dentin because of abnormal dentinoenamel junction. Early loss of enamel results in severe attrition of dentin (Fig. 1.31).

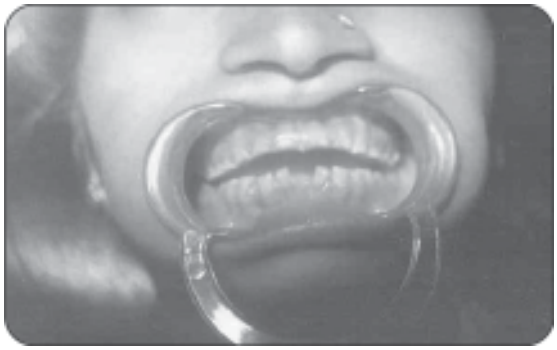

Fig. 1.31: Dentinogenesis imperfecta showing generalized attrition of teeth

- In some cases of dentinogenesis imperfecta, the affected teeth may also exhibit hypomineralized areas on the surface enamel.
- Teeth are not particularly sensitive even when most of the surface enamel is lost, it happens since the dentinal tubules are haphazardly arranged and most of them are devoid of the odontoblastic processes.
- Although the dentin is soft and easily penetrable in dentinogenesis imperfecta, these teeth are **not caries prone**. The possible reason could be the structural change in the dentin itself, which provides little scope for the entry of the cariogenic microorganisms into the tooth since most of the dentinal tubules are obliterated in this disease (Fig. 1.32).
- Type III cases of dentinogenesis imperfecta are often associated with multiple pulp exposures (mostly due to attrition) and periapical pathology.

RADIOGRAPHIC FEATURES

Radiographically dentinogenesis imperfecta reveals the following features (Fig. 1.33):

- The type I and type II diseases are radiographically similar and they often exhibit "**bulb shaped**" or "**bell shaped**" crowns of the teeth with abnormally constricted cervical areas.
- The roots of the teeth are thin and spiked.
- Depending on the age of the patient, the teeth exhibit varying degrees of **obliteration of the coronal as well as the radicular pulp chamber (Fig. 1.34).**
- The cementum, periodontal ligament and the alveolar bone radiographically appear normal.

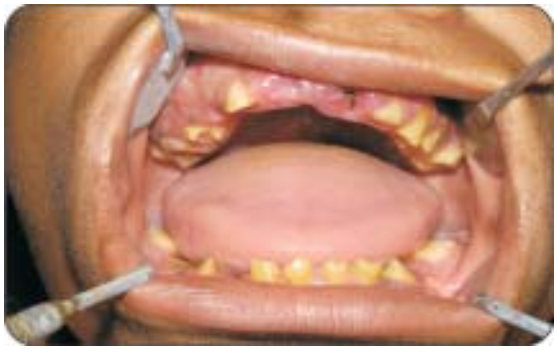

Fig. 1.32: Dentinogenesis imperfecta

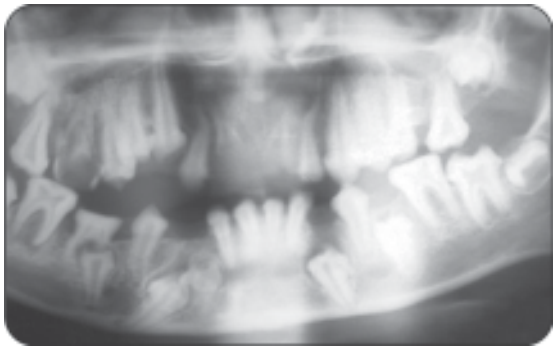

Fig. 1.33: Radiograph of dentinogenesis imperfecta X-ray

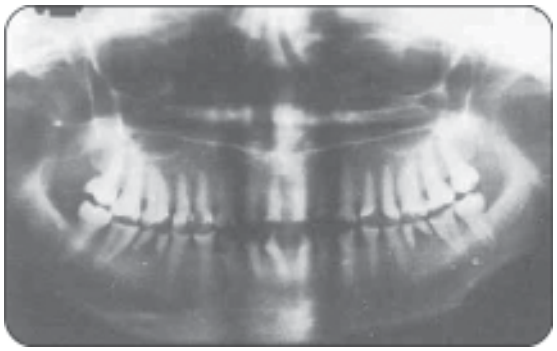

Fig. 1.34: Dentinogenesis imperfecta showing obliteration of the pulp chambers of teeth

- The type III dentinogenesis imperfecta exhibit extremely large pulp chambers surrounded by a thin shell of dentin and enamel.
- Because of their typical appearance, the affected teeth in type III dentinogenesis imperfecta are often called **"shell"** teeth.
- These teeth frequently exhibit multiple pulp exposure and associated periapical pathology.

HISTOPATHOLOGY

- Histologically, the enamel appears normal in dentinogenesis imperfecta.
- The mantle dentin (a narrow zone of dentin immediately beneath the enamel) is also nearly normal.
- The major parts of the remaining dentin are severely dysplastic and exhibit vast areas of amorphous matrix with globular or intergobular foci of mineralization.
- The dentinal tubules are far less in number per square unit area of dentin as compared to the normal dentin.

- These tubules are often distorted, irregular in shape, widely spaced and are often larger in size.
- In many cases the odontoblastic processes are absent in the dentinal tubules, instead there can be presence of some degenerating cellular debris inside these tubules.

Key points of dentinogenesis imperfecta

- This is a hereditary defect of dentin characterized by increased, abnormal synthesis of dentin in the tooth with presence of normal enamel.
- The disease occurs in three forms—Type I, Type II and Type III.
- The affected teeth have an opalescent hue with amber-like color after eruption; with time they become brown or gray with a bluish reflection from enamel.
- Dentinoenamel junction is flat instead of scalloped and it causes poor locking between enamel and dentin; because of this tooth enamel is quickly lost from the dentin surfaces.
- Teeth in dentinogenesis imperfecta a often exhibit severe abrasions.
- Tooth have narrow constricted cervical area.
- Type I and Type II show obliteration of pulp chamber due to abnormal dentin formations. Type III shows abnormally large pulp chamber (shell tooth).

- There may be large areas of atubular dentin present along with areas of noncalcified matrix.
- Degenerating odontoblasts are often trapped inside the dentin matrix.
- The pulp chamber and root canals are often obliterated by abnormal secondary dentin deposition.
- **The dentinoenamel junction appears smooth or flattened instead of being scalloped (Fig. 1.35).** This abnormal configuration is mostly responsible for the early loss of enamel from the tooth surface in dentinogenesis imperfecta.

BIOCHEMICAL PROPERTY OF DENTIN

- Biochemical analysis of the dentin in dentinogenesis imperfecta reveals increased water content and decreased mineral content.

Fig. 1.35: Photomicrograph of dentinogenesis imperfecta showing loss of scalloping of the DEJ

- The microhardness of the dentin is low as compared to the normal dentin.

TREATMENT

The treatment in dentinogenesis imperfecta is mostly aimed at preventing excessive tooth attrition and improving esthetics of the patients.

- Metal and ceramic crowns are given.
- These teeth are not suitable candidates for playing the role of abutments for any bridge work since the roots are small and they also tend to fracture under frictional stress.
- In case of severe generalized attrition, complete denture prosthesis may be necessary.

Conditions associated with enlarged pulp chambers

- Dentinogenesis imperfecta (shell tooth)
- Regional odontodysplasia (ghost tooth)
- Internal resorption of tooth
- Taurodontism
- Vitamin D-resistant rickets (high pulp horns)
- Hypophosphatasia
- Dentin dysplasia type II.

DENTINAL ABNORMALITY DUE TO SYSTEMIC OR ENVIRONMENTAL DISTURBANCES

The environmental or systemic conditions, which can affect dentinogenesis are as follows:

- Vitamin-D dependent rickets.
- Vitamin-D resistant rickets.
- Cytotoxic drugs.
- Juvenile hypoparathyroidism.

- Hypophosphatasia.
- Dentin dysplasia type II (thistle tube pulp).

VITAMIN-D DEPENDENT RICKETS

Dentinal Changes

Dentinal changes in this disease include the following:

- The width or thickness of the predentin is increased.
- Improper and incomplete calcification of the regular dentin.
- Thick band like areas of interglobular dentin can be seen histologically, which correspond to the periods of active phase of the disease.

VITAMIN-D RESISTANT RICKETS (HYPOPHOSPHATEMIA)

Dentinal Changes

- Increased amount of interglobular dentin formation.
- These teeth exhibit large pulp chambers and long pulp horns. The later may even extend to the dentino enamel junction as narrow clefts.
- The overlying enamel is defective and shows numerous cracks, which can serve as the direct pathways for entry of microorganisms into the pulp.
- Many such teeth with this defect often exhibit pulpitis and periapical lesions even in the absence of caries.

HYPOPHOSPHATASIA

Dentinal Changes

- Increased formation of interglobular dentin.
- Widening of the predentine.

Cytotoxic Agents

Presence of many prominent incremental lines in the dentin, which often correspond to the periods of the drug (cytotoxic) administration.

Juvenile Hypoparathyroidism

Dentinal changes include:

- Presence of small sized teeth in the arch.
- Hypoplastic enamel.
- Multiple prominent incremental lines can be seen in the dentine.
- Roots of the teeth are small.
- Histologically radicular dentine reveals many structural abnormally and there can be areas of vascular inclusions in the dentine.

DENTIN DYSPLASIA

DEFINITION

Dentin dysplasia is an autosomal dominant inherited disorder characterized by defective dentine formation and abnormal pulpal morphology, however the enamel in such teeth is absolutely normal. The condition is also known as "**rootless teeth**".

TYPES

The condition is classified into two types:

A. **Type I or radicular dentin dysplasia**.
B. **Type II or coronal dentin dysplasia**.

Dentin Dysplasia Type-I (radicular)

Dentin dysplasia type-I represents a peculiar disturbance in the development of radicular dentin.

Clinical Features

- There is no sex predilection.
- Although, both types of dentin dysplasias are rare entities, however type-I dentin dysplasia is far more common than type-II.
- The anomaly affects both deciduous as well as permanent dentitions.
- Although the roots of the teeth are defective, the crown portions are normal both structurally and morphologically.
- The color of the teeth is usually normal but in some cases the crowns of the teeth reveal a slight bluish or brownish translucency at the cervical region.
- Unlike dentinogenesis imperfecta, the enamel does not chip off from the crown surface.
- The teeth usually erupt at the normal time; although in some cases there can be delayed eruption.
- Because of the presence of functionally unstable short roots, the affected teeth often exhibit severe mobility and they may even exfoliate prematurely due to minor trauma.

- Dentin dysplasia Type-I can occur in association with diffuse generalized osteosclerosis.

Radiographic Features

- The roots of the teeth are characteristically malformed, short, blunt or conical.
- Although presence of rudimentary roots is common, in many cases the teeth may be completely devoid of roots.
- The deciduous teeth often exhibit total obliteration of the pulp chambers and root canals.
- The permanent teeth also present pulp obliterations but there may be presence of very thin crescent shaped remnants of the pulp.
- Obliteration of the pulp chamber in the affected teeth may occur even before the teeth erupt in the oral cavity.
- The mandibular molars often exhibit characteristic **"W" shaped roots**.
- Periapical radiolucencies of unknown etiology (e.g. periapical cyst, abscess or granuloma, etc.) may be found in many normal appearing teeth.

Histopathology

- The enamel and mantle dentins are normal.
- The remaining coronal and radicular dentin appear as a fused nodular mass comprising of tubular dentin, osteodentin and amorphous dentin mass.
- Histologic appearance of such defective mass of dentinal tissue often resembles, what is called "**a series of sand dunes**" or **"lava flowing around boulders".**
- Remnants of pulp tissue may occasionally be seen between the normal and the abnormal dentinal tissue.
- The normal and the abnormal dentin are well demarcated and the later reveals an abnormal distribution and orientation of the dentinal tubules with a typical whorled appearance.

Pathogenesis

Dentin dysplasia type I develops probably due to a defect in the epithelial root sheath of Hertwig, which fragments and becomes incorporated into the dental papilla, where it induces formation of dysplastic dentin.

Treatment

No specific treatment is available. These teeth also do not serve as good abutments since their roots are very short.

Dentin Dysplasia Type-II (Coronal)

Definition

It is an inherited autosomal dominant disorder of dentine, which mostly affects the coronal dentine.

Clinical Features

- Both deciduous and permanent teeth are affected in this disorder.
- The permanent teeth are of normal color, whereas the deciduous teeth exhibit an "ambergray" color with some translucent or opalescent appearance.
- There is no sex predilection.

Radiographic Features

- The deciduous teeth in dentin dysplasia type II reveals obliterated pulp chambers and root canals, thereby resembling dentinogenesis imperfecta.
- Permanent teeth exhibit large pulp chambers with a typical "thistle tube" appearance.
- Pulpal obliteration occurs only after tooth eruption.
- The roots of the deciduous and the permanent teeth are usually of normal shape and length.
- Unlike dentinogenesis imperfecta there is no cervical constriction of the teeth in dentin dysplasia type-II.
- The pulp chambers in permanent teeth are abnormally large instead of being obliterated and have a typical flame shape.
- The pulp chamber contains many pulp stones or denticles.
- Root canals may be partially obliterated in the apical third region.

Histopathology

- The deciduous teeth exhibit a dense amorphous mass of dentin, which contains only few haphazardly arranged dentinal tubules.

- The permanent teeth show normal dentinal structures but may have the presence of abnormal globular or interglobular dentin near the pulpal third area and in the roots.
- The pulp chambers exhibit the presence of numerous pulp stones.

Treatment and Prognosis

No special treatment is required in case of dentin dysplasia type-II. Prognosis is good for the permanent teeth since their root length is essentially normal.

REGIONAL ODONTODYSPLASIA (GHOST TEETH)

DEFINITION

Regional odontodysplasia is an uncommon but unique nonhereditary developmental disturbance of teeth, characterized by defective formation of enamel and dentin, in addition to abnormal pulp and follicle calcifications.

ETIOLOGY

The etiology is not fully understood but it is suggested that the disease develops due to some local ischemic change in the tissue during odontogenesis. Some investigators suggest a viral etiology for this condition.

CLINICAL FEATURES

- Both permanent and deciduous dentitions are affected in this disease although it is more common in permanent dentition.
- There is no sex predilection.
- The maxillary teeth are affected more often than the mandibular teeth.
- The disease is called **regional** since it **affects several contiguous teeth** in a single quadrant of the jaw.
- It frequently occurs unilaterally, often affecting certain parts of maxilla.
- The central and lateral incisors and the cuspids in the maxillary arch are often affected.
- The affected teeth show either delayed eruption or a complete failure of eruption.
- These teeth are often deformed, have a soft leathery surface and are yellowish-brown in color.

Conditions associated with malformation of the roots of teeth

- Dilaceration
- Hypercementosis
- Concrescence
- Supernumerary roots
- Taurodontism
- Enamel pearl
- Benign cementoblastoma
- Dentinogenesis imperfecta
- Dentin dysplasia type–I
- Radiotherapy during childhood
- External resorption of tooth.

RADIOGRAPHIC FEATURES

The teeth is regional odontodysplasia have often been described as **"ghost teeth",** since there is marked decrease in the radio-density of these teeth as a result of defective mineralization.

- The enamel and dentin are very thin and radiographic distinction between these two structures is impossible, this accounts for the subdued or "ghostly" appearance of the involved teeth.
- Pulp chambers of the teeth are **extremely large and open**, and often they contain pulp stones.

HISTOPATHOLOGY

- The enamel layer is attenuated and disrupted.
- Dentin is very thin and globular, and exhibits irregular tubules and a wide predentine layer.
- Large pulp chamber exhibits numerous pulpal calcifications.
- The reduced enamel epithelium persists and the follicular connective tissue contains numerous clusters of tiny droplet calcifications.

TREATMENT

Extraction of the affected teeth and fabrication of a suitable prosthesis is usually recommended.

DISTURBANCE IN STRUCTURE OF CEMENTUM

Cementum is the odontogenic mesenchymal tissue, which covers the root surface of teeth. There are two types of cemental tissues found:

The acellular or primary cementum: Which covers the coronal one third of the roots.

The cellular or secondary cementum: It covers the apical two thirds and furcation areas of the teeth. The cellular cementum often has a thicker layer and it continues to form throughout the life of the tooth.

There are two main types of defects seen in the cementum:

- Hypercementosis
- Hypocementosis.

HYPERCEMENTOSIS

DEFINITION

It represents an increased and abnormal thickness of the cementum, which results from abnormal cementogenesis.

ETIOLOGY

- ***Periapical inflammation:*** Periapical inflammation in a tooth causes cemental resorption at it's centre position, however this also causes cemental opposition on the root a little further away. This may result in either a generalized increase in the thickness of cementum or a localized "knob-like" enlargement.
- ***Mechanical stimulation:*** Although excessive mechanical forces applied to a tooth produce cemental resorption but forces below a certain threshold level may stimulate cemental apposition and subsequent hypercementosis.
- ***Nonfunctional and unerupted teeth:*** These teeth sometimes show cemental resorption but excessive apposition of cementum is also possible.
- ***Paget's disease of bone:*** Hypercementosis is a common feature of Paget's disease of bone. The cementum in this disease is very thick and it often has a mosaic pattern.
- ***Root ankylosis and concrescence:*** Teeth in these conditions may be associated with hypercementosis.

Radiographic changes in various tooth abnormalities

Germination (incomplete)	Two crowns with one root.
Dilacerations	Sharp bend in the tooth (mostly root).
Dens-in-dente	Tooth within a tooth.
Taurodontism	Large crown with small root, too much apically placed bifurcation.
Concrescence	Joining of roots of many teeth with obliteration of periodontal ligament space.
Amelogenesis imperfecta	Little or no enamel on tooth.
Dentinogenesis imperfecta	Obliteration of pulp chamber.
Dentinogenesis imperfecta type III	Abnormally large pulp with thin shell of enamel and dentin surrounding the pulp.
Ghost tooth	Decreased radiodensity of tooth; abnormally large pulp chamber.
Dentin dysplasia	Abnormally short, blunt root, molar roots appear **'w'** shaped.
Hypercementosis	Bulbous root.
Supernumerary tooth	Mostly small and conical shaped.
Pit and fissure caries	Triangular-shaped radiolucency with it's base towards DE Junction.
Smooth surface caries	Triangular-shaped radiolucency with it's base towards surface of the tooth.
External resorption of tooth	Moth-eaten irregular destruction of root surface.
Internal resorption	Well-defined spherical radioluceny of dentine in continuation with the pulp.
Compound odontome	Multiple miniature teeth projecting from a single focus.

HYPOCEMENTOSIS

Hypocemtosis or acementosis is a rare developmental anomaly of tooth characterized by lack of cementum formation in the tooth.

CAUSE

- Cleidocranial dysplasia
- Hypophosphatasia.

Hypocementosis prevents the normal development of the periodontal attachment or even the normal dentin formation. Premature loss of few or all deciduous and permanent teeth may occur in this disease.

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CHAPTER 2

Benign and Malignant Neoplasms of the Oral Cavity

NEOPLASM (TUMOR)

DEFINITION

A neoplasm can be defined as a ceaseless, purposeless, uncoordinated and uncontrolled growth of the tissue resulting from multiplication of its cells. Moreover, the growth of the neoplasm may continue even after the stimulus or the initiating factor is removed.

Neoplasms can occur from virtually any tissue anywhere in the body and the oral cavity is an important location where a large variety of neoplasms often develop with diverse pathogenicity.

Classification of oral neoplasms is very important since it facilitates in the understanding of the pathological nature of the disease in a more specific and comprehensive manner and more-over it also helps in making comparison and evaluation of different neoplastic conditions on the basis of their specific pathological nature.

The modern classification of oral neoplasms is based primarily on the structural basis or in other words, several neoplastic conditions are put into different categories on the basis of their tissue of origin.

Depending on the pathologic state, the oral neoplasms can be divided into two broad categories or groups, namely:

A. ***Benign neoplasms*** and

B. ***Malignant neoplasms***

In the following section, we will see how a benign neoplasm may differs clinicopathologically from its malignant counterpart.

Generally, the benign tumor is designated by attaching the suffix "oma" to the cell type from which it arises. For example, a benign tumor arising from the fibrous tissue is called a "fibroma" while a benign cartilaginous tumor is called a "chondroma". A benign epithelial tumor arising from the gland is known as "adenoma".

A malignant tumor arising from the epithelial tissue is called "carcinoma" and a malignant tumor arising from the connective tissue is known as "sarcoma". Recent literatures have documented about another malignancy, which is called "carcinosarcoma" and it is characterized by simultaneous malignant transformation of both the epithelial and mesenchymal components of the tissue.

LOCAL INVASION

When a tumor penetrates into the adjoining tissues due to its increased rate of growth, it is known as invasion. Most of the malignant tumors as well as few benign tumors show this behavior. Invasion is an important pathological change in any malignant neoplasm, which determines the future course of the neoplasm as well as the prognosis.

METASTASIS

Metastasis can be defined as the distant spread of tumor cells anywhere in the body away from its primary location. This is an important characteristic of the malignant tumor. The tumor which occurs initially is called the **primary tumor;** while the newly formed tumor developing as a result of metastasis at a distant site is called the **metastatic or secondary tumor**.

During metastasis, the tumor cells spread either via the lymphatic channels or the blood vessels, besides this, in some cases, the metastatic cells can spread via the nerve sheath or even through other natural tissue spaces. With some exceptions, the carcinomas generally metastasize via lymphatic channels while the sarcomas metastasize via blood vessels.

Differentiating features of benign and malignant tumors

	Features	*Benign*	*Malignant*
On the basis of clinical features	Size of the tumor	Usually small	Usually large
	Rate of growth	Slow	Very fast
	Pain	Absent	Mostly painful
	Hemorrhage	Not usual	Very common
	Ulceration	Absent	Present
	Paresthesia	Does not occur	Commonly occurs
	Induration	Absent	It is often present
	Symptoms	Asymptomatic	Always symptomatic
	Metastasis	Usually Absent	Very common
On the basis of histopathologic features	Cell multiplication rate	Slow	Very fast
	Cell maturation	Good	Cells are often immature
	Cell uniformity	Uniform	Irregular size and shape
	Cell morphology	Not changed	Normal cell morphology is lost
	Cell function	Restored	Mostly lost
	Stroma	Almost normal	Exhibits invasion
	Tissue architecture	Intact (Resembles normal tissue)	Mostly lost or altered
	Capsule	Usually present	Absent
	Superadded infection	Usually absent	Commonly present
	Necrotic areas	Usually absent	Commonly present
	Prognosis	Good	Mostly poor

CLASSIFICATION OF ORAL NEOPLASMS (TUMORS)

In the oral cavity, several types of neoplasms often develop and these entire variety of neoplastic lesions are broadly divided into two categories:

A. Odontogenic neoplasms and

B. Non-odontogenic neoplasms.

Odontogenic neoplasms: These are a group of neoplastic conditions either benign or malignant, which develop from the dental formative tissues or their remnants.

Non-odontogenic neoplasms: These are the neoplastic lesions, which arise from virtually any tissue in the oral cavity excepting from those arising from the dental formative organs.

The nonodontogenic neoplasms can develop from several tissues like skin or mucous membrane, fibrous connective tissue, blood vessels, muscles, bone, cartilage, neural tissue and lymphoid tissue, etc. It is important to remember that unlike the odontogenic neoplasms which can arise only in the oral cavity or its surrounding areas, the nonodontogenic neoplasms are not always confined to the oral region, rather they can develop in other parts of the body as well.

CLASSIFICATION OF ORAL NON-ODONTOGENIC NEOPLASMS

NEOPLASMS OF EPITHELIAL TISSUE ORIGIN

Benign neoplasms	Malignant neoplasms
Papilloma	Basal cell carcinoma
Keratoacanthoma	Squamous cell carcinoma
Pigmented cellular nevus	Verrucous carcinoma
Papillary hyperplasia	Adenoid squamous cell carcinoma
	Malignant melanoma
	Spindle cell carcinoma
	Primary intra-alveolar carcinoma
	Multicentric oral carcinoma

NEOPLASMS OF MESENCHYMAL TISSUE ORIGIN

Benign neoplasms	Malignant neoplasms
NEOPLASMS OF FIBROUS CONNECTIVE TISSUE	**NEOPLASMS OF TISSUE FIBROUS CONNECTIVE**
Fibroma	Fibrosarcoma
Fibromatosis	Malignant fibrous Histiocytoma
Desmoplastic fibroma	
Pyogenic granuloma	

Fibroepithelial polyp
Giant cell fibroma
Peripheral ossifying fibroma
Central ossifying fibroma
Peripheral giant cell granuloma
Central giant cell granuloma
Benign fibrous histiocytoma
Nodular fascitis
Myxoma

NEOPLASMS OF ADIPOSE TISSUE	NEOPLASMS OF ADIPOSE TISSUE
Lipoma Angiolipoma	Liposarcoma

NEOPLASMS OF VASCULAR TISSUE	NEOPLASMS OF VASCULAR TISSUE
Hemangioma Lymphangioma Juvenile angiofibroma Hereditary hemorrhagic telangiectasia Glomus tumor	Hemangiopericytoma Hemangioendothelioma Angiosarcoma Kimura's disease

NEOPLASMS OF OSSEOUS TISSUE	NEOPLASMS OF OSSEOUS TISSUE
Osteoma Osteomatosis Osteoid osteoma Osteoblastoma Osteoclastoma Torus palatinus Torus mandibularis	Osteosarcoma Parosteal osteosarcoma Ewing's sarcoma

NEOPLASMS OF CARTILAGINOUS TISSUE	NEOPLASMS OF CARTILAGINOUS TISSUE
Chondroma Chondroblastoma Chondromyxoid fibroma	Chondrosarcoma Mesenchymal Chondrosarcoma

NEOPLASMS OF NEURAL TISSUE	NEOPLASMS OF NEURAL TISSUE
Neurolemmoma Neurofibroma Neurofibromatosis Multiple endocrine neoplasia syndrome Melanotic neuroectodermal tumor of infancy Neuroblastoma Ganglioneuroma Traumatic neuroma Plexiform neuroma	Neurosarcoma Olfactory neuroblastoma

NEOPLASMS OF SMOOTH MUSCLE TISSUE	NEOPLASMS OF SMOOTH MUSCLE TISSUE
Leiomyoma Angiomyoma	Leiomyosarcoma Angiomyosarcoma

NEOPLASMS OF STRIATED MUSCLE TISSUE	NEOPLASMS OF STRIATED MUSCLE TISSUE
Rhabdomyoma Granular cell myoblastoma Congenital epulis of newborn	Rhabdomyosarcoma

NEOPLASMS OF LYMPHOID TISSUE	NEOPLASMS OF LYMPHOID TISSUE
No benign neoplasm	Hodgkin's lymphoma Non-Hodgkin's lymphoma Burkitt's lymphoma Mycosis fungoides Leukemias Multiple myeloma Plasmacytoma

NEOPLASMS OF MIXED TISSUE	NEOPLASMS OF MIXED TISSUE
Teratoma	

NEOPLASMS OF SALIVARY GLAND TISSUE	NEOPLASMS OF SALIVARY GLAND TISSUE
See the chapter of salivary gland neoplasm.	

BENIGN NEOPLASMS OF THE EPITHELIAL TISSUE ORIGIN

PAPILLOMA

DEFINITION

Papilloma is a common benign neoplasm of the oral cavity, arising from the epithelial tissue. It is characterized by an exophytic papillary growth with a typical '**cauliflower like**' appearance.

This lesion constitutes about 2 percent of all oral neoplasms and it is believed by many investigators that they are caused by Human papilloma virus (HPV).

HPV virus subtypes 6 and 11 have been detected from neoplastic tissues of papilloma in about 50 percent cases, whereas it is found in normal oral tissues in less than 5 percent cases.

CLINICAL FEATURES

Age: Any age but mostly third, fourth and fifth decade.

Sex: Both sexes are equally affected.

Site: Tongue, lips, buccal mucosa, gingiva, hard and soft plate, etc.

CLINICAL PRESENTATION (FIGS 2.1 AND 2.2)

- Clinically, papilloma appears as a slow growing, exophytic, soft, usually pedunculated, painless, nodular growth often with a typical "cauliflower-like" appearance.
- Papillomas often characteristically have numerous finger-like projections on their surface, which can be either blunt or pointed.
- Because of these projections, the papilloma often appears as an ovoid swelling with a rough, corrugated surface.
- The size of the lesion is usually small and that varies from few millimeters to about one centimeter in diameter.
- The base of the lesion can be either pedunculated or sessile (broad based) but papilloma is mostly a well-circumscribed growth.
- The lesion is mostly white in color and is firm in consistency as the surface is highly keratinized.

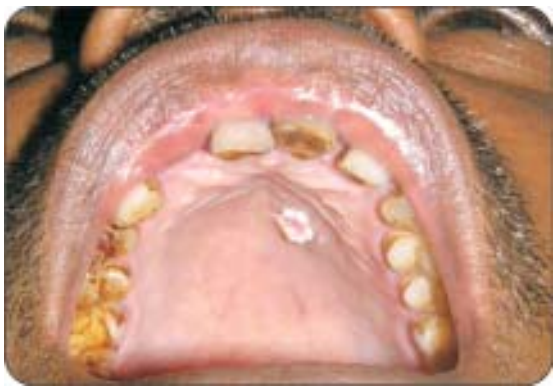

Fig. 2.1: Papilloma

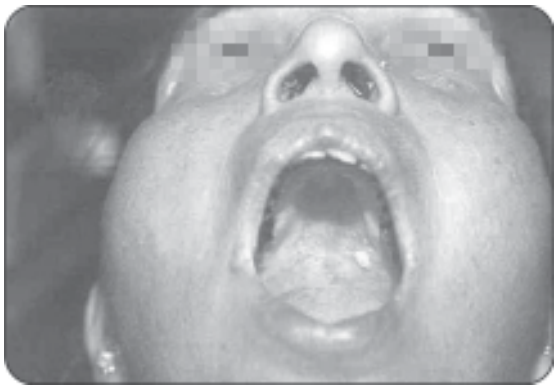

Fig. 2.2: Papilloma of the palate

- Sometimes superficial ulceration and secondary infection may occur especially in those lesions in the oral cavity, which are often subjected to trauma.
- A papilloma with non-keratinized surface may also occur and in such cases it will appear pinkish or greyish in color and moreover, this type of lesion is usually softer in consistency.
- On rare occasions, papillomas may grow in an inwardly direction (inverted type) instead of growing in the usual exophytic manner. Such lesions are mostly seen in the lateral nasal wall, paranasal sinuses and in the maxillary antrum, etc. Moreover, they have great tendency for local destruction and malignant transformation.
- Multiple papillomas may sometimes coalesce together and form a large lesion in the oral cavity and the condition is commonly known as 'papillomatosis' (Figs 2.3 and 2.5).
- Papillomatosis of oral mucosa may sometimes occur in association with skin disorders e.g. Focal dermal hypoplasia syndrome, Nevus unius lateris, Cowden syndrome and Acanthosis nigricans, etc.
- "Nevus unius lateris" is a dermal condition in which papillomatous growths can be seen in the trunk and limbs, with a unilateral distribution. Oral papillomatous lesions can occur in this disease and involves the lips, tongue and the palate.

HISTOPATHOLOGICAL FEATURES

Microscopically, papillomas present the following features (Fig. 2.4):

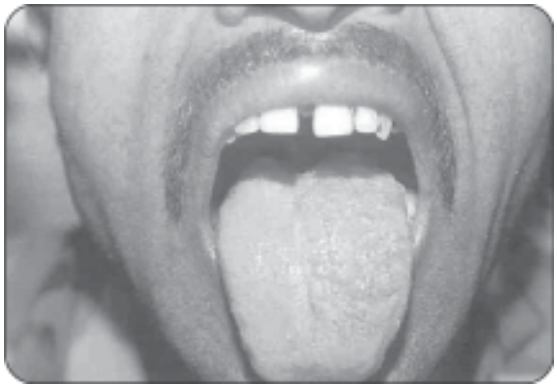

Fig. 2.3: Papillomatosis of the tongue

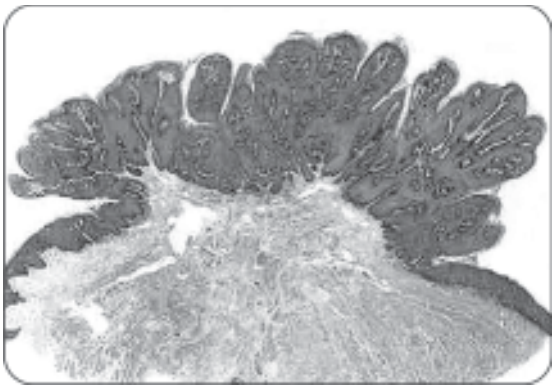

Fig. 2.4: Photomicrograph of papilloma

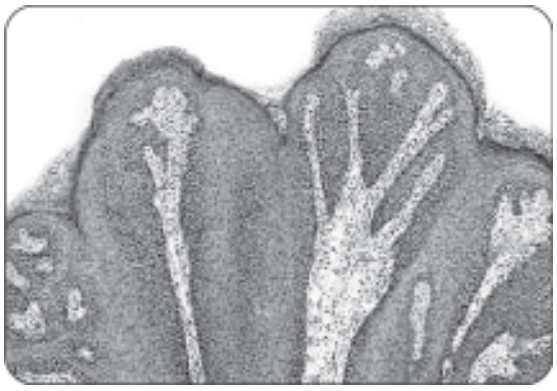

Fig. 2.5: Photomicrograph of papillomatosis

- Proliferating keratinized stratified squamous epithelium in the form of **multiple fingers-like projections**.
- Every single finger-like projection has a fibrovascular connective tissue core in the center, which contains few inflammatory cells.
- The covering squamous epithelium shows hyperkeratosis and acanthosis. Thickening of the keratin is seen in lesions which are clinically whiter.
- Although most of the papillary projections are long and finger-like, there can be some projections, which are short, round and blunt.
- In the spinus cell layer 'koilocytes' are sometimes seen, these are virus-altered epithelial clear cells with small dark (pyknotic) nuclei.
- In some lesions, slightly increased mitotic activity can be seen in the basal layer of the epithelium, which results in mild epithelial hyperplasia.
- There can be little cellular atypia in some papillomas, however, the dysplastic changes in the epithelium is rarely found.
- Papilloma is not a premalignant lesion and malignant transformation in pre-existing oral papillomas has not been documented.

DIFFERENTIAL DIAGNOSIS

- Verruca vulgaris
- Focal dermal hyperplasia
- Verruciform xanthoma
- Verrucous carcinoma
- Condyloma acuminatum.

TREATMENT

Conservative surgical excision of the lesion including the base is the common treatment. Recurrence is rare.

KERATOACANTHOMA

DEFINITION

Keratoacanthoma is a benign endophytic epithelial tissue neoplasm with profound clinical and histological **resemblance to well-differentiated squamous cell carcinoma**. It commonly occurs in the sun-exposed skin of the face and it usually appears as a circumscribed keratin filled crater.

ORIGIN

Keratoacanthoma of the skin surfaces probably develops from the hair follicles above the sebaceous glands.

On the mucosal surfaces these lesions are extremely rare but if they occur at all, they probably develop from the superficial epithelium of the sebaceous ducts.

CAUSES

- Chronic sun exposure
- Human papilloma virus infection
- Immunosuppression
- Heredity

CLINICAL FEATURES

Age: Middle aged adults are frequently affected between the age group of 50 to 70 years.

Sex: Male to female ratio in this tumor is about 2:1.

Site: Keratoacanthoma chiefly develops over the sun-exposed skin surface of the lips (both upper and lower lips) near the outer edge of vermilion border. Besides this, the lesion can also occur on the cheeks, nose, eyelids and ear. Intraoral lesions of keratoacanthoma are rare, although few have been reported in the palate and gingiva.

PRESENTATION (FIG. 2.6)

- Keratoacanthoma initially begins as a small, red macule that soon turns into a well-circumscribed, elevated and umbilicated, **crater-like lesion with a central depression**.
- The lesion is firm, painless and sessile in nature; and can be single or multiple in number.
- The fully developed lesion of keratoacanthoma clinically presents a well-circumscribed, elevated nodule, which has a sharply delineated, rolled margin and a central keratotic core.
- Clinically, the outer surface of the lesion shows normal skin color or slight erythema, while the central keratin plug appears yellow, brown or black with an irregular crusted appearance.
- The disease is often painful and sometimes it may have an associated lymphadenopathy.

STAGES OF DEVELOPMENT OF KERATOACANTHOMA

- The lesion initiates as a small lump or a bud like growth on the sun-exposed skin surface of the face, it grows rapidly and achieves the maximum size (1 to 2 cm in diameter) over a period of about 4 to 8 weeks.
- After the initial growth, the disease remains static for an indefinite period of upto 4 to 8 weeks and then it starts to regress spontaneously.
- Within the next 6 to 12 months time, the lesion regresses completely leaving only a small depressed scar.

HISTOPATHOLOGY

- Keratoacanthoma clinically and histologically appears very similar to well-differentiated squamous cell carcinoma and because of this, it is often known as **"self-healing" cancer (Fig. 2.7).**
- The cells appear mature and often there is individual cell keratinization and even keratin pearl formation in the tumor.
- The lesion consists of a thick hyperkeratinized covering epithelium with a central zone of keratin or parakeratin plugging.
- Pseudoepitheliomatous hyperplasia may be observed in some cases, the spinous cell layer is thick and rate ridge formation is often seen.
- Pathognomonic nonmalignant feature of this neoplasm can be indentified **at the margin, where the lesion shows a crater-like area, plugged with keratin and is surrounded by hyperplastic normal epithelium.**
- This abrupt transition of the normal surrounding epithelium at the margin of the crater-like area is an important diagnostic clue for keratoacanthoma.

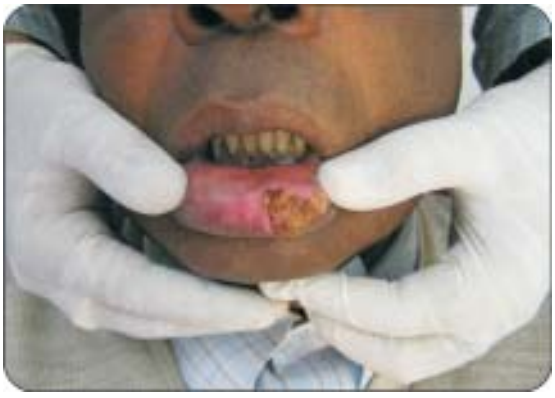

Fig. 2.6: Keratoacanthoma

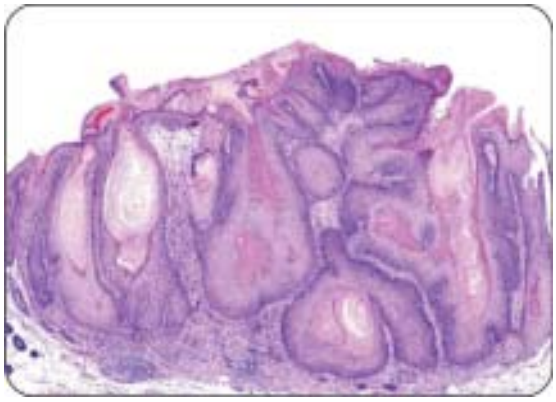

Fig. 2.7: Photomicrograph of keratoachanthoma

- In keratoacanthoma, the surrounding connective tissue reveals a moderate to marked infiltration by chronic inflammatory cells.
- Although, keratoacanthomas are benign and self limiting conditions, serial sectioning is always required of the available tissue sample for confirmation of the diagnosis.
- Moreover, careful long-term follow-up evaluations are necessary since the neoplasm is often confused with squamous cell carcinoma.

The distinction between keratoacanthoma and squamous cell carcinoma

- The epithelium in this neoplasm exhibits a pseudocarcinomatous rather than a true carcinomatous growth pattern.
- Dyskeratosis is always absent in keratoacanthoma.
- The epithelium is composed of well-differentiated spinous cells with abundant cytoplasm, minimal nuclear pleomorphism, infrequent mitotic figures and no abnormal mitosis.

DIFFERENTIAL DIAGNOSIS

- Basal cell carcinoma
- Squamous cell carcinoma.

TREATMENT

Surgical excision is the treatment of choice for keratoacanthoma, usually before the lesion reaches its maximum size of 2 to 2.5 cm diameter. Waiting for spontaneous regression of the lesion is not advisable for the following reasons:

- Confusion with squamous cell carcinoma.
- The scar developing after spontaneous regression is depressed and cosmetically unacceptable.
- Surgical treatment always provides good tissue specimen for confirmation of the diagnosis.

PIGMENTED CELLULAR NEVUS

DEFINITION OF NEVUS

A nevus can be defined as **a congenital, developmental, tumor-like malformation** of the skin or mucous membrane.

The term "nevus" has got several meanings; in Latin terms nevus means birth marks, however, the common lay term used for nevus is **"mole".**

Nevus is composed of **"nevus cells"** which are **neuroectodermal in origin**, these cells, except for their tendency to form cell nests and their less prominent dendritic processes, are nothing but melanocytes or their precursors. After their formation, nevus cells migrate through the peripheral nerves and finally reach to the basal layer of the skin or mucous membrane. Nevi are usually present at birth or they can be seen any time after birth.

The function of nevus cells is to produce melanin, this pigment, after being synthesized within the nevus cells is passed on to the adjacent keratinocytes of the oral mucous membrane. Although nevus cells produce melanin pigments, not all these cells are always equally pigmented. The amount of pigmentation in a nevus does not depend on the number of pigment producing nevus cells present in it, instead, it depends solely upon the amount of pigment produced by its individual constituent cell.

Different types of nevi

- Intradermal (intramucosal) nevus.
- Junctional nevus.
- Compound nevus.
- Blue nevus.

INTRADERMAL (INTRAMUCOSAL) NEVUS

The term intradermal nevus and intramucosal nevus are synonymous, the former occurs on the skin surfaces while the later occurs over the mucous membrane.

CLINICAL FEATURES

- Intradermal nevus is a very common lesion of the skin and it usually occurs in children.
- This lesion is often referred to as common "mole".
- Intradermal nevus clinically appears as a raised or flat area on the skin surface, with a typical tan or dark brown color.
- These lesions often contain more hair follicles then the normal skin of the surrounding area.

- Intramucosal nevi in the oral cavity are relatively uncommon lesions as compared to their cutaneous counterparts.
- The mucosal lesions clinically appear as asymptomatic, slightly elevated papules or flat macules with a pigmented surface.
- The color of these nevi varies from brown to black.
- Intraoral nevi are commonly seen over the hard palate or the gingiva.
- The intraoral lesions are often slow growing and their size is usually less than 1 cm in diameter.

HISTOPATHOLOGY

- Microscopically intramucosal nevus reveals **clusters or nests of nevus cells which are confined within the connective tissue (Fig. 2.8).**
- The cells may appear as **epitheloid cells or lymphocyte like cells**; however few cells may be even spindle-shaped.
- Multiple multinucleated giant cells may be found in some cases.
- Normally, there is no evidence of increased mitotic activity in these cells.
- Intramucosal nevus often characteristically presents a narrow zone of connective tissue devoid of nevus cells, which separates the zone of nevus cells from the overlying epithelium.
- The amount of melanin produced by these nevus cells varies; some cells are heavily pigmented whereas other cells are almost nonpigmented.

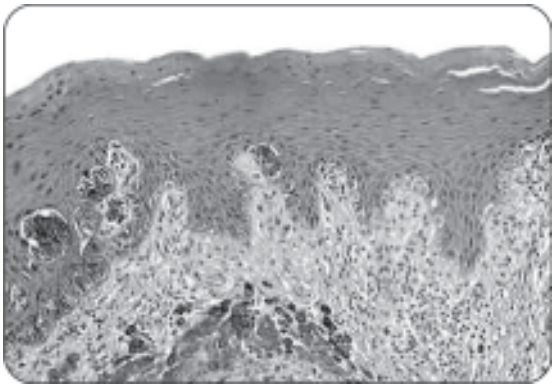

Fig. 2.8: Photomicrograph of intradermal nevus

TREATMENT

Intramucosal nevi usually do not require any treatment. However, when these lesions are subjected to persistent trauma during mastication, surgical excision should be preferred.

Once excised, they usually do not recur.

JUNCTIONAL NEVUS

CLINICAL FEATURES

- Junctional nevus is usually a less common variety as compared to the intradermal nevus.
- It appears as an asymptomatic, brown or black macule, affecting both skin as well as the oral mucosal surfaces.
- Intraorally these lesions are commonly seen over the hard palate and gingiva.

HISTOPATHOLOGY

- Histologically, junctional nevus reveals focal areas of **proliferating nevus cells** or in some cases clusters of cells **at the basement membrane zone** of the epithelium.
- The cluster of nevus cells is often specifically present at the apex of the epithelial rete-pegs.
- Nevus cells are not seen in the adjacent connective tissue stroma.
- Occasionally, junctional nevus may undergo malignant transformation and gives rise to the development of malignant melanoma.

TREATMENT

Junctional nevus should be excised surgically. Post-surgical recurrence is uncommon.

COMPOUND NEVUS

The compound nevus characteristically presents the combined features of intradermal nevus and the junctional nevus.

CLINICAL FEATURES

- This lesion occurs far more commonly in skin as compared to the oral mucosa.
- Intraorally they appear as pigmented papules or macules over the hard palate or the gingiva.

HISTOPATHOLOGY

Microscopically, compound nevus reveals the presence of **nevus cells, which are distributed both in the basal layer of the epithelium as well as in the adjacent superficial connective tissue**.

TREATMENT

Surgical excision is the treatment of choice for compound nevus.

BLUE NEVUS

Blue nevus is a relatively common pigmented lesion of the oral cavity.

CLINICAL FEATURES

- Clinically, it often appears either as a dome-shaped, **dark blue papule** or as a flat pigmented macule over the skin or the oral mucous membrane.
- Intraoral blue nevi are commonly seen on the mucosal surfaces of the hard palate.

HISTOPATHOLOGY

- The melanin producing cells of the blue nevus often morphologically differ from those of the other nevi.
- Instead of being round or epitheloid in shape, the cells of blue nevus are usually **elongated, bipolar and spindle-shaped.**
- Sometimes, fusiform dendritic cells can also be present in these lesions.
- The spindle-shaped cells are mostly oriented parallel to the overlying epithelium and are not arranged in clusters.
- Few pigmented macrophages may be present among these dendritic nevus cells and they are known as 'melanophages'.

TREATMENT

Blue nevus often clinically resembles a melanoma and therefore surgical excision of the lesion with subsequent histopathological evaluation is the common practice. However, it has been observed that blue nevi do not have much tendency to undergo malignant transformation.

MALIGNANT NEOPLASMS OF THE EPITHELIAL TISSUE ORIGIN

SQUAMOUS CELL CARCINOMA

DEFINITION

Squamous cell carcinoma is the **most common malignant epithelial tissue neoplasm of the oral cavity**, which is derived from the stratified squamous epithelium. Since oral squamous cell carcinomas constitute bulk of the oral malignancies (above 90 percent) it is thus commonly referred to as oral cancer (although there are several other malignancies of the oral cavity besides squamous cell carcinoma).

EPIDEMIOLOGY

- Squamous cell carcinoma is also termed as epidermoid carcinoma and it is by far the most common malignant neoplasm of the oral cavity, representing about 90 percent of all oral cancers. For this reason, oral squamous cell carcinomas are often designated as "oral cancers".
- The incidence of oral squamous cell carcinoma varies in different countries and also in different population groups.
- On an average, oral squamous cell carcinomas represent about 3 percent of all cancers in males and about 2 percent of all cancers in females.
- This disease is responsible for 2 percent of all annual deaths in males and 1 percent of all annual deaths in females.
- The incidence of oral cancer varies in different countries depending upon the frequency of tobacco usage and other related habits throughout the world.
- The general trend indicates that the incidence of oral squamous cell carcinoma increases alarmingly in the societies, where extensive tobacco use begins in the early life and is continued for a longer period.
- The incidence of oral squamous cell carcinoma increases with age and most of the cases occur usually after the age of 40 years.
- Although, oral squamous cell carcinomas can arise from virtually any intraoral site, but they develop more frequently from the lower lip, lateral borders of the tongue, buccal mucosa and floor of the mouth, etc.

- In the ICD (International Classification of Diseases-WHO-1977), oral cancer is described in a group comprising of different numbers depending upon the site of involvement of the disease.
- According to this ICD classification, oral cancers are numerically categorized in the following manner:
  - lip cancer–ICD No. 140,
  - tongue cancer–ICD No. 141,
  - cancer of the gingiva and alveolar mucosa–ICD No. 143,
  - Cancer of the floor of the mouth–ICD No. 144
  - Cancer of other parts of the mouth-ICD No. 145.
- The annual age-adjusted incidence rates of oral cancer per 100,000 (one lakh) population varies from continents to continents, from countries to countries and also from places to places within the same country.
- In Europe, it varies from 2.0, in UK to 9.4, in France, in USA it varies from 4.4, in Columbia to 13.4 in Canada.
- In Asia, the annual incidence rates of oral cancer per one lakh population varies from 1.6 in Japan to as high as 13.5 in India.
- Australia and New Zealand also exhibits similar trends and here the incidence varies from 2.6 in New Zealand to 7.5 in South Australia.
- In Sri Lanka, the oral cancers constitute about 40 percent of all malignancies.
- In the Manipuri districts in India, the annual incidence rate of oral cancer is about 21.4 per one lakh population (Wahi 1968).
- Survey among textile mill workers in Ahmedabad (Gujarat), India, indicates that the average incidence rate of oral cancer among individuals above 35 years of age is 25 per one lakh population (Malaowalla et al).
- In a house to house 10 year follow-up study, Gupta et al (1980) have reported the annual age-adjusted incidence rate of oral cancer in Ernakulam and Srikakulam districts as 16 and 21 respectively per one lakh population.
- In UK, oral cancers account for 1 percent of all malignancies, in USA, they account for about 2 to 4 percent, however in India they account for about 30 to 40 percent of all malignant tumors and in some cases the figure may be as high as about 50 percent.
- Recent trends besides few exceptions, indicate that the incidence and mortality rates of oral cancer are declining and it can be due to the reduced exposure to various etiological agents.

ETIOLOGY OF ORAL CANCER

A large number of etiological factors have been implicated in the development of oral cancer, specifically the oral squamous cell carcinomas, these include the following:

- ***Tobacco smoking***
  - Cigarettes
  - Beedes
  - Pipes
  - Cigars
  - Reverse smoking.
- ***Use of smokeless tobacco***
  - Snuff dipping
  - Tobacco sachets (Gutkha)
  - Tobacco chewing
  - Tobacco as a toothpaste.
- ***Consumption of alcohol***
  - Drinking spirits
  - Drinking wines
  - Drinking beers
  - Tobacco and alcohol synergism (smoking and chewing tobacco with drinking of alcohol).
- ***Diet and nutrition***
  - Vitamin A, B-complex and C deficiency.
  - Nutritional deficiency with alcoholism.
- ***Dental factors***
  - Chronic irritation from broken teeth.
  - Ill-fitting or broken prosthesis.
- ***Radiations***
  - Actinic radiation, X-ray radiation
- ***Viral infections***
  - Herpes simplex virus (HSV)
  - Human papilloma virus (HPV)
  - Human immunodeficiency virus (HIV)
  - Epstein-Barr virus (EBV)
- ***Immunosuppression***
  - AIDS
  - Organ transplants
- ***Chronic infections***
  - Candidiasis
  - Syphilis

- *Occupational hazards*
  - Woolen textile workers
- *Genetic factors*
  - Oncogenes
  - Tumor-suppressor genes
- *Pre-existing oral diseases*
  - Lichen planus
  - Plummer-Vinson syndrome
  - Oral submucous fibrosis
  - Leukoplakia
  - Discoid lupus erythematosus.

ROLE OF TOBACCO IN ORAL CANCER

- One person dies in every 10 seconds in the world due to the use of tobacco.
- Epidemiological and experimental studies categorically indicate that tobacco plays an important role in the development oral cancer.
- Tobacco is used in various smoking forms like-cigarettes, cigars, pipes and beedes, etc.
- It can also be used in smokeless forms like pan-beetel quid, snuff, tobacco sachets (khaini), zarda and other popular forms.

Mechanism of Action of Tobacco in Carcinogenesis

There are about 300 carcinogens found in tobacco smoke, which include: aromatic hydrocarbon benzopyrine and tobacco specific nitrosamines (TsNs), N-nitrosonornicotine (NNN), N-nitro-sopyrrolidine (NPYR), N-nitrosodimetheylamine (NDMA) etc. In our body these carcinogenic agents produce DNA adduct (it is a piece of DNA covalently bonded to a cancer causing chemical) called O-6-methylguanine, which interferes with the DNA replication and thereby cause mutation. Mutations open the floodgate of molecular chain of events leading eventually to carcinogenic change in cells.

There are several supportive evidences, which can establish the relationship between the use of tobacco and the occurrence of oral cancer:

- Studies indicate that the incidence of oral cancer is four times greater among pipe or cigar smokers as compared to the non- smokers. The common tobacco related diseases include (a) carcinoma of the lung, bladder, pancreas, oral cavity, esophagus, pharynx and larynx, etc. (b) chronic obstructive pulmonary disease and (c) coronary arterial diseases.
- Pipe and cigarette smoking have been linked with carcinoma of the lips for many years.
- Different studies also indicate that persons those who are smoking forty or more cigarettes per day have a significantly increased risk of oral cancer (ranging from about 10 to 20 times) more than that of the non-smokers.
- The type of tobacco (variation in tar, nicotine and nitrosamine content), its curing technique used by the manufacturer, species of tobacco and methods used by the patient for smoking can influence the relative risk of oral cancer to a large extent. For example, high incidence of oral cancer in India could be partly due to the widespread smoking of beedes (country made cigarette made up of crude tobacco).
- The habit of reverse smoking (if the burning end of the cigarette is kept inside the mouth while smoking) definitely increases the risk of oral cancer especially among women.
- Reports indicate that the relative risk of oral cancer for reverse smokers is about forty times higher than those who do not smoke.
- Long-term follow-up studies also indicate that about one third of the patients who have been successfully treated for oral or oropharyngeal cancers will develop new (second) cancers if they continue smoking after treatment. On the other hand, smokers who stop smoking after getting their fast cancer, successfully treated will carry only a small risk of developing another lesion.
- Research indicates that excessive use of tobacco, heavy consumption of alcohol and poor diet together cause increased incidence of oral cancer.

Smokeless Tobacco-Betel Quid (Pan) and other Chewing Habits

- Chewing of pan is a popular habit all over the world and it is practiced by over 200 million people in different countries.

- This habit is particularly more common in Southeast Asia and India.
- Pan is made up of several ingredients like betel nut, lime, tobacco, catechu and other spices, which are wrapped within a betel leaf.
- The constituents vary according to the custom, individual taste and economic status, etc.
- The carcinogenic effect of pan chewing could be due to the presence of tobacco as one of its main ingredients.
- Moreover, the possible interactions between different ingredients of pan may results in the formation of some chemicals which might be harmful, for example, shaked lime used in pan may hydrolyze one of the alkaloids of the betal nut called arecoline to produce arecoidene, the later is experimentally proved to be carcinogenic.
- The habit of placing a mixture of tobacco and lime (commonly known as khaini) in oral vestibule is a popular practice in India and Pakistan, which contributes to the occurrence of large number of oral and oropharyngeal cancer cases.
- A large number of people in these countries, particularly the younger generation, are also adapted to the habit of chewing tobacco sachets, which acts as a strong carcinogenic agent. As a result of this, people inclined to such habits develop oral cancer very often.
- Tobacco users can develop oral cancers in their mouth either as direct lesions (de-novo lesions) or such habits may result in the development of precancerous lesions in their mouth like oral submucous fibrosis or leukoplakia, etc. which may turn into malignancy in future, if the habits are continued for long.

ALCOHOL

- Several epidemiological studies have indicated about alcohol as a possible risk factor for oral cancer.
- Both the quantity and quality of alcohol consumed and duration of the habit are crucial factors in this regard. People consuming more amount of alcohol per day, for more number of years will have an increased risk for developing oral cancer than others.
- Inferior quality of the alcohol also increases the risk of oral cancer since these liquors may contain some carcinogenic byproducts.
- Although alcohol has some important role in carcinogenesis, many studies have shown a marked increase in the relative risk of oral cancer when smoking and drinking are practiced together, suggesting a synergistic effect.

Mechanism of Action of Alcohol in Carcinogenesis

Alcohol acts as a solvent and facilitates penetration of other carcinogens (especially nitrosonornicotine) across the oral mucous membrane.

Alcohol can cause atrophic change in the oral mucosa, which can therefore make the tissue more vulnerable to the effect of other carcinogenic agents. This often leads to mutagenic change in the epithelial cells. Moreover, the dehydrating effect of alcohol on oral mucosa may further increase the risk of tobacco related damage.

- Long-term alcoholic habit often produces cirhossis of liver. This disease may be associated with the development of oral cancers in many patients, simply because the damaged liver can not detoxify the carcinogenic chemicals in the blood.

DIET AND NUTRITION

- Iron deficiency anemia often causes dysphagia, glossitis and atrophy of the oral mucosa; these changes may increase the risk of malignant transformation of oral mucosa in presence of other carcinogenic agents.
- Deficiencies of certain dietary factors like vitamin A, D, C and E, etc. may cause atrophy of the oral epithelium and thereby make the tissue more vulnerable to various carcinogenic agents.
- The beneficial effect of dietary factor is often badly hampered by the use of alcohol.
- Fresh fruits and vegetables (rich in carotene) provide increased protection against cancer of the mouth, pharynx and larynx, etc.
- Deficiency of certain trace elements like zinc, manganese, magnesium and molybdenum, etc. disturbs the structural integrity of the oral epithelial tissue, as a result of which, the epithelium becomes more vulnerable to the free

radical injury. The later may cause development of oral cancer.

DENTAL FACTORS

- Ill fitting dentures, poor oral hygiene, faulty restorations, sharp or broken teeth, etc cause persistent irritation and trauma to the oral mucosa and therefore may act as possible predisposing factors in this development of oral cancer.
- Moreover, carcinogenic potential of tobacco and/or alcohol may be increased significantly in the presence of these orodental factors.
- Chronic oral sepsis is another important contributing factor in the development of oral cancer.

ULTRAVIOLET RADIATION

- Ultraviolet radiation is often believed to be responsible for the development of carcinoma of the lip, in fair-skinned people, especially those who are engaged in outdoor activities or professions, e.g. farming, forestry, postal delivery, outdoor games and fishing, etc.
- The ultraviolet radiation penetrates their exposed part of the body easily and thus makes them more vulnerable to cancer.
- Lip cancer caused by ultraviolet radiation is less common among the black or the brown skinned people, since heavy melanin pigmentation in their skin acts as a protective barrier against the ultraviolet radiation.
- The lesion which develops initially is called 'solar keratosis' near the vermilion border of the lip and it is a premalignant lesion of long duration. The lip lesion of solar keratosis may gradually turn into squamous cell carcinoma with time.

IONIZING RADIATION

Squamous cell carcinoma may develop in those areas of the oral cavity, which were exposed to long-term radiation therapy in the past.

VIRUSES

- Laboratory investigations have shown that certain human cancers may be produced by the oncogenic viruses. For example, the Human papilloma virus (HPV) as well as the Human immunodeficiency virus (HIV) increase the risk of oral cancer and the Herpes simplex virus (HSV) type- II increases the risk of cervical cancer among females and oral cancer in males.
- It is often believed that the oncogenic viruses can initiate oncogenesis by altering the DNA and the chromosomal structure of the infected cells and also by inducing some proliferative changes in the host cells.
- The common viruses which might be having some oncogenic potential are as follows:

Human Papilloma Virus (HPV)

These viruses probably play some important role in the development of oral premalignant lesions and oral squamous cell carcinomas.

Herpes Simplex Virus (HSV) and Epstein-Barr Virus (EBV)

The exact role of these viruses in the development of oral squamous cell carcinomas is not well understood and they are probably incidental passenger viruses.

Experimental animal studies indicate that development of oral cancers may result from interaction between the oncogenic viruses and the effect of tobacco or smoke, etc.

Human Immunodeficiency Virus (HIV)

Oral squamous cell carcinomas may develop in patients having HIV infection or AIDS, however, the exact role of these viruses in the pathogenesis of oral cancer is not clearly known.

IMMUNOSUPPRESSION

- Immunosuppression may be associated with an increased risk of oral cancer and it can be seen in patients with HIV infection, who often develop Kaposis sarcoma and oral squamous cell carcinoma.
- The role of immunosuppression in the development of oral carcinoma can further be emphasized by the fact that the HIV infected patients often develop oral cancers at an early age (as compared to the normal age of occurrence for these tumors) and moreover, these tumors develop without the presence of any tobacco or alcohol related habits.

- Increased risk of oral cancers has been reported in patients receiving immunosuppressive drugs following renal or other organ transplant treatments.

CHRONIC ORAL INFECTIONS

Candidiasis

- Chronic oral candidiasis may occur in association with leukoplakia, the later disease often undergoes malignant transformation.
- It is believed that candidial infections probably act as cofactors in the transformation of oral premalignant lesions into oral squamous cell carcinomas.
- Chronic hyperplastic candidiasis often appears as a leukoplakic lesion and it may have some premalignant or malignant potential.

Syphilis

Like tobacco and alcohol, syphilis has also been traditionally associated with oral cancers.

- Tertiary syphilis has often been linked with oral squamous cell carcinomas, particularly the lip or tongue lesions.
- Experimental studies indicate that long standing syphilitic infections may cause atrophy of the oral epithelium and such atrophic changes may render the epithelial tissue more susceptible to the carcinogenic effects of tobacco, alcohol and other agents.
- Definite correlations between syphilitic glossitis and oral cancer has been suspected in the past, however occurence of such mucosal lesions secondary to syphilis, and their coexistence with oral cancers have become rare in recent times.

ATMOSPHERIC POLLUTION

Vehicular and industrial exhausts contain excessive amount of harmful chemicals, e.g. sulphur, nitrogen, carbon monoxide, carbon dioxide and several hydrocarbons; these agents increase the risk of oral cancer among people living in cities or in industrial areas.

OCCUPATIONAL HAZARDS

- People in some occupations may have more risks for developing oral cancers as compared to others. Exposure to hazardous chemicals such as nitrosamines and polycyclic aromatic hydrocarbons etc make the people susceptible to oral cancers.
- It has often been reported that textile workers those who are regularly exposed to particles created by the initial carding of raw cotton wool are especially at risk for this disease.
- Oral cancer incidence is particularly high among people those who are working in rubber, asbestos, woods or chemical industries; and also those who are regularly exposed to gas and soot.
- Apart from this, heavy metal factory workers and people in the printing trade also have an increased tendency for developing oral cancers as compared to others.

GENETIC FACTOR (ONCOGENES AND TUMOR SUPPRESSOR GENES)

Oral cancers may occur due to the uncontrolled neoplastic proliferation of cells as a result of some abnormal genetic activity.

- It is a multi step event involving multiple sequential mutations to the genes which regulate the system of cell growth and cell multiplication.
- Since the basal cells of the oral epithelium normally have a higher rate of mitotic activity, any factor that causes disturbance in the quality and quantity of the cell regulating proteins can induce a neoplastic growth. .
- Some of these proteins (kinases) interact with the proteins that coordinate the process of cell replication (cyclins). Others are regulatory proteins, which influence the events associated with mitosis. These proteins are produced under the directions of some specific genes on specific chromosomes.
- The specific gene loci responsible for producing proteins that can upset the normal replication cycle of cells are known as "oncogenes".
- When oncogenes are stimulated to over-produce proteins that stimulate the process of mitosis, the result is neoplastic growth. Alteration in the oncogene activity may be associated with environmental factors such as tobacco habits, alcohol, nutritional deficiency and chronic infections, etc.

TUMOR SUPPRESSOR GENES

These are suppressor gene loci responsible for producing proteins, which can stop or control unnecessary cell cycling.

Neoplastic growths can occur if there is deactivation of these tumor suppressor genes.

PRE-EXISTING ORAL LESIONS

Beside the chronic infective lesions such as syphilis and candidiasis, etc. there can be few other oral lesions, from which oral squamous cell carcinomas may sometimes develop and these lesions include the following:

- Erythroplakia
- Oral submucous fibrous
- Oral lichen planus
- Oral leukoplakia
- Plummer-Vinsons syndrome
- Epidermolysis bullosa
- Discoid lupus erythematosus
- Xenoderma pigmentosum, etc.

CLINICAL FEATURES OF ORAL SQUAMOUS CELL CARCINOMA

Age: Carcinomas mostly occur in the older age while sarcomas occur in the younger age. Fourth, fifth, sixth and seventh decade of life is the common age range for oral squamous cell carcinoma.

Sex: The disease affects male people more after than the females and it happens because male people are more frequently exposed to the various deleterious oral habits. Among the oral lesions, lip carcinomas are commonly seen in females. However, recent trends indicate that there is an average increase in the incidence of oral squamous cell carcinomas among females because ladies are becoming more and more attracted towards smoking, drinking alcohol and other related habits.

Sites: The incidence of oral squamous cell carcinomas in various anatomic locations is significantly different, some oral sites are relatively immune to the disease while other sites are particularly more prone to it. Among all oral anatomic areas, lower lip is the most common site, the second most common site is the lateral borders of the tongue. Among all intraoral sites, dorsum of the tongue and hard palate are the least common sites for oral squamous cell carcinoma.

Relative incidence of squamous cell carcinoma in various oral sites

Site	*Relative incidence*
Lower lip	35
Lateral/Ventral tongue	25
Floor of the mouth	20
Soft palate (near the tonsillar pillars)	15
Gingiva/Alveolar ridge	4
Buccal mucosa (above occlusal line)	1

Taking into account of the above incidence rates of cancer in different intraoral sites, **a horse-shoe shaped imaginary zone** can be drowned, which will **indicate the more prone oral sites** for this disease. The zone includes the following areas— ***anterior floor of the mouth, lateral borders of the tongue, tonsillar pillars and lateral part of soft palate.***

CLINICAL PRESENTATION OF ORAL SQUAMOUS CELL CARCINOMA

Oral squamous cell carcinoma has a number of different clinical features depending upon its location and its duration of presence in the mouth (Figs 2.9 to 2.13)).

- The most common early appearance of oral squamous cell carcinoma could be extensive oral leukoplakia and erythroplakia.
- The initial lesion may also present an asymptomatic, white or red, varigated patch or a nodule or fissure over the oral mucosa.

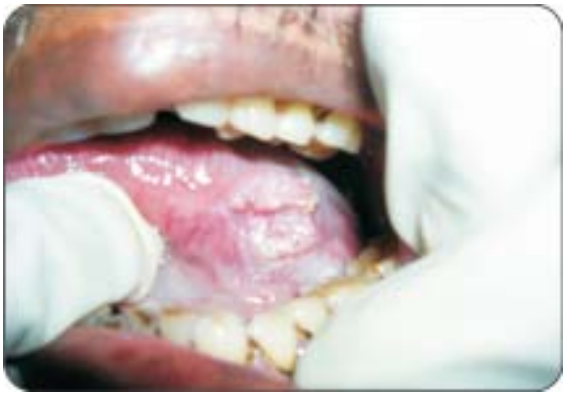

Fig. 2.9: Squamous cell carcinoma of tongue

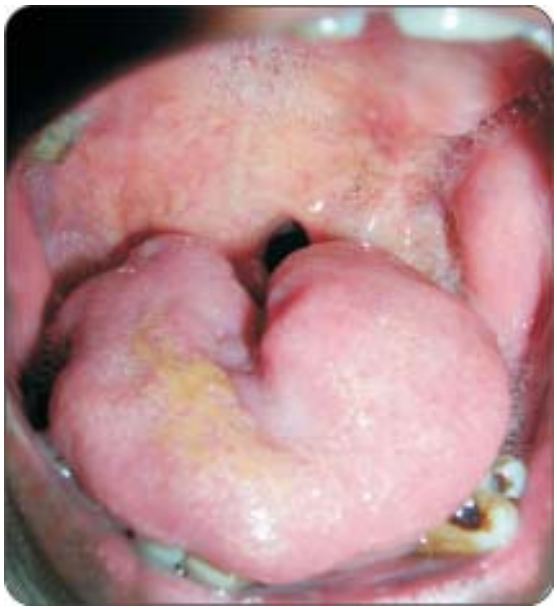

Fig. 2.10: Oropharyngeal carcinoma

Fig. 2.11: Squamous cell carcinoma-I

Fig. 2.12: Squamous cell carcinoma-II

- Initially the condition is usually painless and quite innocuous looking however an early biopsy often reveals the real nature of this disease.

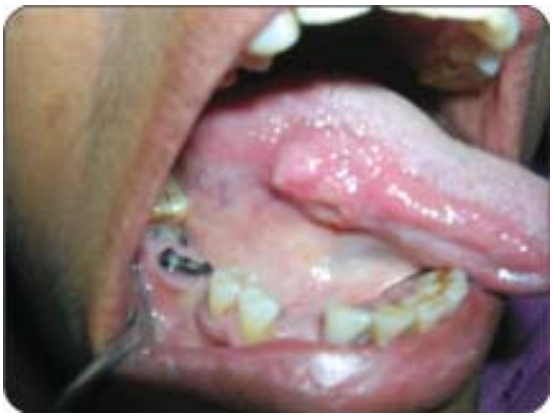

Fig. 2.13: Squamous cell carcinoma-III

- More advanced lesions present either as a **fast enlarging, exophytic or invasive ulcer** or sometimes as a **large tumor mass or a verrucous growth**.
- The ulcerated lesion often shows **persistent induration** around the periphery with an **elevated and everted margin**.
- In many cases, there is presence of superadded candidial infections.
- The induration is caused by infiltration of the tumor cells deep into the surrounding connective tissue. Moreover, the elevated and everted margin of the lesion occurs due to an increased rate of growth of the epithelial tissue (because of the extensive mitosis of the tumor cells) as compared to the surrounding normal epithelium.
- The lesion can be **painful** either due to **secondary infection** or due to **involvement of the peripheral nerves** by the tumor cells. The lesion can also bleed easily.
- Floor of the mouth lesions often cause **fixation of the tongue** to the underlying structures with difficulty in **speech** and **inability to open the mouth (trismus).**
- When malignant tumor cells **invade into the alveolar bone** of either maxilla or mandible, they usually cause **mobility or exfoliation** of regional teeth.
- Involvement of inferior alveolar nerve often causes **paresthesia** of the lower teeth and the lower lip.
- Regional lymph nodes are often **enlarged, tendered and fixed**; some of these nodes can be **stony hard** in consistency.

- In oral squamous cell carcinoma, enlarged lymph nodes do not always indicate metastatic spread of the tumor cells, since this enlargement of lymph nodes may also represent only nonspecific reactive hyperplasias.
- Extensive maxillary lesions may often **invade into the maxillary antrum**, which often results in nasal bleeding and pressure sensation in the eyeball.
- Untreated lesions of squamous cell carcinoma may sometimes destroy the oral tissues and extend into the skin on the outer surface of the face to produce a nodular or lobulated growth on the facial skin, which appears as an **extraoral discharging sinus**.
- Involvement of facial skin is significant in squamous cell carcinoma since it indicates a very poor prognosis of the tumor.
- Carcinoma of the floor of the mouth and the tongue are sometimes asymptomatic at least in the early stage of the disease.
- Long standing oral squamous cell carcinomas also produce severe facial disfigurement, difficulty in taking food and difficulty in phonation, etc.
- **Pathological fracture** of the jaw bone may sometimes occur in untreated cases due to extensive destruction of the bone by the tumor.
- Untreated patients mostly die of **cachexia, hemorrhage, secondary infections and aspiration bronchopneumonia, etc.**

Special Aspects of Oral Cancer

Multiple cancer: Multiple cancer refers to the condition in which a patient develops **cancer in multiple organs of the body at a time**. For example, a patient with oral squamous cell carcinoma may also have cancer of the small intestine, cancer in the lung and in the kidney, etc.

Multicentric cancer: Multicentric cancer means **occurrence of two or more separate malignant lesions within a single organ or area of the body**, which develop either concurrently (synchronous) or subsequently (metachronous). For example, a patient with tongue cancer may also separately have cancer of the lip or of the buccal mucosa or soft palate, etc. All these malignant lesions may occur either simultaneously or they can develop at certain time intervals.

Oral multicentric cancers probably occur as a result of the phenomenon called "**field cancerization**", in which a large wide area of the oral epithelium becomes vulnerable to cancer either by itself or by the influence of certain carcinogenic agents.

Key points of squamous cell carcinoma

- Fast enlarging swelling or large ulcer, which does not respond to conventional therapies.
- Few lesions may appear as extensive leukoplakic or erythroplakic patches.
- The ulcer is indurated or everted, painful and bleeds frequently.
- Difficulty in speech, difficulty in taking food and difficulty in opening the mouth.
- Regional lymph nodes are enlarged, tendered and are often fixed.
- Regional teeth are often mobile and these can exfoliate spontaneously.
- Most of the lesions exhibit superadded candidial infections.
- There may be anesthesia or paresthesia of the affected area.
- Severe weakening of the jawbone with occasional pathological fractures.
- Long standing lesions may spread extraorally by perforating the facial skin.
- Maxillary lesions can invade the antrum and cause pain, swelling and nasal bleeding, etc.

ORAL CANCER IN DIFFERENT INTRAORAL LOCATIONS OR SUBSITES

Separate descriptions of oral squamous cell carcinomas occurring at different intraoral sites may be necessary since this can help in gathering reliable informations regarding variations in the etiology, clinical features and prognosis of the disease.

CARCINOMA OF THE LIP

- Squamous cell carcinoma of the lip accounts for about thirty to forty percent of all oral cancers and in most of the cases, it is caused by actinic radiation.

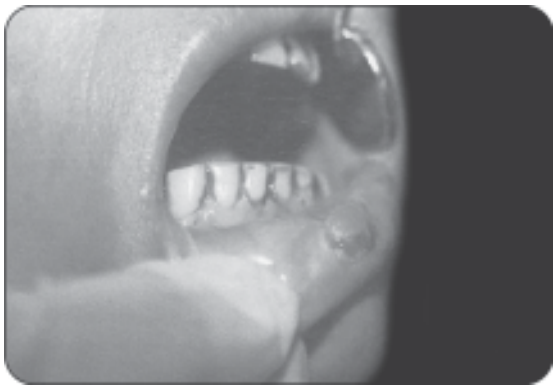

Fig. 2.14: Carcinoma of the lip

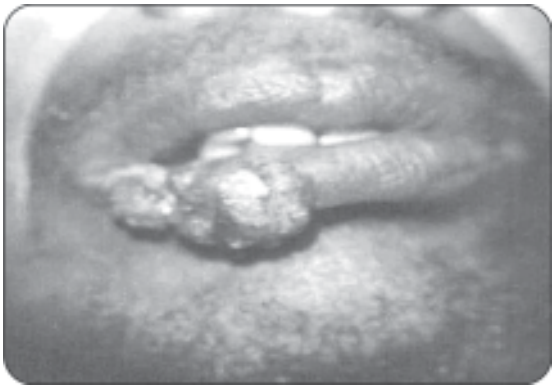

Fig. 2.15: Carcinoma of the lip extending to the angle of the mouth

- Carcinomas of the lip (Fig. 2.14) account for about 12 percent of all head and neck cancers and about 21.5 percent of all intraoral cancers.
- The lesion occurs **more commonly among males** as compared to females (uncommon in females) and most often the patients are in their fifth to eighth decade of life. However, several cases are also found in young patients below 40 years of age.
- Carcinoma of the lip commonly affects either the left or the right side of the vermilion border and seldom the midline.
- Among the lip carcinomas (Figs 2.15 and 2.16), the lower lip is affected in about 85 to 95 percent cases; the upper lip is affected in only about 2 to 7 percent cases, while the vermilion border is affected in about 1 to 4 percent cases.
- The lesions are **mostly preceded by the precence of long standing keratotic leukoplakia or actinic cheilitis, etc.** which are characterized by innocuous looking white plaques on the lip. These conditions are followed by recurrent ulceration or encrustration or an exophytic tumor.

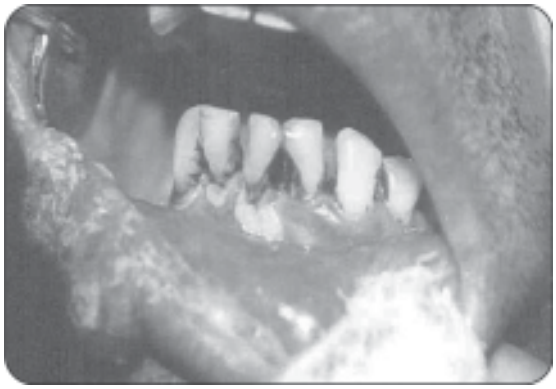

Fig. 2.16: Intraoral view of same patient

- The ulcer spreads diffusely and the lip becomes everted; and later on the ulcer develops a rolled border with induration of the surrounding tissue.
- Pain, bleeding and paresthesia are common features of lip carcinoma, moreover patient often have difficulty in speech, difficulty in taking food and inability to close the mouth.
- Most lesions in lip carcinoma are small and measure about below 2 centimeter in diameter; however some lesions can be extremely large, which extend either to the facial skin in the adjacent area or to the underlying connective tissue or bone.
- Lip carcinomas are slow to metastasize, however long standing, untreated cases may metastasize to submental lymph nodes and also to the submandibular nodes.
- Carcinoma of the lower lip and commissure are often associated with skin pigmentations.
- Histologically, lip carcinomas are mostly well-differentiated malignancies (85 percent cases) and if the treatment is done before the metastasis has taken place, prognosis could be as good as 100 percent.

CARCINOMA OF THE TONGUE

Tongue is anatomically divided into two parts, **anterior two-third area (movable tongue)** and **posterior one-third area (base).** Anterior two-third

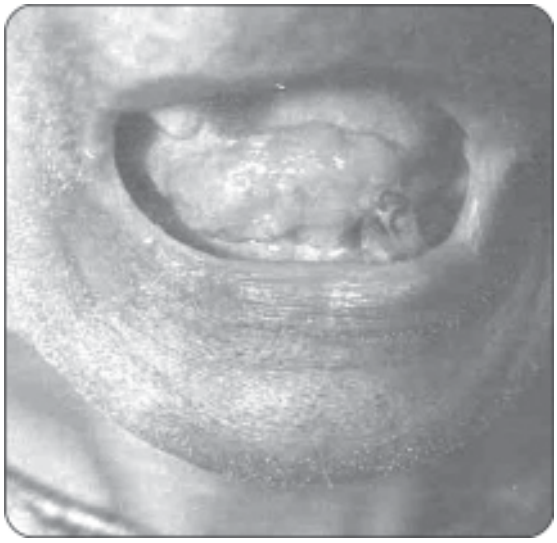

Fig. 2.17: Carcinoma of tongue

area is the portion lying anterior to the line of circumvalate papilla on the top and the junction of the ventral surface of tongue to the floor of the mouth below. The posterior one-third area of the tongue is the portion extending from the circumvalate papilla to the junction with the epiglottic vallecula and it includes the pharyngo-epiglottic and glossoepiglottic folds.

Carcinoma of the tongue, constitutes about fifty percent of all oral malignancies and out of this, about 25 percent cases affect the lateral borders of posterior one third area of the tongue and 75 percent lesions occur on the anterior two-third area.

- The lateral borders of the tongue and the anterior, right and left floor of the mouth, the retromolar pad and the adjacent parts of the soft palate constitute a **"U" shaped zone** in the oral cavity, which is considered to be a **high-risk area** for the development of squamous cell carcinomas (Fig. 2.17) .
- The **dorsum of the tongue is a relatively resistant site** for the initiation of this lesion, although extension from adjacent areas frequently occurs.
- The initial lesions often appear as painless, erythematous macules or nodules or fissured areas over the tongue. There may be some cases of nonhealing ulcers on the lateral border.
- In some cases, the lesion can appear only as an extensive leukoplakic patch, which later on ulcerates and gives rise to a raised, painful and indurated lesion.
- The advanced lesions often produce fast enlarging, painful, exophytic and large, extensively indurated ulcers with elevated and everted margin.
- Squamous cell carcinoma of tongue in advanced stages often spreads to involve the adjacent areas like- gingiva, floor of the mouth, base of the tongue and mandible, etc.
- Tongue lesions usually have excessive bleeding tendency upon silght provocation and often there is presence of superadded candidial infection.
- Squamous cell carcinomas often cause **fixation of the tongue to the floor of the mouth**, which results in difficulty speech and swallowing, etc.
- Paresthesia of the tongue frequently occurs due to invasion of the lingual nerve by tumor cells.
- Tumor cells from the anterior two-third area of tongue often spread via lymphatics to submandibular, mid-anterior jugular and sub-digastric lymph nodes.
- Long standing invasive lesions of posterior one-third area of tongue may spread to any of the following areas, e.g. anterior part, pre-epiglottic space, pharyngeal or laryngeal wall and the mandible, etc.
- Untreated tumors at the tip of tongue tend to spread to the submental and to the jugulo-omohyoid lymph nodes.
- Tumors at the posterior part of the tongue usually spread to the submandibular and jugulodigastric lymph nodes of either the ipsilateral or the contralateral side.
- Tongue carcinomas have tremendous tendency for metastasis to the neck; the metastatic lymph nodes are enlarged, tendered and are often fixed to the surrounding tissue.
- Tongue lesion extending to the floor of mouth often increases the possibility of nodal metastasis; moreover lesions which cross the median longitudinal raphe can cause contralateral or bilateral nodal involvement.
- Sometimes distant metastasis may occur and in such cases, the malignant tumor cells often spread to the bone or lung or to the brain, etc.
- The prognosis of tongue carcinoma is often excellent if an early diagnosis is made and prompt treatment could be given.

CARCINOMA OF THE FLOOR OF THE MOUTH

Floor of the mouth is the mucosal area spreading over anterior and lateral floor of the oral cavity. Anteriorly and laterally it is bordered by the lingual surface of lower alveolar ridge, its posterior boundary is formed by the base of tongue and anterior tonsilar pillar. The lingual frenulum divides the floor of mouth into right and left halves, moreover from the front upto the posterior edge of lower second molar is called the **anterior zone** and the area behind that is called the **posterior zone** of floor of the mouth.

Floor of the mouth can be the site of about 20 percent of all oral carcinomas and moreover, it is the third most common location of all intraoral squamous cell carcinomas.

- Carcinomas of the floor of the mouth mostly occur in the anterior part (72 percent cases), near the opening of the Wharton's duct.
- There is absolute male predominance as per as carcinoma of floor of the mouth is concerned (70 to 90 percent lesions occur in males), however recently the female percentage is also on the rise.
- Almost all the patients are either heavy smokers or alcoholics or both.
- The initial lesions often appear either as erythroplakia or speckeled leukoplakia; or a 'sore spot' as described by most patients. These lesions gradually undergo central ulceration and exhibit induration at the periphery.
- Carcinomas of the floor of the mouth are among the **most fatal and aggressive lesions** of oral cavity as they can spread easily to the adjoining structures; moreover as it is the area of rich lymphatic drainage and upto 40 percent patients have nodal involvement during first reporting.
- Gradually the advanced lesions become nodular, ulcerated or indurated, and moreover extension of the tumor cells to the deeper tissues of the tongue often results in fixation of the later.
- These lesions can also extend to the adjoining gingival tissues and cause pain, swelling and bleeding of the gingiva with mobility of the regional teeth.

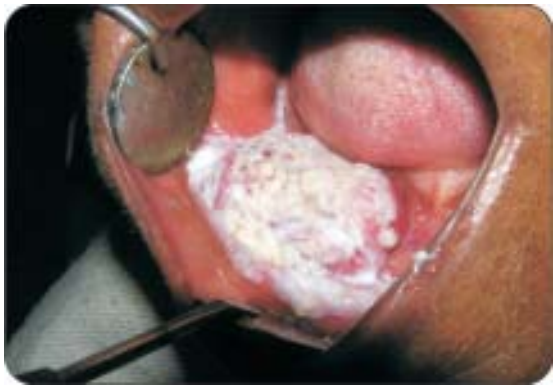

Fig. 2.18: Squamous cell carcinoma of floor of the mouth

- Squamous cell carcinomas of the floor of the mouth usually spread to the submandibular lymph nodes (Fig. 2.18). Distant metastasis is also a common.

CARCINOMA OF THE PALATE

Palate is divided into two parts, anteriorly hard palate and posteriorly soft palate. From the inner aspect of superior alveolar ridge upto the posterior edge of palatine bone is the hard palate and from there upto the end of uvula is the soft palate.

Squamous cell carcinoma of the soft palate constitutes about 15 percent of all intraoral carcinomas.

- Squamous cell carcinomas affect the soft palate in about 75 percent cases and hard palate in nearly 25 percent cases.
- Lesions affecting the soft palate very often develop from the posterolateral surface adjacent to the anterior faucial pillars.
- History often reveals that most of these patients with carcinoma of the soft palate are **heavy smokers with high affinity towards alcohol.**
- Clinically the lesions often appear either as mixed red-white patchy areas or extensive erythroplakic plaques with late ulceration.
- Invasion into deeper structures occurs usually before the surface ulceration begins.
- Carcinoma of the hard palate is very rare in western population, however it is fairly common in the Indian population, especially among **reverse smokers**. Young female reverse smokers of south India are particularly prone to this.

- Carcinomas of the hard palate mostly occur as lateral ulcers in the glandular zone and these lesions often invade into the **underlying bone, floor of the nasal cavity, maxillary antrum, gingiva and the soft palate, etc.**
- Carcinomas of both hard and soft palate are generally moderately or poorly differentiated lesions and these tumors generally spread to the internal jugular and submandibular lymph nodes.

CARCINOMA OF THE BUCCAL MUCOSA

Buccal mucosa is that part of oral epithelium which covers the inner aspect of cheeks and lips.

It is a common site for the occurence of squamous cell carcinoma especially among people of the Indian subcontinent.

Such higher incidences of squamous cell carcinoma can be attributed to the widespread use of betel nut and tobacco in various forms among the people of this region. However, in the worldwide scenario, buccal mucosa is not a very prominent site for oral cancers and they constitute only about 1 to 2% of all intraoral carcinomas.

- Carcinoma of the buccal mucosa frequently occurs in the **posterior part** of the buccal mucosa.
- Clinically, these lesions often present as white speckled patch or small nodule or well-defined ulcer with surrounding induration or may be as verrucous type of growth.
- Exophytic ulcers are commonly seen in the commissural areas while deep excavating lesions are mostly seen in the area **along the occlusal line** of buccal mucosa. The later group of lesions often exhibit rapid invasion into the surrounding tissues.
- In the advanced stage of the disease or in untreated cases, the lesion often presents **large, painful, indurated ulcers, which may perforate the cheek and reach to the external surface of the face as a nodular protruding mass (Fig. 2.19).**
- Lesions from this area can also spread to the underlying bone or to the pharyngomaxillary fossa or to the muscles, etc.

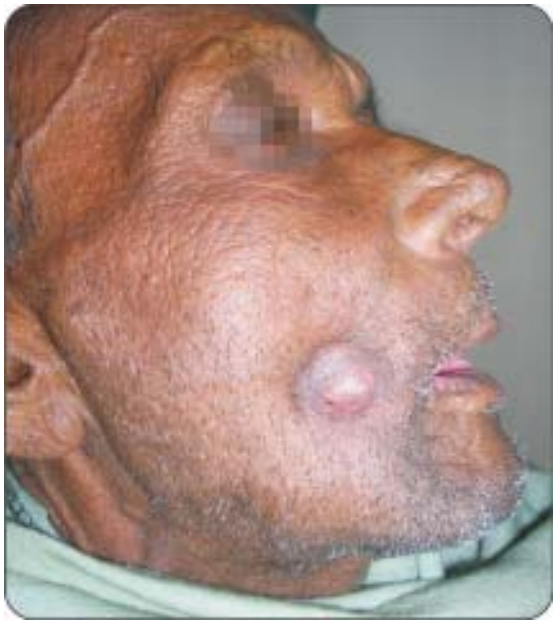

Fig. 2.19: Squamous cell carcinoma of buccal mucosa causing skin fixation

- Buccal mucosal carcinomas are usually moderately differentiated lesions and they often metastasize to the submandibular lymph nodes. Recurrence after treatment is also very high.

CARCINOMA OF THE GINGIVA/ ALVEOLAR RIDGE

Carcinoma of the gingiva and alveolar ridge (both upper and lower) represents approximately about 4 to 6% of all oral carcinomas (Figs 2.20 to 2.22). The most common predisposing factor is tobacco and betel nut chewing.

- Mandibular gingiva is affected more often (70 percent) than the maxillary gingiva (30 percent) and elderly people (predominantly males) are commonly affected usually after the age of 60 years.
- Attached gingiva is affected more than the free gingiva and edentulous people develop the disease more often than the dentulous people.
- The initial lesion appears either as a verrucous leukoplakia or as a small ulceration with indurated margin.

Fig. 2.20: Squamous cell carcinoma causing pathological fracture of jaw-I

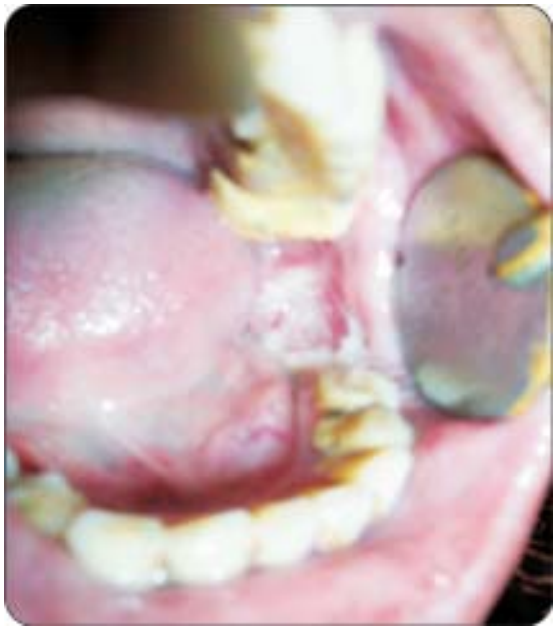

Fig. 2.21: Intraoral view of squamous cell carcinoma causing pathological fracture of jaw-II

- Carcinoma of the gingiva is often mistaken for other ordinary diseases like—**chronic gingivitis, gingival abscess or periodontitis, etc.**
- Early invasion of the bone takes place, mostly via the periodontal ligament and this causes extensive mobility and premature loss of the regional teeth.
- Extraction of tooth often leads to early bone invasion, which causes nonhealing or delayed healing of the extraction socket.
- Mandibular lesions often extend to the adjoining structures, e.g. labial mucosa, tongue, bone, floor of the mouth and the retromolar areas.
- Carcinoma of the maxillary gingiva often extends to hard palate, maxillary antrun, buccal mucosa, lip and facial skin, etc.
- Metastasis occurs often to the submandibular and deep cervical lymph nodes.

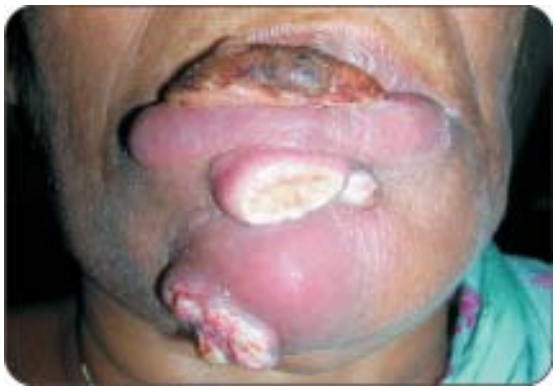

Fig. 2.22: Untreated case of squamous cell carcinoma

CARCINOMA OF THE MAXILLARY ANTRUM

Squamous cell carcinomas sometime involve the maxillary antrum (Figs 2.23 and 2.24) and these lesions often present the following features:

- **Pain and heaviness of the upper face** on the involved side, with occasional **epistaxis**.
- **Anesthesia or paresthesia** of the affected area is very common.
- There can be **pain in the upper molar teeth with pressure sensation on the eyeball.**
- Edentulous patients often feel pain and **discomfort under the artificial denture.**
- In advanced stages of the disease, there can be mobility of the upper molar teeth as well as swelling of the face.
- Radiograph **(Waters' view)** often reveals **clouding** of the antral space and sometimes destruction of the bony walls of the antrum (Fig. 2.25).

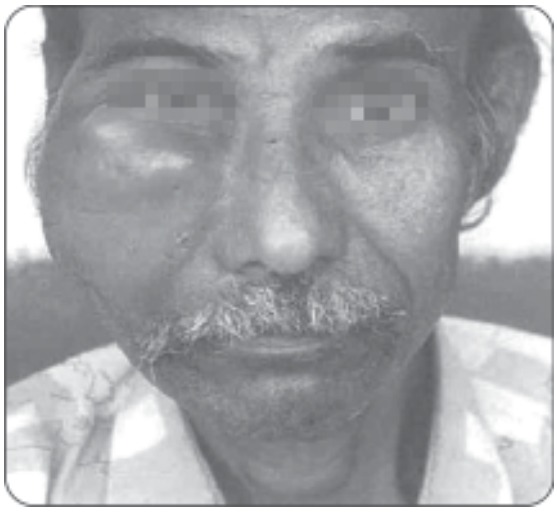

Fig. 2.23: Carcinoma of the maxillary antrum

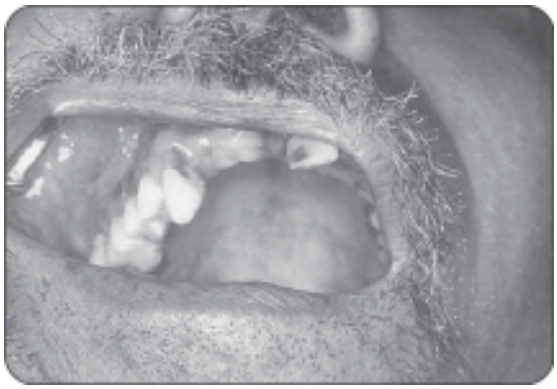

Fig. 2.24: Intraoral view of the same patient

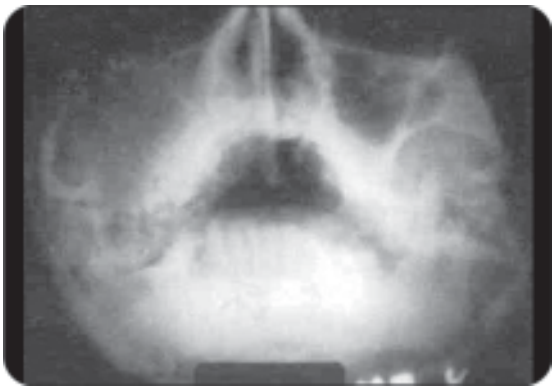

Fig. 2.25: Occipitomental view radiograph showing expansion of the Rt. antrum in carcinoma

DIFFERENTIAL DIAGNOSIS OF SQUAMOUS CELL CARCINOMA

A large numbers of neoplastic or nonneoplastic lesions often resemble squamous cell carcinoma either clinically or histhopathologically and therefore these lesions should be distinguished from squamous cell carcinoma while making the diagnosis.

Following are the lesions, which can simulate squamous cell carcinoma:

- Keratoacanthoma
- Lymphoma
- Ewing's tumor
- Neuroblastoma
- Metastatic tumor from a primary lesion located elsewhere in the body
- Granular cell myoblastoma
- Pseudoepitheliomatous hyperplasia
- Epithelial overgrowths at the periphery of a nonmalignant chronic ulcer
- Tangential sectioning of hyperplastic oral epithelium, which often microscopically looks like an invading squamous cell carcinoma.
- **Organ of Chievitz** often resembles squamous cell carcinoma (it is seen in the bucco-temporalis fascia on the medial surface of the mandible).

RADIOLOGICAL FEATURES OF SQUAMOUS CELL CARCINOMA (FIG. 2.26)

Variable degrees of bone destruction may occur when malignant cells of the squamous cell carcinoma invade into the jaw bones. This type of bony involvement can be seen more frequently, if the primary tumor occurs in gingiva or alveolar ridge or in the floor of the mouth, which extends to the jaw bone. Moreover, metastatic carcinomas also frequently affect the jawbone and cause bony changes which could be detected by radiographs.

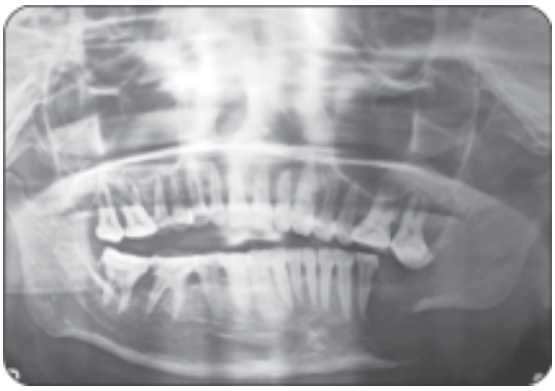

Fig. 2.26: Radiograph of squamous cell carcinoma

The common imaging techniques used for the detection of the jawbone malignancies

- Anteroposterior (AP) and posteroanterior (PA) view radiograph of the jaw.
- Orthopantomogram of the jaw (OPG).
- Standard occlusal radiograph of the jaw.
- Water's view radiograph of the jaw.
- Intraoral periapical (IOPA) radiograph of the jaw.
- CT Scan of the jaw and skull.
- Magnetic Resonance Imaging (MRI).

Radiographic Features of Jaw Malignancy

- Radiographically the involved bone often exhibits large, irregular and ill-defined radiolucent areas with a typical **"moth-eaten"** appearance.
- Border of the lesion is often **hazy** and not clearly demarcated.
- Irregular **expansion and destruction of the cortical plates** of the jawbone is common.
- Destruction of the interdental or inter-radicular bone may be seen frequently and this causes expansion of the periodontal ligament space in the localized area, displacement or exfoliation of the regional teeth.
- In advanced cases, the bone destruction could be so extensive that it may lead to **pathological fractures** of the affected jawbone.
- Clouding of the maxillary antrum and destruction of the lateral antral wall is commonly seen in case of antral carcinoma.

HISTOPATHOLOGY

Histopathology is the most important tool for making the diagnosis of squamous cell carcinomas. It is performed by obtaining a biopsy from the representative site of an existing lesion with subsequent histopathological evaluation.

Under microscope, the neoplasm presents the following features:

In squamous cell carcinoma, the malignant epithelial cells grow out of control and tend to spread throughout the body.

Histologically, there are at least three very important criterias for malignancy exhibited by squamous cell carcinoma.

A. **Dysplastic changes** in the malignant tumor cells with varying grades of differentiation.
B. **Invasion of the tumor cells** into the underlying connective tissue.
C. Inherent potential or tendency of the malignant cells to spread to distant sites or organs throughout the body **(metastasis).**

- Histologically, squamous cell carcinoma exhibits **excessive proliferation of malignant squamous epithelial cells** due to increased and abnormal mitosis.
- These tumor cells exhibit variable degrees of **cellular pleomorphism** and **nuclear hyperchromatism**.
- Besides this, there can be other neoplastic changes in these cells which include increased nuclear cytoplasmic ratio, individual cell keratinization and loss of polarity of cell, etc.
- The malignant epithelial cells often cause **breakdown of the basement membrane** and **invade** into the underlying connective tissue stroma.
- The connective tissue stroma into which the tumor cells infiltrate generally shows intense inflammatory cell infiltration mostly by the lymphocytes and the plasma cells.
- Squamous cell carcinomas often exhibit some histologic variations, which depend upon the degree of differentiation of their constituent malignant tumor cells.

Histologic Gradation (Differentiation) of Squamous Cell Carcinomas

The term **'differentiation'** refers to the extent to which the tumor cells resemble their mother cells (cell of origin) both structurally and functionally. And according to the degree or grade of differentiation of its neoplastic cells, squamous cell carcinomas are divided into three histologic types—**well-differentiated squamous cell carcinoma, moderately-differentiated squamous cell carcinoma and poorly-differentiated squamous cell carcinoma.**

Well-Differentiated Squamous Cell Carcinoma

- Most of the squamous cell carcinomas histologically belong to the well-differentiated category (about 80%) (Fig. 2.27).
- In this lesion, the malignant tumor epithelial cells to a large extent **resemble the cells of the**

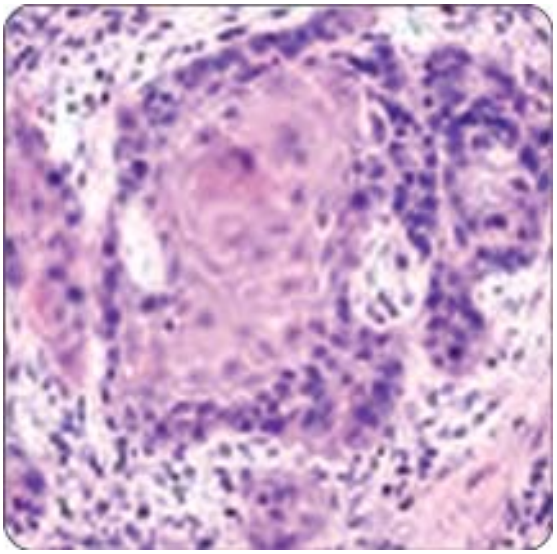

Fig. 2.27: Well-differentiated squamous cell carcinoma

squamous epithelium both structurally and functionally.

- Moreover, the tissue architecture seen in the tumor also reveals certain similarities to that of the stratified squamous epithelium.
- Besides this, tumor cells of well-differentiated squamous cell carcinomas produce large amount of keratin (a special fibrous protein normally produced by the keratinocytes of stratified squamous epithelium) in the form of **"keratin pearls" (Fig. 2.28).**
- The malignant tumor cells **invade into the underlying connective tissue**, where the cells proliferate further and give rise to the formation of many **epithelial islands** within the connective tissue stroma.
- The epithelial islands or the **cell nests** are bordered at the periphery by the basal cells and there is progressive differentiation or maturation of the tumor epithelial cells at the center of these islands or nests, which often results in the formation of keratin of variable maturity.
- The tumor cells often exhibit dysplastic features like—**cellular pleomorphism, nuclear hyperchromatism, individual cell keratinization and altered nuclear-cytoplasmic ratio**, etc.
- Moreover, in well-differentiated squamous cell carcinoma, malignant cells **exhibit some degrees of epithelial maturation, e.g. keratinization, strafication and existence of intercellular bridge,** etc. and therefore simulate the normal stratified squamous epithelium to a large extent.
- Squamous cell carcinoma of well-differentiated type is usually associated with a better prognosis.

Moderately-Differentiated Squamous Cell Carcinoma

- In moderately-differentiated squamous cell carcinoma (Fig. 2.28A), the **tumor cells are usually more severely dysplastic than that of the well-differentiated type.**
- The malignant epithelial cells produce **little or no keratin** and these cells exhibit **greater number of mitotic cell divisions.**
- The formation of epithelial islands or cell nests, etc. are diminished since these tumor cells do not differentiate or mature as much as the well-differentiated type of cells do.

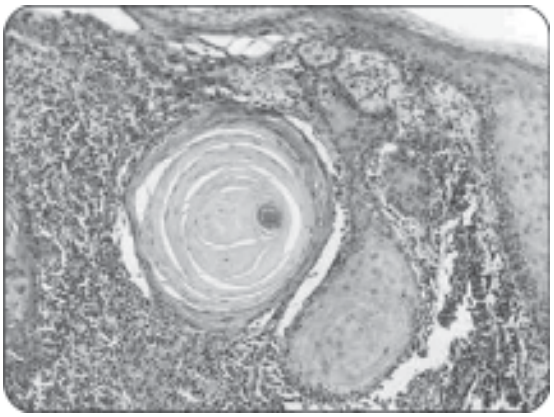

Fig. 2.28: Photomicrograph of well-differentiated squamous cell carcinoma showing large keratin pearl

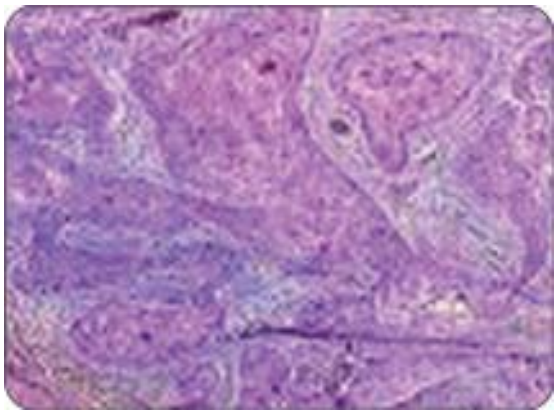

Fig. 2.28A: Photomicrograph of moderately-differentiated squamous cell carcinoma

Key points of histopathological aspect of squamous cell carcinoma

- Excessive proliferation of malignant epithelial cells.
- There will be cellular pleomorphism, nuclear hyperchromatism and increased abnormal mitosis of the malignant epithelial cells.
- Formation of epithelial islands and keratin pearls.
- Malignant cells invade into the underlying connective tissue by breaking the basement membrane.
- The well-differentiated squamous cell carcinoma exhibits cells which resemble their mother cells (stratified squamous epithelial cells) both structurally and functionally.
- The well-differentiated cells produce large amounts of keratin in the form of 'keratin pearls'; also produce large epithelial islands and prominent intercellular bridges.
- The moderately differentiated squamous cell carcinoma produces keratin pearls and their rate of mitosis is faster, the malignant cells resemble the mother cels but not as convincingly as the well-differentiated type.
- Poorly differentiated squamous cell carcinoma reveals extremely high rate of mitotic cell divisions, the cells look immature, there is no keratin pearl formations and nor any intercellular bridges.
- The poorly differentiated squamous cell carcinomas are difficult to diagnose as the cells have no structural or functional resemblance to their mother cells.

- There are only fewer tendencies for these malignant cells to produce normal stratification.
- However, despite their significant deviation from normal, the malignant tumor cells of moderately differentiated squamous cell carcinoma could still resemble their mother cells (stratified squamous epithelial cells).
- This tumor also carries a reasonably good prognosis.

Poorly-Differentiated Squamous Cell Carcinoma

- In poorly-differentiated squamous cell carcinoma, the malignant tumor cells produce no keratin and neither these cells bear any structural or functional resemblance whatsoever to the cells of the stratified squamous epithelium (mother cells).
- The tumor exhibits extensive cellular abnormalities with lack of normal architectural pattern and loss of intercellular bridges between the tumor cells.
- Moreover, in these tumor cells, the rate of mitotic cell division is extremely high and because of this, the neoplastic cells are often very immature and primitive looking and it is often very difficult even to recognize them as squamous epithelial cells.
- Diagnosis of poorly differentiated squamous cell carcinoma will require special investigative techniques like immunohistochemistry and flow cytometry, etc.
- These tumors always have a very poor prognosis.

SCREENING TESTS FOR SQUAMOUS CELL CARCINOMA

Exfoliative Cytology

Exfoliative cytology can often be helpful in making the diagnosis of oral squamous cell carcinoma. This method is not an alternative but an adjunct to the system of standard histopathology.

- In malignant neoplasms, the neoplastic cells become less cohesive (due to loss of intercellular bridges) and often these cells tend to exfoliate or shed into the surface fluid or secretions.
- During exfoliative cytology, these **exfoliated neoplastic cells are obtained** from the tumor surface by gentle scrapping of the area with a blunt instrument.
- The material obtined is then taken on to a slide and a smear is prepared. Staining of the slide is done with a special stain called **"Papanicolaou stain".**
- Microscopic evaluation of the stained cytologic slide often reveals dysplastic changes in the shed tumor cells, indicative of their cancerous origin.
- This type of cytological interpretation may give indication towards a positive diagnosis in large number of suspected oral squamous cell

carcinoma cases and is therefore considered as an important diagnostic tool.
- However, there can be false negative or false positive results in little percentage of cases in exfoliative cytology and therefore, all suspected cases must be confirmed by biopsy with subsequent standard histopathological evalution.

OTHER SCREENING TESTS

The toludine blue test and acridine binding method have been regarded as reliable screening methods during detection of oral cancer.

TOLUIDINE BLUE TEST

It is an *in vivo* test for detection of dysplastic lesions.

Methods

First of all, the surface of the suspected lesion is gently painted with 1% aqueous solution of toludine blue and then after 10 seconds, decolorization of the surface is done with 1% acetic acid solution.

Results

If the color of toludine blue is retained, malignancy or dysplasia is suspected in the lesion. If the color is washed away following application of acetic acid solution, the lesion should be considered nonmalignant.

Efficacy

The efficacy of this method depends upon the amount of DNA present, which relates to the number and size of superficially stained nuclei in the tissue to which the toludine blue is applied.

ACRIDINE BINDING METHOD

In this mothod the uptake of acriflavine by the desquamated buccal cells are measured.

Since the DNA content of the dysplastic cells are more, they will be stained more intensely than normal cells.

BRUSH BIOPSY

Brush biopsy is a usefull screening method in squamous cell carcinoma, in this technique a round stiff bristle brush is rotated vigorously in one particular spot of a suspected lesion till bleeding starts. Because of this rotation, cells, from the surface as well as the subsurface layer of the lesion will be collected by the brush, which are then transferred onto a slide and viewed microscopically after the the smear is prepared.

SPECIAL INVESTIGATIONS IN ORAL CANCER

Special investigations like immunocytochemistry, flow cytometry and DNA probe analysis may be necessary for the detection of some poorly differentiated oral cancers which cannot be diagnosed by conventional histopathology or cytology, etc. These techniques help in evaluating the nature of cancer cells and also help to determine the prognosis of some critical oral malignant lesions.
- These techniques can be applied to exfoliated cancer cells, biopsy specimens or even tissue aspirates, etc.
- **Detection of cytokeratin by immunoperoxidase staining** helps in differentiating between a poorly differentiated carcinoma and a large cell lymphoma.
- **Southern blot analysis** helps in making distinction between two different malignant tumors by detecting the clonal rearrangement of the antigen receptor genes.
- **Flow cytometric detection** of differentiation specific antigens in different tumor cells can separate one tumor from the other.
- **DNA probe analysis** can help in determining the DNA content of tumor cells and it can aid in evaluating the prognosis of the tumor.

TUMOR MARKERS

When a tumor develops in the body, certain tumor markers are produced in the blood in response to it. **Carcinoembryonic antigen (CEA) and α-fetoprotein** are two important such tumor markers.

The presence of these tumor markers in blood indicates that there is a tumor developing somewhere in the body or it might have already developed. These tumor markers disappear from blood once the tumor is surgically removed or

treated by other means. However, they can reappear once again if the tumor recurs.

IMMUNOLOGY OF ORAL CANCER

In the recent times it has become very clear that immunity has a strong influence in the development of any malignant or benign neoplasm or any precancerous lesion in the body. According to different investigators initiation of a tumor (oncogenesis) may occur in the body as results of any of the following immunological lapses or short comings:

- Failure of recognition of tumor cell antigens by the immunosurvilence system of the body.
- Breakdown of cell mediated and humoral immune system.
- Oncogenesis stimulated by the body's own immune system itself.

FAILURE OF RECOGNITION OF TUMOR CELL ANTIGENS BY THE IMMUNOSURVEILLANCE SYSTEM OF THE BODY

The immunosurveillance system distinctly recognizes (identifies and differentiates) between the normal cells and the tumor cells, since tumor cells are antigenically different from their normal progenitor cells, they are readily recognized within the body by the immunosurvilence system of the host.

Once these tumor antigens are recognized, they are immediately killed by the bodies own defense system, so that these cells do not make any further progress towards oncogenesis. The destruction process is generally carried out by cytotoxic T-lymphocytes, natural killer cells and macrophages, etc.

Causes of Failure of Immunosurveillance System

- ***Loss or reduced expression of major histocompatibility antigens:*** Sometimes, the tumor cells fail to express normal levels of HLA-class I or HLA-class II antigens and because of this, they may escape the immunosurveillance network as well as the attack from cytotoxic-T-cells.
- ***Selective growth of antigen negative variants:*** Strongly immunogenic subclones may be eliminated during tumor progression.
- ***Shedding or modulation of tumor antigens:*** Sufficient shedding of tumor antigens may inhibit tumor cell recognition.
- ***Sneaking through:*** Emerging tumors may sometimes produce a very small antigenic response, which results little or no immune reaction against it.
- ***Immunosuppression:*** Many oncogenic agents like chemicals, ionizing radiation, etc. may actually suppress the host immune response against the tumor cells.

BREAKDOWN OF CELL MEDIATED AND HUMORAL IMMUNE SYSTEMS

In vitro and *vivo* tests reveal that breakdown of the body's immune systems (both cell mediated and humoral) may result in the development of malignancies including the oral cancers.

- Cell mediated immune systems may become suppressed in case of liver damage, due to chronic alcoholism and such patients could be more vulnerable to many cancers.
- Skin tests reveal absence or impairment of delayed hypersensitivity reactions in patients with squamous cell carcinoma.
- Peripheral blood T-lymphocyte count is decreased in patients with squamous cell carcinoma.
- The cytotoxic effects of T-8-lymphocytes are reduced in case of head and neck carcinomas.
- Since the natural killer cells (NK Cells) help in tumor rejection, depressed number of natural killer cell in the body may be associated with increased tumor susceptibility.
- Changes in the humoral immunity is less well-defined in patients with oral cancers as compared to the patients having defects in cell-mediated immunity.
- Raised levels of IgA and IgG are often expressed during the development of malignant tumors and these levels are further raised in tumors where metastasis has occured.

Oncogenesis Stimulated by the Body's Own Immune System Itself

The specific genes responsible for producing proteins that can upset the normal replication cycle of cells are known as "oncogenes".

When oncogenes are stimulated to over-produce proteins that stimulate the process of mitosis, the result is neoplastic growth. Alteration in the oncogene activity may be associated with environmental factors such as tobacco habits, alcohol, nutritional deficiency and chronic infections, etc.

Metastasis in Squamous Cell Carcinoma

Definition of metastasis—spread of cancer from a primary site to distant organ or organs elsewhere in the body is called **metastasis**. When there is more than one metastasis, they are called **metastases**.

Basic steps in metastasis

- Detachment of malignant tumor cells.
- Invasion and intravasation of tumor cells.
- Tumor cells in the circulation.
- Stasis of the tumor cells.
- Invasion and extravasation of tumor cells.
- Proliferation of the tumor cells at the distant site and development of secondary or metastatic tumor.

Routes of Metastasis

Squamous cell carcinomas of the oral cavity usually spread by involving the lymphatic vessels and sometimes via perineural sheath.

Mechanism of Metastasis

- Malignant cells have no intercellular bridges and are not bound to one another as seen in normal epithelium.
- These free malignant cells destroy the basement membrane and invade into the underlying connective tissue.
- Here the malignant cells invade into vessels for further travel into distant organs; generally the carcinoma cells take the lymphatic route while the sarcomatous cells take route via blood vessels.
- Once the tumor cells get inside the lymphatic vessel, some cells are carried to the regional lymph nodes while other cells move on till they reach to a suitable distal organ, e.g. lung, bone, liver, brain and skin, etc.
- The newly arrived cells become implanted in the respective organs and continue to proliferate further to produce secondary or metastatic tumor.
- Metastasis through blood vessels or perineural infiltration is rare in oral squamous cell carcinoma.
- Inside the lymph node, the proliferating tumor cells cause enlargement of the nodes and later on, these cells extends further beyond the capsule of the lymph node and spread into the surrounding tissue. In such cases the nodes become 'fixed'.
- The involved lymph nodes are palpable, enlarged, firm in consistency.
- Bilateral involvement of the lymph nodes is uncommon unless the tumor is very large and it crosses the midline.

Lymph nodes where metastasis of oral cancers commonly occur

- Submandibular lymph nodes—about 32% cases.
- Submental nodes about—12% cases.
- Superior deep cervical nodes about—10% cases.
- Jugulo-digastric and jugulo-omohyoid nodes about—30% cases.
- Midcervical lymph nodes about—4% cases.
- Posterior supraclavicular nodes about—2% cases.

Treatment

Squamous cell carcinomas of the oral cavity are usually treated by surgical excision, radiotherapy and chemotherapy, etc.

- Depending upon the size, the anatomical location and the histological gradation of the tumor, surgical treatment may consist of either only local excision or a combination of local excision and regional lymph node dissection.

Survival

Since most of the oral squamous cell carcinomas are well differentiated (about 80% lesions), prognosis is often expected to be good for them. Unfortunately however, excepting the lip carcinomas, most of the other intraoral cancers have a rather poor prognosis and it is mostly due to their late diagnosis and failure of initiating prompt treatment.

The survival rates for oral squamous cell carcinomas depend on the clinical staging of the disease, degree of differentiation of the tumor cells and the specific intraoral site of involvement.

According to one study (Hibbert *et al* 1983), the overall 5 year survival rate of oral squamous cell carcinoma is under 55%. According to Herkey (1979), the survival rate is equal among men and women in case of lip cancers. However, the survival rate is always better for women in case of other intraoral cancers as compared to men.

CLINICAL STAGING OF CARCINOMAS OF HEAD AND NECK (TNM SYSTEM)

In a patient with carcinoma, clinical staging is used to designate the extent of the disease and to determine the most appropriate treatment necessary for that patient during that particular stage of the disease.

Finally the method helps in making an overall evaluation regarding the prognosis of the disease.

The designations used in the TNM system are as follows:

T for primary tumor
N for regional lymph node
M for distant metastasis.

All these criterias incorporated in the system are major factors, which definitely influence the prognosis of the disease.

Another clinical staging system has been introduced in recent times, which is called the STNMP system. In this system, two new variables have been included besides the original TNM factors and these are—**"S" (site of the tumor) and "P" (pathology of the tumor).**

According to many investigators, the STNMP staging system has promised considerable improvement regarding the prognostic evaluation and differentiation of a tumor over the TNM system.

TNM System: Definition and staging groups

T—Primary Tumor

TX Primary tumor can not be assessed
To No evidence of primary tumor
TIS Carcinoma-*in situ*.
T1 Tumor size–2 cm or less in greatest dimension.
T2 Tumor size more than 2 cm but not more than 4 cm in greatest dimension.
T3 Tumor size more than 4 cm in greatest dimension.
T4 Tumor invades adjacent structures.

N—Regional Lymph Node

NX Regional lymph nodes can not be assessed.
No No regional lymph node metastasis.
N1 Metastasis in single ipsilateral lymph node, 3 cm or less in greatest dimension.
N2 Metastasis in single ipsilateral lymph node, more than 3 cm but less than 6 cm in greatest dimention, or in multiple ipsilateral nodes, or in bilateral or contralateral nodes (none more than 6 cm in greatest dimension).
N2a Metastasis in single ipsilateral lymph node, more than 3 cm but less than 6 cm in greatest dimension.
N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension.
N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
N3 Metastasis in lymph node, more than 6 cm in greatest dimension.

M—Distant Metastasis

MX Presence of distant metastasis can not be assessed.
Mo No distant metastasis.
M1 Clinical or radiographic evidence of metastasis.

TNM clinical staging of oral carcinoma

	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1 T2 T3	N1 N1 N0 N1	M0 M0 M0
Stage IV	T4 Any T Any T	N0 N1 N2 N3 Any N	M0 M0 M1

PREVENTION OF ORAL CANCER

Now a days the evidence is overwhelming that tobacco chewing and smoking are the major causes of oral cancer. It is estimated that about 90% cases of oral cancers especially in South and South East Asia can be attributed to these two major habits.

Studies indicate that the risk of oral cancer increases due to an increase in the use of tobacco and moreover, the incidence is higher among people, who start chewing tobacco at an early age or who chew tobacco for a longer time. It has also been observed that people who chew tobacco more frequently or who keep the tobacco quid in the mouth overnight carry increased risked for developing oral cancer.

METHODS OF PREVENTION

A. Primary prevention.
B. Secondary prevention.

Primary Prevention

In primary prevention, the risk of cancer development is minimized by avoiding the exposure to tobacco and other deleterious habits.

The primary prevention can be attempted either on individual basis or on community basis, and its implementation requires active support from media like—television, films, radio, newspapers and posters, etc.

This can also be achieved through intensive personal communications by doctors and social workers at the clinics, hospitals and in community health care centers.

Methods

Primary prevention can be implemented in the form of a community approach and the common measures taken towards this include the following:

- Reducing tobacco habits by making tax hike for tobacco related products.
- Making changes in the manufacturing process of tobacco items.
- Making genetic changes in tobacco plants.

Advantage

Primary prevention tackles the problem at the grass-root level.

Limitations

- Requires long-sustained efforts and close monitoring.
- Requires long-time to achieve a significant amount of success.

Secondary Prevention

This form of prevention includes early detection and treatment of already developed cancer cases and prompt management of potentially risky precancerous lesions and conditions.

The treatment of early cancers will result in their better prognosis, while an early management of suspect precancerous lesions and conditions will prevent their progress to cancer.

The basic aim of secondary prevention is to improve the prognosis.

Limitations

Requires adequate number of trained professionals and significant financial as well as technical resources.

BASAL CELL CARCINOMA (RODENT ULCER)

DEFINITION

Basal cell carcinoma is a common, locally aggressive, non-metastasizing malignant neoplasm of the skin, which is usually composed of medullary pattern of basaloid cells.

ORIGIN

The disease arises from either the basal layer of epidermis or from the hair follicles and it affects the facial skin more often than any other part of the body.

ETIOLOGY

Chronic occupational or recreational exposure to direct sunlight (actinic radiation) is the most common and wellknown etiologic factor for this neoplasm.

In the tropical black populations, this lesion is very uncommon and it could be attributed to the natural pigmentation of the skin of these people, which provide adequate protection from actinic radiation and thereby prevent the development of basal cell carcinoma among them.

CLINICAL FEATURES

Age: Basal cell carcinoma develops mostly in middle aged people, preferably in the 4th decade of life.

Sex: Males are more commonly affected than females.

Geographical area: The incidence of basal cell carcinoma is particularly high in geographic areas with high temperature and low humidity. For this reason large numbers of cases have been reported from Queensland in Australia and Arizona in United States.

Site: The neoplasm commonly occurs (over 85 percent cases) over the **hair-bearing areas of facial skin (especially the mucocutaneous areas)** in blonde, white males.

The orofacial areas particularly vulnerable to these lesions are the upper lip, nasolabial folds, periorbital region, cheek, forehead and ear, etc.

The lesion **does not arise from the oral mucous membrane**; however it can sometimes invade the mucous membrane by directly spreading from the adjacent skin oral lesions could otherwise be misdiagnosed either as salivary gland neoplasms or odontogenic neoplasms.

PRESENTATION

- The neoplasm initiates as a slow growing, firm, slightly elevated, small nodule.
- It gradually enlarges and develops a **central crusted ulcer** with an elevated, smooth, **rolled border.**
- The lesion may heal partially by scarring in the central area but it keeps on spreading centrifugally.
- One or more telangiectatic blood vessels may be seen coursing over the lesion and moreover, a characteristic pearly opalescence is noticed when the tumor is digitally pressed.
- The untreated neoplasm enlarges and invades adjacent tissues and organs by direct extension but it rarely metastasizes.
- The synonym "**rodent ulcer**" is given to this tumor since it makes a slow but relentless progress over months or years and increases in size by invading and destroying the adjoining tissues.
- There may be intermittent bleeding from the ulcer followed by ulcer.
- Some lesions of basal cell carcinoma may be pigmented due to melanosis and they often appear tan, brown or black in color.
- A sclerosing or '**morphea**' form of basal cell carcinoma is also recognized, which appears as a pale, poorly demarcated scar tissue over the skin.
- Basal cell carcinoma usually occurs as a solitary lesion, however there can be development of multiple lesions at a time when the tumor develops in association with Gorlin-Goltz syndrome.

HISTOPATHOLOGY

- Histologically, basal cell carcinoma is characterized by neoplastic proliferation of basaloid epithelial cells in the form of **multiple solid islands or strands (Fig. 2.29)**.
- These cells arise from the basal cell layer of the epidermis and they invade into the underlying dermis.
- The cells in the periphery of the tumor islands are columnar in shape and they often resemble basal layer of the oral epithelium with hyperchromatic nuclei.
- These tumor cells do not show any feature of abnormal mitosis.
- The cells are uniform in shape and size, and in their staining reaction. Moreover, these cells often have a palisaded arrangement.
- The central cells of the tumor islands may be polyhedral, oval, round or even spindle shaped.

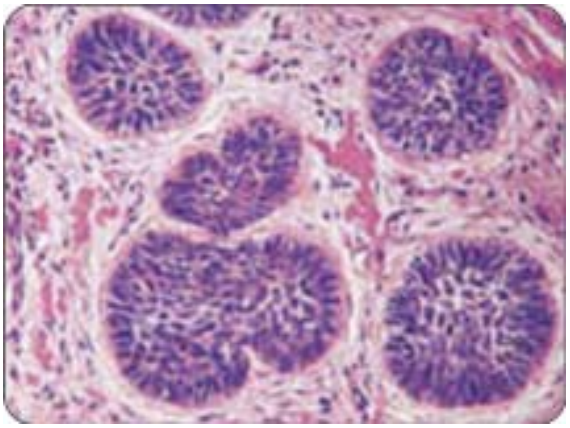

Fig 2.29: Photomicrograph of basal cell carcinoma

- Intercellular bridges are often absent in routine tissue sections and apoptosis (individual cell death) of the tumor cells are commonly seen.
- In addition to create solid island—like masses, these neoplastic cells may also proliferate to give rise to adenoid or cystic growth patterns.
- In some cases squamous metaplasia may occur is the tumor, with the formation of foci of keratin and hair follicle like structures.
- Basal cell carcinoma may sometime resemble 'follicular ameloblastoma' very closely.
- The fibrous connective tissue stroma reveals varying degrees of cellularity and it contains large number of elastic fibers.

DIFFERENTIAL DIAGNOSIS

The following lesions are included in the differential diagnosis of basal cell carcinoma:

- Ameloblastoma
- Salivary gland neoplasms
- Squamous cell carcinoma.

TREATMENT

Surgical excision or electrocautery along with radiotherapy is the treatment of choice. Prognosis is extremely good and cure rate is about 95%.

VERRUCOUS CARCINOMA

DEFINITION

Verrucous carcinoma is a diffuse, papillary, non-metastasizing, well-differentiated malignant neoplasm of the oral epithelium.

It is also known as **'Ackerman's tumor'** since it was first recognized as a distinct entity by Ackerman in 1948. According to the biological nature, verrucous carcinoma stands between benign hyperplasia of squamous epithelium and the conventional squamous cell carcinoma.

ETIOLOGY

Verrucous carcinoma commonly occurs in people with tobacco chewing and snuffs dipping habits.

CLINICAL FEATURES

Age: The tumor usually affects individuals over 60 years of age and never before 35 years of age (range is between 50 – 80 years).

Sex: Predominantly affects males.

Site: Intra orally buccal mucosa accounts for more than half of the cases, besides that the other common intraoral locations for verrucous carcinoma include gingiva and alveolar mucosa, etc.

Hard-palate and floor of the mouth can also be affected but less frequently.

Moreover, verrucous carcinomas can often develop from the mucosal surfaces of the larynx, nasal cavity, glans penis, vagina and perineum, etc.

PRESENTATION (FIGS 2.30 TO 2.34)

- Clinically verrucous carcinoma presents slow enlarging, soft, exophytic neoplasm, consisting of closely packed, papillary growths of heavily keratinized epithelium.
- The surface of the lesion is often raised and `pebbly' or sometimes it is `**warty**' and shows multiple **rauge-like folds** with deep clefts in between.
- The fully developed tumor appears as an exophytic, grayish-red, bulky lesion with a rough shaggy fungating surface.
- The tumor is generally slow growing, but few lesions can be fast growing as well.
- A small lesion of verrucous carcinoma often looks like a `papilloma'.

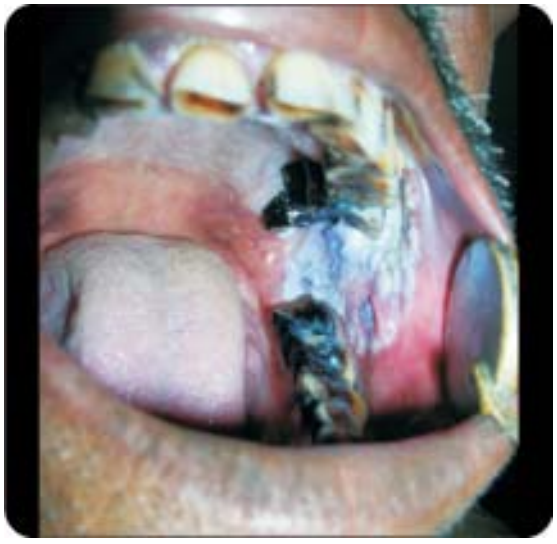

Fig. 2.30: Verrucous carcinoma-I

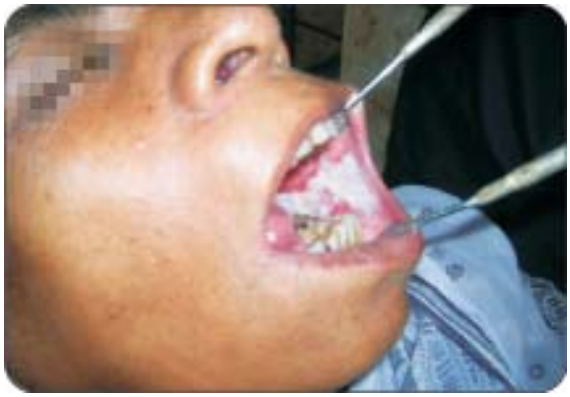

Fig. 2.31: Verrucous carcinoma-II

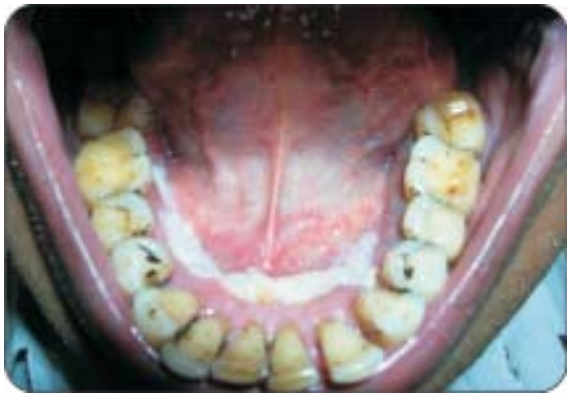

Fig. 2.32: Verrucous carcinoma-III

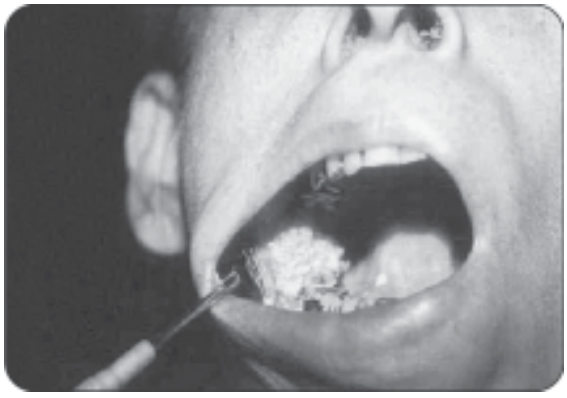

Fig. 2.33: Verrucous carcinoma of the buccal mucosa

- Verrucous carcinoma may occur either as a single entity or there can be multiple lesions developing from different parts of the oral cavity simultaneously.
- Sometimes, 'leukoplakia' may occur in association with verrucous carcinoma or in other cases the tumor may actually develop from within a preexisting leukoplakia.

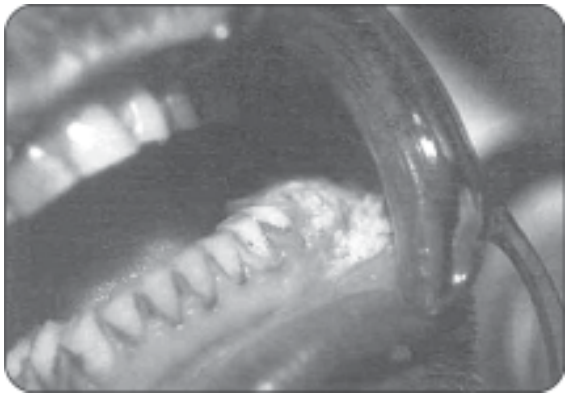

Fig. 2.34: Verrucous carcinoma of the gingiva

- In verrucous carcinoma, majority of the lesions are exophytic and well circumscribed in nature; however, there can be few lesions which are of invasive type and they quickly invade into the underlying tissues including the bone.
- The lesions on the buccal mucosa are sometimes very extensive and they often cause pain, tenderness and difficulty in taking food.
- Verrucous carcinoma of the gingiva or the alveolar mucosa **rapidly becomes fixed to the underlying periosteum** and causes gradual invasion and considerable amount destruction of the jaw bone (Fig. 2.34).
- The regional lymph nodes are often enlarged and tendered. However, these features are only due to the inflammatory reactions in the lymph nodes as a result of secondary infection and are not due to the metastatic spread of the tumor cells.

HISTOPATHOLOGY

Histologically verrucous carcinoma presents the following features:

- The tumor is composed of highly differentiated malignant epithelial cells, which proliferate as broadly papillary structures.
- The tumor cells are locally invasive in nature although distant metastasis is rare in verrucous carcinoma.
- Verrucous carcinoma is a low grade malignancy and the neoplastic cells often lack the usual cytologic criteria of malignancy.
- The hyperplastic epithelium often exhibits a papillary surface, being covered by a thick layer of parakeratin.

- The continuity of the surface is maintained by filliform or broader processes of well differentiated squamous cells and these processes often resemble **"church spires"**.
- The lesion is slow growing and the neoplastic cells spread laterally more rather than vertically.
- Massively enlarged, **bulb-like, acanthotic rete-ridges** are seen, which often invaginate into the underlying connective tissue stroma.
- Many deep cleft-like spaces lined by thick layer of parakeratin, often extend from the surface of the epithelium and project deep into the center of the bulbous rete rides, this phenomenon is known as "**parakeratin-plugging**."
- All the bulbous rete-ridges of the epithelium tend to project into the underlying connective tissue at more or less the same level and this is known as **"pushing margin".**
- In verrucous carcinoma the malignant epithelial cells are usually well- differentiated, mitosis is rare or absent and the cells exhibit almost normal level of maturation.
- The epithelial cells **seldom exhibit severe dysplastic changes** and there is usually no abnormal mitotic activity found in these cells.
- Moreover, besides having some basilar or parabasilar hyperchromatism, there is not even any cytologic atypia seen in the epithelium.
- Formation of epithelial pearls and microcysts are often seen in verrucous carcinoma. The interface between the tumor and the adjacent normal epithelium is well demarcated.
- The basement membrane is almost always intact and the underlying connective tissue shows an intense inflammatory reaction, with numerous chronic inflammatory cell infiltrations in the area.
- Long standing verrucous carcinoma lesions sometimes cause compression of the underlying superficial muscle bundles and saucerization of the cortical bone.
- If left untreated for years together, focal areas of neoplastic cells within verrucous carcinoma may turn into invasive squamous cell carcinoma and cause metastasis.

DIFFERENTIAL DIAGNOSIS

- Papillary hyperplasia
- Verrucous leukoplakia
- Pyostomatitis vegetans
- Squamous cell carcinoma
- Chronic hyperplastic candidiasis
- Pseudoepitheliomatous hyperplasia.

TREATMENT

Surgical excision or laser therapy. Prognosis is good. Anaplastic transformation may sometimes be seen following radiotherapy in verrucous carcinoma.

MALIGNANT MELANOMA

DEFINITION

These are malignant neoplasms arising from the **melanocytes** of the skin or mucous membrane. Malignant melanomas can develop either as 'de novo' lesions or they form due to the malignant transformation of the preexisting '**nevi**'. The neoplasms commonly have an initial radial growth phase, which is followed by a vertical growth phase.

Malignant melanomas are biologically the most unpredictable tumors and are recognized as the most aggressive as well as deadly among all malignant tumors occurring in humans.

Predisposing factors in melanoma

- Sun exposure
- Exposure to artificial ultraviolet rays
- Fair skin, red hair and freckles
- Genetic (familial) factor
- Higher socioeconomic status with regular holidaying habit.

CLINICAL FEATURES

Age: Ranges between 20 to 90 years of age, however maximum number of cases develop in the 5th to 7th decade of life.

Sex: Both sexes are affected but there is a slight male predilection.

Sites: Upto 70 percent lesions occur in the skin, particularly the sun exposed skin of the fair skinned races.

Oral cavity is the primary site for 0.2 to 8 percent of all melanomas. These lesions most frequently affect the **hard palate** and **maxillary alveolar ridge or gingiva**. However, the lips, lower jaw, floor of the mouth, tongue, buccal mucosa and parotid glands are also sometimes affected. For malignant melanomas the other susceptible mucosal areas include the eyes, vulva and vagina, anus and rectum, and upper respiratory tract, etc.

CLINICAL TYPES OF MELANOMA

Superficial spreading melanoma: This type mostly shows radial growth phase, however in long standing lesions vertical growth phase may be seen.

Nodular melanoma: Nodular lesions exhibit only vertical growth phase.

Lentigo maligna melanoma: Also known as 'melanotic freckle of Hutchinson', it characteristically develop as a macular lesion over the malar region, mostly among Caucasian females.

Acral lentiginous melanoma: This lesion occurs as a macular, lentiginous pigmented area around a nodule and is commonly seen over the palms and soles, and fingers and toes.

Mucosal lentiginous melanoma: These are aggressive lesions and are commonly seen on the mucosal surfaces of eye, respiratory tract, esophagus, oral cavity and genitourinary system, etc.

Amelanotic melanoma: Instead of being dark brown or bluish black as the conventional melanomas look like, these lesions appear red or **reddish or pinkish** due to lack of melanin pigmentations.

PRESENTATION (FIGS 2.35 TO 2.37)

- Oral melanomas initiate as macular pigmented focal lesions.
- In melanoma, most of the lesions are pigmented excepting few non-pigmented lesions which are referred to as "**amelanotic melanomas**", and which appear as "slightly" inflamed-looking areas.
- The pigmented lesions are often **dark-brown** or **bluish-black** or simply **black** in appearance.

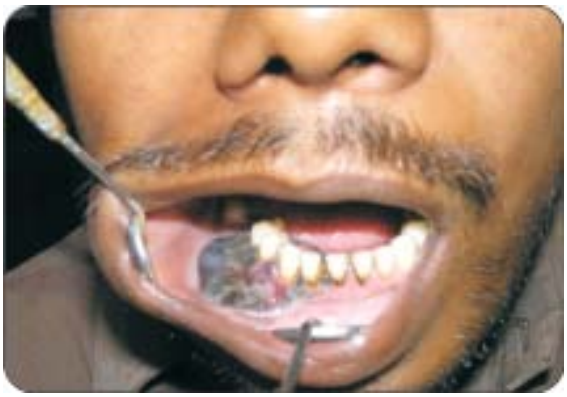

Fig. 2.35: Malignant melanoma-I

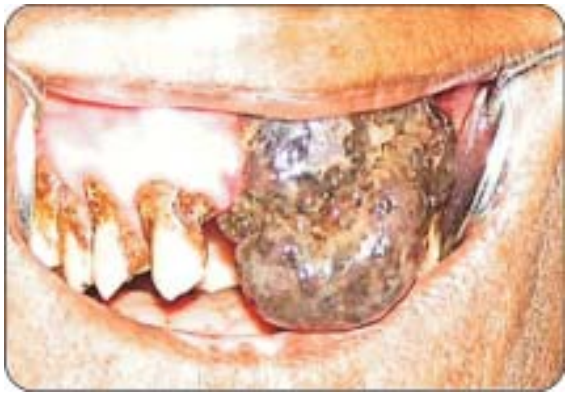

Fig. 2.36: Malignant melanoma-II

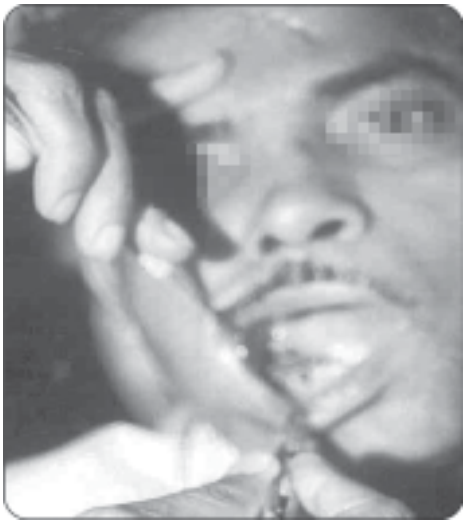

Fig. 2.37: Malignant melanoma of the buccal mucosa

- The initial macular lesions grow very rapidly and often result in a large, painful, diffuse mass.
- Surface ulceration is very common and besides this, hemorrhage, paresthesia and superficial fungal infections are often present.

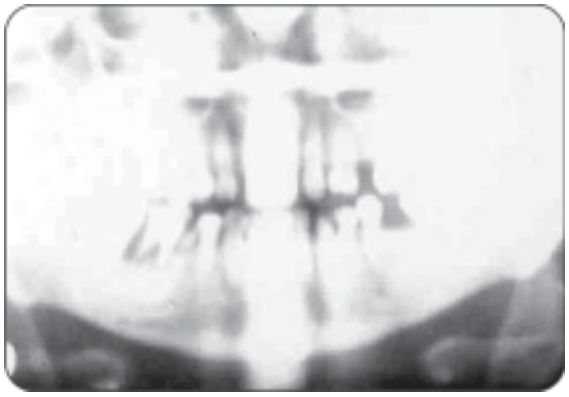

Fig. 2.38: Melanoma causing bone destruction in Rt. lower molar region

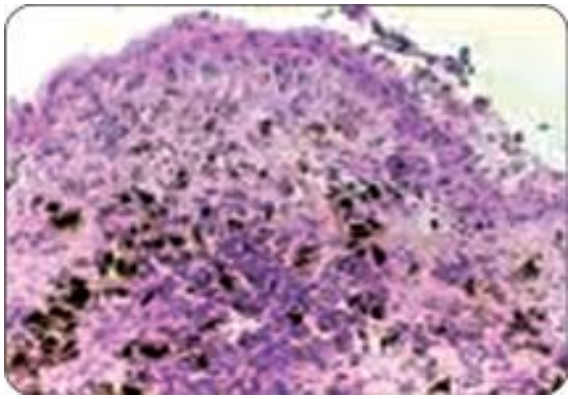

Fig. 2.39: Photomicrograph of malignant melanoma-I

- As the tumor continues to grow, small satellite lesions can develop at the margin of the primary tumor.
- Unlike other epithelial malignant tumors, melanomas exhibit **little or no induration** at the periphery.
- Oral melanomas often cause **rapid invasion and extensive destruction** of bone (Fig. 2.38). This often results in loosening and exfoliation of the regional teeth in the jaw.
- Widespread dissemination of the tumor cells occurs frequently in the lymph nodes as well as in the distant sites, e.g. the lung, liver, bone and brain, etc.
- Survival rates for oral melanomas are extremely low and only less than 5% patients remain alive for 5 years.
- A superficial form of melanoma called "melanotic freckle of Hutchinson" is sometimes reported, which has a more favorable prognosis. This lesion appears as a flat, pigmented spot on the skin or oral mucous membrane.

HISTOPATHOLOGY (FIGS 2.39 AND 2.40)

- Microscopically, malignant melanoma reveals **excessive proliferation of neoplastic melanocytes** in the form of large masses within the dermis or epidermis (Fig. 2.39).
- These malignant melanocytes often exhibit extensive cellular pleomorphism and nuclear hyperchromatism.
- The cells may be round, polyhedral or fusiform in nature and these are either mononucleated or multiancleated.

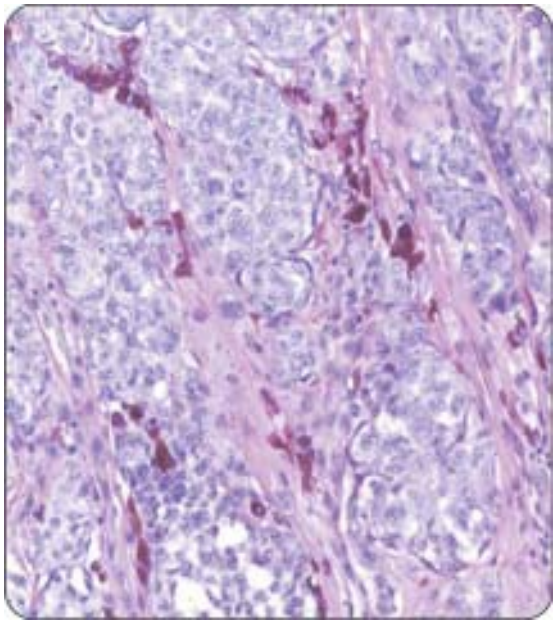

Fig. 2.40: Photomicrograph of malignant melanoma-II

- Mitotic activity is usually numerous and these tumor cells often produce huge amounts of **melanin pigments**.
- However, in some lesions melanin production by the tumor cells can be very little and on few occasions there can be virtually no melanin production.

According to the arrangement of the tumor cells, malignant melanomas can be divided into three specific histologic patterns:

- Hutchinson's freckle type
- Superficial spreading type
- Invasive type.

Hutchinson's Freckle Type

- Histologically, these lesions are characterized by proliferation of pleomorphic, palisaded, malignant melanocytes in a **horizontal direction along the epidermal-dermal junction**.
- These atypical tumor cells do not invade into the upper layers of the epithelium.

Superficial Spreading Type

- This type of melanoma is histologically characterized by the presence of numerous, large, atypical melanocytes within the epithelial layer and the cells exhibit abundant pale cytoplasm.
- The cells are arranged in **small, round clusters at the epidermal-dermal interface** with few areas of focal microinvasions.
- The term **"pagetoid"** is often used to describe the clear cells in the unique intraepithelial growth pattern in this superficial spreading type of melanoma.
- Excessive amount of melanin is often produced by these atypical malignant, melanocytes, moreover, melanin can also be present within the macrophages which are present in the vicinity.

Invasive Type

- The invasive types of melanomas are usually nodular lesions and are characterized by **vertical pattern of growth** of the malignant, melanocytes, which **frequently invade** the underlying connective tissue.
- The malignant pleomorphic cells can be either spindle or ovoid shaped and some cells can be even polygonal in appearance. These cells produce variable amount of melanin pigments.

DIFFERENTIAL DIAGNOSIS

- Kaposi's sarcoma
- Pigmented basal cell carcinoma
- Hemangioma
- Seborrheic keratitis
- Amalgam tattoo
- Hereditary hemorrhagic telangiectasia
- Benign intraoral nevus
- Hematoma

Grades of malignant melanoma

Depending upon the depth unto which the malignant cells have invaded or infiltrated into the connective tissue, malignant melanomas are categorized into 5 grades:	
Grade I	Malignant cells are confined within the epithelium.
Grade II	Malignant cells have invaded into the papillary dermis.
Grade III	Malignant cells have invaded up to the level of reticular dermis.
Grade IV	Malignant cells have completely invaded the reticular dermis.
Grade V	Malignant cells have extended into the subcutaneous fat.

- Venous lake
- Oral melanotic macule
- Dermatofibroma.

TREATMENT

The key to the successful treatment of malignant melanoma is early diagnosis as long as the lesion remains in the radial growth phase. Radical surgery with prophylactic neck dissection is often advised. Regardless of the treatment modalities, the tumors in the vertical growth phase often exhibit very poor prognosis.

SPINDLE CELL CARCINOMA

DEFINITION

Spindle cell carcinoma is a rare, unusual form of poorly differentiated squamous cell carcinoma, consisting of elongated **(spindle-shaped)** epithelial cells. This lesion is also known as **sarcomatoid carcinoma**.

CLINICAL FEATURES

- Spindle cell carcinoma occurs primarily in males and the lesion frequently affects the lower lip, tongue and the alveolar ridge. Some lesions develop in the larynx, pharynx and esophagus as well.
- Clinically, the lesion produces pain, ulceration and swelling, etc. However, the tumor may also

exhibit a characteristic fleshy and polypoid growth pattern.
- Size of the lesion varies from 0.5 to 6 centimeter, very large lesions sometimes cause life threatening air way obstruction.
- The surface of the tumor is almost always extensively ulcerated with a fibrinonecrotic exudate covering it.
- The superficial part of the tumor is a friable granulation tissue, chunk of which may come out while coughing.

HISTOPATHOLOGY

- Spindle cell carcinomas histologically exhibit **two types of cells,** one is the **conventional squamous cells** and the other is the malignant **pleomorphic spindle cells,** both cell types derive from sarcomatous metaplasia of the malignant epithelial cells.
- Although both cell types are present, the **spindle type of cells predominate** in the tumor and proliferation of numerous fusiform or spindle-shaped cells (closely resemble malignant fibroblasts) often make the tumor look like a fibrosarcoma.
- The tumor cells often exhibit marked nuclear hyperchromatism, cellular pleomorphism, increased abnormal mitosis, etc. In some lesions, there may be presence of **tumor giant cells**.
- The squamous type of epithelial cells in the tumor histologically look invasive or *in situ* or verrucous type or they may exhibit only some dysplasia.
- The epithelial cells may loose their cohesive character and often **appear round in shape** and as a result of this, these cells often produce a **pseudosarcomatous** appearance.
- The malignant epithelial cells in spindle cell carcinoma exhibit minimum degrees of epithelial dysplasia with little or no keratin formation.
- The underlying connective tissue stroma reveals inflammatory cell infiltration by lymphocytes, neutrophils and eosinophils, etc.

DIFFERENTIAL DIAGNOSIS

- Fibrosarcoma
- Synovial sarcoma
- Leiomyosarcoma
- Malignant fibrous histiocytoma.

TREATMENT

Spindle cell carcinomas are usually less aggressive than conventional squamous cell carcinomas and these lesions produce late metastasis. Surgical excision is the most effective mode of treatment.

PRIMARY INTRA-ALVEOLAR CARCINOMA

DEFINITION

These are rare malignant neoplasms of epithelial tissue origin, which develop as central jaw lesions with no indication that they have originated from the surface epithelium or they have metastasized from other distant sites.

ORIGIN

The tumor arises from the **cell rests of the odontogenic epithelium** or from the **epithelial remnants** at the site of fusion between two embryonic processes.

CLINICAL FEATURES

Age: Middle aged adults are often affected.

Sex: There is slight male predication.

PRESENTATION

- Primary intra-alveolar carcinoma often causes rapid expansion and destruction of the jaw bones.
- Pain and paresthesia are very common features of this lesion.
- Often there is unexplained loosening of the teeth.
- Perforation of cortical plates and pathological fractures of bone may sometimes occur.
- Extraction of teeth often results in nonhealing of the socket and sometimes the tumor mass may protrude from the nonhealed wound.

RADIOLOGICAL FEATURES

Radiographically primary intra-alveolar carcinoma presents a multilocular radiolucent area with ill-defined borders.

- Expansion and distortion of the cortical plates of the jawbone are common.
- There can be perforation of the cortical plates or occasional pathological fractures.
- There can be severe destruction of the alveolar bone with loosening and displacement of the regional teeth.

HISTOPATHOLOGY

Primary intra-alveolar carcinoma histologically reveals the following features:

- Excessive proliferation of neoplastic epithelial cells either in the form of diffuse sheets or epithelial islands.
- The neoplastic cells often exhibit definite signs of malignancy, e.g. cellular pleomorphism, nuclear hyperchromatism and increased abnormal mitosis, etc.
- Areas of acanthotic changes with epithelial pearl formation are often seen and the overall histologic features closely **resemble the squamous cell carcinoma**.
- Importantly, the odontogenic nature of the tumor is exhibited by the presence of a rim of **ameloblast-like cells** in the position, which is usually assumed by the basal cells in conventional squamous cell carcinoma.

DIFFERENTIAL DIAGNOSIS

- Osteomyelitis
- Osteosarcoma
- Ameloblastoma
- Metastatic carcinoma.

TREATMENT

Radical surgical excision with regional lymph node dissection. Prognosis is poor.

NEOPLASMS OF MESENCHYMAL TISSUE ORIGIN

BENIGN NEOPLASMS OF FIBROUS CONNECTIVE TISSUE

FIBROMA

DEFINITION

Fibroma is a benign neoplasm of fibrous connective tissue origin. It is characterized by excessive proliferation of fibroblast cells with synthesis of large amount of collagen. Although a large number of fibrous over-growths are found inside the oral cavity, most of these are reactive lesions occurring as a result of trauma or local irritation and therefore true fibromas are extremely rare.

CLINICAL FEATURES

Age: Fibromas commonly develop in the third, fourth and fifth decade of life.

Sex: They are more common among females.

Site: Intraoral fibromas often develop from the gingiva, however, these lesions may also develop from buccal mucosa, tongue, lips and palate as well.

CLINICAL PRESENTATION (FIGS 2.41 TO 2.43)

- Clinically, fibromas appear as small, asymptomatic, round or oval, well-circumscribed, slow enlarging, nodular growths in the oral cavity.
- The size varies between 1 to 2 cm in diameter.
- These lesions can be either pedunculated or sessile and their surface is usually smooth.
- On palpation, these lesions are either soft or firm in consistency and the overlying covering epithelium often appears normal in color.
- Persistent trauma or injury to these lesions often causes pain, inflammation or surface ulceration, etc.
- Sometimes , the surface may be hyperkeratotic.

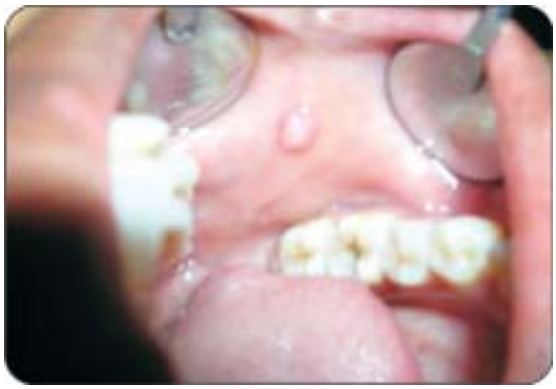

Fig. 2.41: Fibroma-I

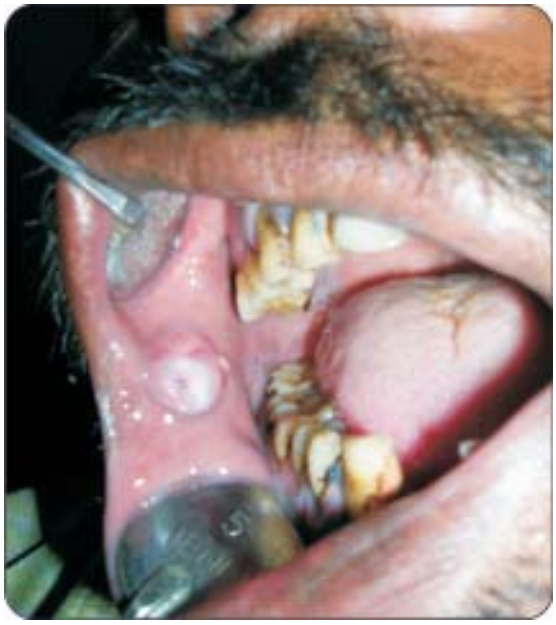

Fig. 2.42: Fibroma-II

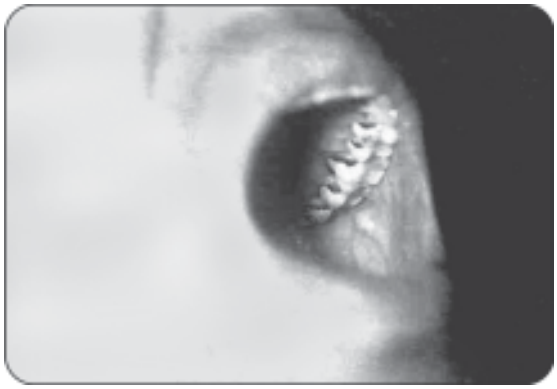

Fig. 2.43: Fibroma of the left cheek

DIFFERENTIAL DIAGNOSIS

- Giant cell fibroma
- Neurofibroma
- Peripheral giant cell granuloma
- Mucoceles
- Salivary gland (minor) neoplasms.

HISTOPATHOLOGY

- Histologically, the neoplasm reveals unencapsulated, solid, nodular mass of dense and sometimes hyalinized connective tissue, which is often arranged in haphazard fascicles (Fig. 2.44).
- The proliferating neoplastic fibroblast cells are large in numbers and they exhibit production of excessive amount of collagen.

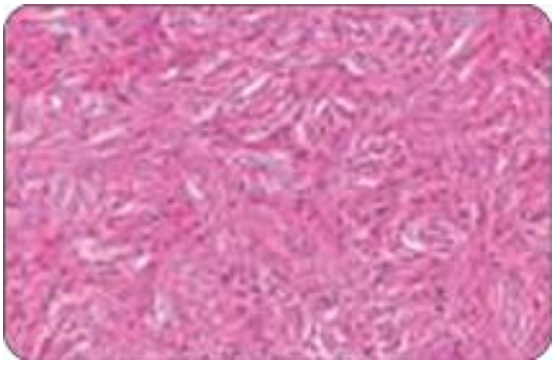

Fig. 2.44: Photomicrograph of fibroma

- The neoplastic fibroblast cells often appear "**spindle-shaped**" and they have prominent hyperchromatic nuclei.
- **Thick bundles of collagen fiber** are characteristically present throughout the lesion. Sometimes, concentric layers of collagen fibers may produce a **capsule** or **pseudocapsule** around the periphery of the lesion.
- The overlying epithelium is **thin** and it often shows **flattening of the rete pegs**. Sometimes it may be hyperplastic or hyperkeratotic.
- Connective tissue stroma is relatively avascular and in some lesions there may be presence of small foci of calcified or ossified tissue within it.
- In few cases, chronic inflammatory cell infiltration may be found within the connective tissue stroma, especially, those lesions which are often traumatized or ulcerated.

TREATMENT

By surgical excision.

DESMOPLASTIC FIBROMA

DEFINITION

These are rare benign primary fibroblastic neoplasms arising from the mesenchymal tissue of the jawbone but are not necessarily related to the teeth. The tumor is characteristically composed of well-differentiated collagen producing cells.

CLINICAL FEATURES

Age: First, second and third decade of life. Older patients are rarely affected.

Sex: Both sexes are equally affected.

Site: Mandible is affected more often than maxilla and majority of the lesions occur posterior to the premolar region (molar, angle and ascending ramus areas).

CLINICAL PRESENTATION

- These intraosseous fibromas are generally asymptomatic neoplasms, however some lesions may produce painless swelling in the jaw.
- Lesions are nontendered on palpation and moreover percussion of the regional teeth also does not elicit any tenderness.
- Long standing lesions may cause expansion or perforation of the cortical plates of jaw bone.
- Few lesions even corode through the cortical bone of the jaw and protrude outside as a soft tissue lump.
- Few lesions are locally infiltrative and may cause painful swelling in the jawbone.
- Difficulty in mouth opening is frequently associated with desmoplastic fibroma.

RADIOGRAPHIC FEATURES

- Radiographically desmoplastic fibromas reveal unilocular or occasionally multilocular, well-defined, radiolucent areas in the bone.
- Occasionally these lesions can be poorly defined and in most of the cases there is resorption of the roots of the adjoining teeth.
- Expansion, thinning and even perforation of the cortical plates may be seen in some cases.

DIFFERENTIAL DIAGNOSIS

- Ameloblastoma
- Central giant cell granuloma
- Myxoma
- Central ossifying fibroma.

MACROSCOPIC FEATURES

- Macroscopically desmoplastic fibroma often appears as a small, circumscribed growth of fibrous tissue, which is firm in consistency.
- The cut surface of the lesion appears as a greyish-white mass, with interlacing strands of fibers running across it.

HISTOPATHOLOGICAL FEATURES

- The neoplasm consists of numerous small, elongated, proliferating young fibroblasts, which are arranged in a whorled pattern.
- The neoplastic cells produce varying amounts of collagen fibers in the tumor.
- In some areas of the tumor, the collagen fibers produce thick bundles and in these areas the fibroblast cells are only few in numbers.
- In other areas, the fibroblasts are numerous and there is only little amount of collagen present. Intratumor ossification is usually not seen.
- The collagen fibers are usually thin and delicate with fasciculation, often these collagen bundles produce a `**herring-bone'** or '**chevron**' or '**stori-form'** configuration.
- Few bony spicules may be seen at the interface between neoplasm and the adjacent bone.
- In some cases the tumor mass may extend into the adjacent normal tissues by perforating the cortical plates of bone.

TREATMENT

Radical surgery is not indicated for the treatment of desmoplastic fibromas. Local excision and curettage can be enough. However even in properly treated cases recurrence is expected in about 25% cases.

GIANT-CELL FIBROMA

DEFINITION

Giant cell fibromas are distinct neoplastic entities which arise from the fibrous connective tissue.

CLINICAL FEATURES

Age: Most of the giant cell fibromas develop in the first, second or third decade of life. (Mostly diagnosed in persons aged between 10–30 years).

Sex: Slightly more prevalent among females.

Site: Maxillary or mandibular gingiva is most frequently affected (50 percent of all intraoral cases), moreover mandibular gingiva is affected twice as often as maxillary gingiva. Besides this tongue, palate (Fig. 2.45), and buccal mucosa may also be affected.

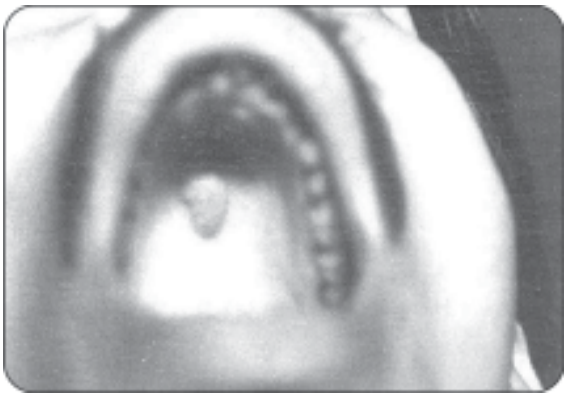

Fig. 2.45: Giant cell fibroma of the palate

PRESENTATION

The unique clinical characteristic of the lesion is its asymptomatic, pedunculated type of nodular growth. Sometimes it can be sessile.

- The lesion usually has a papillary or warty (bosselated) surface and thus sometimes can be mistaken for a papilloma.
- The size is generally less than 1 cm in diameter.
- Some tumors may present a painless, non-ulcerated growth and it generally measures about less than 1 centimeter in size.

DIFFERENTIAL DIAGNOSIS

- Squamous papilloma
- Fibroepithelial polyp
- Peripheral giant cell granuloma
- Irritation fibroma.

HISTOPATHOLOGY

- Giant cell fibroma microscopically presents an unencapsulated mass of fibrous connective tissue.
- Often there are numerous, actively proliferating, large, plump spindle-shaped or stellate fibroblasts in the tumor with formation of several collagen bundles.
- Presence of **multiple multinucleated giant cells** is the hallmark in the histopathology of this lesion.
- The nuclei within the giant cells are large, hyperchromatic and vesicular. The cytoplasm exhibits prominent dendritic processes and it also contains several melanin granules.
- In the tumor the giant cells are predominantly seen near the periphery while the center of the tumor is often filled with typical fusiform fibroblast cells.
- Numerous small blood capillaries are often present within the tumor and few inflammatory cells may also be seen occasionally.
- The covering epithelium is generally corrugated and atrophic, however the rete pegs are thin and elongated.

TREATMENT

By conservative surgical excision. Recurrence is rare.

MYOFIBROMA

DEFINITION

Myofibroma is a rare benign solitary neoplasm characterized by proliferation of spindle shaped myofibroblasts (cells with both smooth muscle and fibroblastic features).

CLINICAL FEATURES

***Age*:** Children and young adults.

Sex: Both sexes equally affected.

Site: Lips, cheek, tongue and mandible, etc.

CLINICAL PRESENTATION

Myofibroma typically produces a slow enlarging, painless, well circumscribed mass. Some lesions can be fast enlarging and when multiple myofibromas occur the condition is known as 'myofibromatosis'. Intraosseous lesions cause bony hard swelling with expansion of cortical plates of the jaw.

RADIOGRAPHIC FEATURES

Intraosseous myofibromas cause unilocular or multilocular radiolucent areas in the jaw with poorly defined borders.

HISTOPATHOLOGICAL FEATURES

Neoplastic proliferation of spindle shaped myofibroblast cells containing tapered or blunt nuclei. Some areas of the tumor is highly cellular, while the other areas are hyalinized with little cellularity. The central area often has a hemangiopericytoma like appearance.

TREATMENT

By local excision.

PERIPHERAL OSSIFYING FIBROMA

DEFINITION

Peripheral ossifying fibroma is an exophytic nodular growth, which commonly occurs on the gingiva and is consisting mosly of hyperplastic connective tissue with focal areas of bone.

ORIGIN

The neoplasm develops as a result of reactive proliferation of either the periodontal or the periosteal tissues. Since both the periodontal and the periosteal tissues contain cells which have some osteogenic potential, it is believed that ossification within peripheral ossifying fibroma is a reflection of the inherent nature of its tissue of origin. Local irritation always plays a significant role in the development of this lesion.

CLINICAL FEATURES

Age: It predominantly occurs among children and young adults.

Sex: More common among females.

Site:

- Peripheral ossifying fibromas occur exclusively on the gingiva (mostly on the superficial part of the interdental papilla). More than half of the cases occur within the incisor-cuspid area and lesions have slight predilection for the maxillary arch.
- Occasionally it can develop from the buccal or lingual attached gingiva.
- Rarely, the lesion may be seen on the edentulous ridge.

PRESENTATION (FIG. 2.46)

- The neoplasm clinically presents a small, painless, lobulated or nodular swelling on the gingiva.
- It can be either pedunculated or sessile growth, which typically projects from the interdental papilla.
- The overlying mucosa often appears normal, although in some cases it appears reddish.

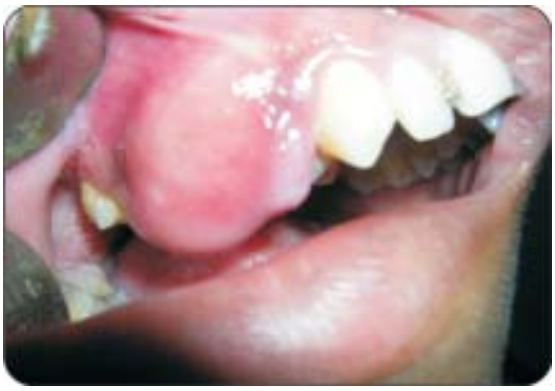

Fig. 2.46: Peripheral ossifying fibroma

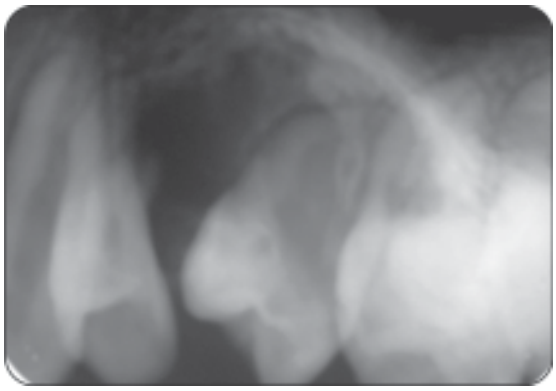

Fig. 2.47: Radiograph of peripheral ossifying fibroma

- The surface of the lesion is usually smooth, although in some cases there can be ulceration on the surface.
- The regional teeth are mostly unaffected. However, there can be migration or loosening of teeth in few cases due to pressure from of the lesion.
- These lesions are either hard or firm on palpation and often they are fixed to the underlying tissue.
- Most lesions are less than 2 centimeter in diameter, although larger lesions may occasionally develop.

RADIOGRAPHIC FEATURES

- Radiograph often reveals the presence of some radiopaque foci within tumor mass, having varying radiodensities (Fig. 2.47).

HISTOPATHOLOGY

- Histologically peripheral-ossifying fibroma exhibits diffuse sheets of proliferating,

immature fibroblasts with plump monomorphic nuclei.
- Hyalinization of the collagen fibers is sometimes noticed, however, the overall picture represents a hypercellular reactive tissue.
- Varying amounts of calcified materials are often present in the lesion, which may be osteoid, cementoid or dystrophic in nature.
- The osteoids can be of varying shape and size; and are often randomly deposited within the fibrous tissue mass.
- Besides the osteoids, the mineralized components of the neoplasm also contain cementum like materials as well as some areas of dystrophic calcifications.
- The remaining area (other than the area of calcification) of the tumor resembles simple fibroma.
- The covering epithelium appears normal but sometimes it can be ulcerated. Whenever the epithelium is ulcerated it is mostly covered by a fibrinopurulent membrane with a subsequent zone of granulation tissue.
- Dystrophic calcification occurs more often in ulcerated lesions either as several small globules or large basophilic masses.
- The bone within the neoplasm is generally of woven or trabecular type, however on rare occasions, thick mature foci of bony trabeculae may be present within the lesion.
- On few occasions multinucleated giant cells can be present in the neoplasm in association with the calcified tissue.
- There is no capsule in this tumor and the hypercellular zone gradually merges with the normal healthy fibrous tissue at the periphery.

DIFFERENTIAL DIAGNOSIS

- Peripheral giant cell granuloma
- Fibroma
- Fibroepithelial polyp
- Peripheral ameloblastoma
- Peripheral odontogenic fibroma
- Pyogenic granuloma
- Inflammatory gingival hyperplasia.

TREATMENT

By surgical excision down to the periosteum along with thorough curettage. The associated teeth are preserved.

CENTRAL OSSIFYING FIBROMA

DEFINITION

Central ossifying fibroma represents a well-demarcated, encapsulated, expansile, central jaw lesion that is composed of cellular fibrous tissue, with spherical calcifications and irregular randomly oriented bony structures. It is a rare but true neoplasm of bone with significant growth potential.

CLINICAL FEATURES

Age: Greatest numbers of cases occur in children and young adults.

Sex: More predilection for females.

Site: Mandible is far more commonly affected than maxilla. The disease often involves posterior to the canine area.

PRESENTATION (Figs 2.48 and 2.49)

Central ossifying fibroma clinically presents the following features:
- There will be a localized, painless, non-tendered, bony hard swelling in the jaw (Fig. 2.50).
- In most of the cases a single lesion usually develops, but sometimes more than one lesion may also be seen in the jaw.
- The tumor is normally slow growing and gradual increase in its size causes facial deformity.
- Expansion and distortion of the cortical plates and displacement of the regional teeth are often seen.
- Pain and paresthesia generally do not occur in case of central ossifying fibroma.
- Although most of the lesions follow a simple benign course, some lesions especially those affecting the children may be rapidly growing and locally aggressive in nature (Fig. 2.50A). The fast growing lesion produce a massive swelling, and are often referred to as "aggressive ossifying fibromas" and they cause severe disfigurement of the face.

RADIOGRAPHIC FEATURES (Figs 2.51 and 2.52)

- Radiographically, central ossifying fibroma presents a well-defined, mostly unilocular or

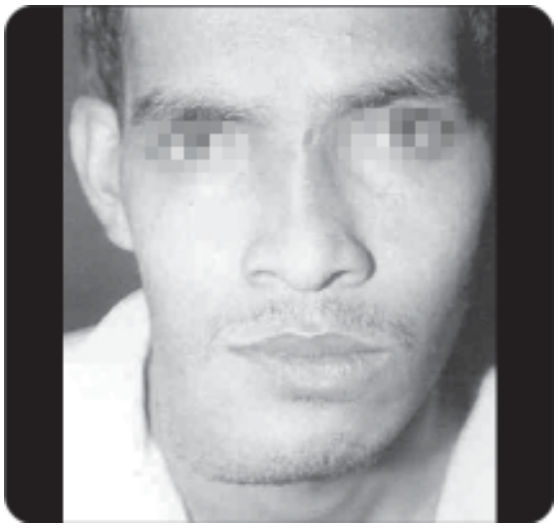

Fig. 2.48: Central ossifying fibroma of mandible

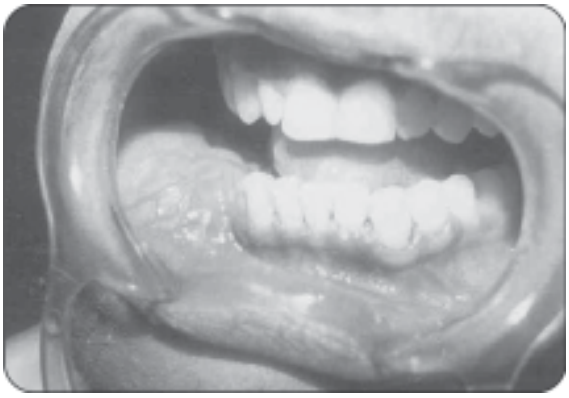

Fig. 2.49: Intraoral view of the same patient

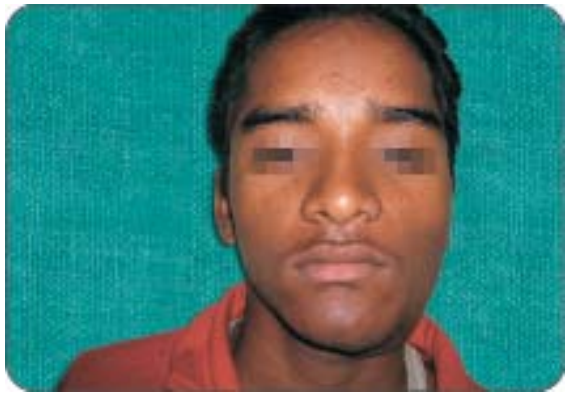

Fig. 2.50: Central ossifying fibroma

sometimes multilocular radiolucent area with clearly demarcated borders (Fig. 2.51).

- Expansion of the cortical plates and a smooth, downward bowing expansion of the lower border of the mandible are commonly observed.

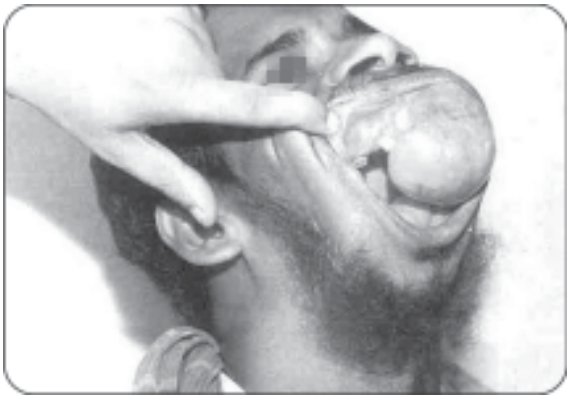

Fig. 2.50A: Aggressive ossifying fibroma

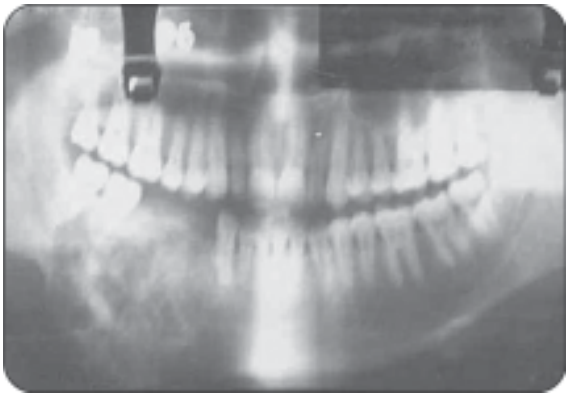

Fig. 2.51: Central ossifying fibroma showing large area of radiolucency interspersed with irregular radiopacities on Rt. side of mandible

- The lesion often extends between the roots of the teeth and causes root divergence and displacement of teeth. Root resorption may sometimes occur.
- In the earlier stages, the lesion is small and is almost completely radiolucent.
- As the lesion enlarges multiple, small radiopaque areas gradually appear within it.
- In the more mature stages of the disease, large radiopaque masses are seen within the lesion that almost completely fill up the area with only a thin rim of radiolucency separating the lesion from the surrounding normal bone.
- In ossifying fibroma, the neoplasm does not blend with the surrounding normal bone, rather it is always demarcated from it by a thin zone of fibrous tissue capsule.

MACROSCOPIC FEATURES

- The cut surface of central ossifying fibroma often exhibits a whitish-yellow mass, with

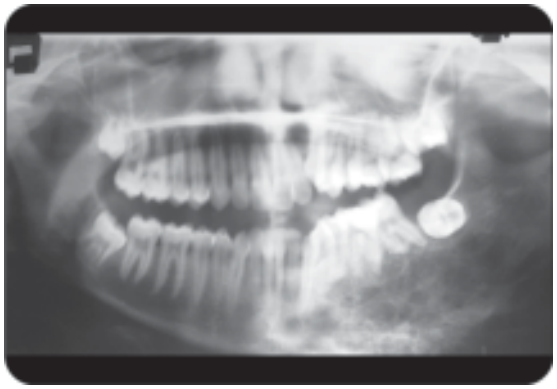

Fig. 2.52: Radiographic view of central ossifying fibroma

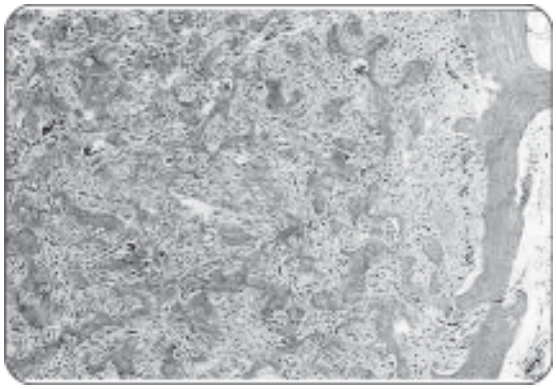

Fig. 2.53: Photomicrograph of central ossifying fibroma

variable consistency and the tissue always has a gritty surface.

HISTOPATHOLOGY

Histologically central ossifying fibromas reveal the following features (Fig. 2.53):

- A highly cellular fibroblastic stroma with the presence of delicate collagen fibers, which are arranged in a typical "**whorled pattern**".
- The lesion is well demarcated from the normal bone by a thin zone of fibrous capsule.
- Numerous blood capillaries run across in stroma although intralesional major hemorrhage is rarely seen.
- In early lesions, the fibrous elements often predominate and there can be presence of multiple small foci of osteoid trabaculae of variable size and shape, the osteoids at this stage are poorly calcified.
- In more mature stages of the disease, osteoid tissues within the lesion increase in size, as small individual osteoid trabeculae fuse together and give rise to large irregular calcified masses.
- Besides osteoids, there may be presence of mature bone as well as poorly cellular, basophilic spherules that resemble cementum.
- These spherules of cementum like material often exhibit peripheral brush borders that blend into the adjacent connective tissue.
- In central ossifying fibroma various types of calcified materials are seen such as osteoids, bone and cementum like—spherules, etc. This structural pattern typically differs from fibrous dysplasia as the later exhibits a more uniform pattern of osseous differentiation.
- There is little or no mitotic activity seen in the cellular elements and no cellular atypia is usually evident in ossifying fibroma.

DIFFERENTIAL DIAGNOSIS

- Fibrous dysplasia of bone
- Desmoplastic fibroma
- Central giant cell granuloma
- Myxoma
- Schawnnoma.

TREATMENT

Surgical enucleation is the treatment of choice and can be easily accomplished in smaller lesions. The aggressive lesions of central ossifying fibroma may require radical treatments like resection and bone grafting, especially in cases of repeated recurrences.

PERIPHERAL GIANT CELL GRANULOMA

DEFINITION

Peripheral giant cell granuloma is the most common of the giant cell lesions, which arises from the tooth bearing areas of the jaw and appears as a purplish-red nodule.

ORIGIN

The lesion probably develops from the connective tissue of the periosteum of jaw bone or from the periodontal ligament tissue.

CLINICAL FEATURES

Age: The lesion usually arises either during the mixed dentition period or during the third and forth decade of life.

Sex: Definite predilection for females. (M:F—3:1.)

Site: From the interdental papilla in dentulous patients. Sometimes, it can also develop from the edentulous alveolar ridge. Mandible is more frequently affected than maxilla.

CLINICAL PRESENTATION (FIGS 2.54 TO 2.56)

- Peripheral giant cell granuloma clinically appears as a small, exophytic, well-circumscribed, pedunculated lesion on the gingival surface (Fig. 2.56).
- The lesion is usually painless, firm and lobulated and the surface is either smooth or granular.

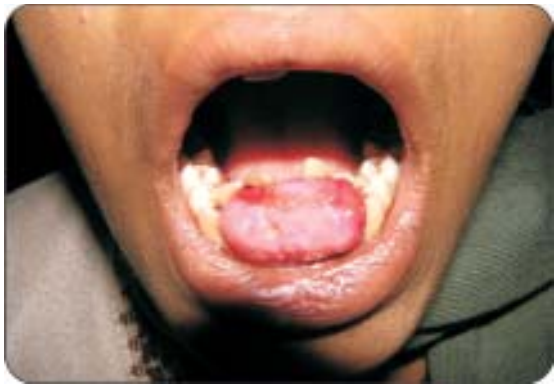

Fig. 2.54: Peripheral giant cell granuloma-I

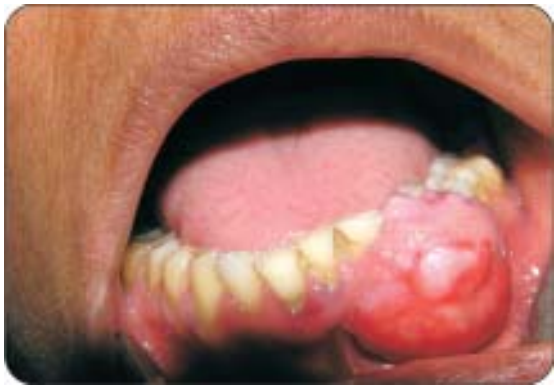

Fig. 2.55: Peripheral giant cell granuloma-II

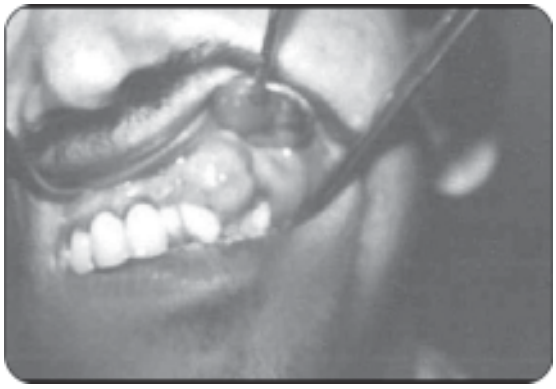

Fig. 2.56: Peripheral giant cell granuloma of the gingiva

- Most lesions of peripheral giant cell granulomas measure less than 2 centimeter in diameter, however larger lesions are also occasionally seen.
- The color of the lesion varies from purplish-red to dark-red and the overlying epithelium is often ulcerated.
- Some of the lesions could be firm in consistency and these are often relatively pale in appearance.
- There can be bleeding from the surface of the lesion either spontaneously or upon provocation with an instrument.
- Careful examination of the lesion reveals multiple, small areas of hemosiderin pigmentation on the surface of the lesion.
- Since the lesion develops and descends from the deeper periodontium, it may increase the space between the affected teeth.
- Sometimes, peripheral giant cell granulomas can be aggressive in nature and such lesions may attain a very large size and they may involve several teeth.
- Like any other reactive gingival growths, this lesion may also frequently occur in pregnant women.
- In some cases the lesion may develop with an 'hour-glass' shape and in such cases the waist of the lesion is located between the teeth and the lobulated extremities projecting both buccally and lingually.
- Clinically, peripheral giant cell granuloma often looks very similar to pyogenic granuloma, however, peripheral giant cell granulomas are more firm in consistency and are bluish-purple in color, whereas pyogenic granulomas are

much softer in consistency and are more reddish in color.

RADIOGRAPHIC FEATURES

Peripheral giant cell granuloma has the potential to erode the underlying alveolar bone and on radiograph this type lesion is often known as "**peripheral cuffing**" of bone (Fig. 2.57).

MACROSCOPIC FEATURES

- Macroscopically, peripheral giant cell granuloma appears as a lobulated, firm growth having a pedunculated base.
- The cut surface of the lesion often presents a homogeneous, reddish-brown, granulomatous tissue.
- Some lesions may exhibit a peripheral brownish zone that is interrupted by pale radiating streaks.
- The surface epithelium is often ulcerated and there is also presence of several pigmented spots (blood pigments).

HISTOPATHOLOGY

Peripheral giant cell granuloma usually presents the following histologic features (Fig. 2.57A):

- The overlying covering epithelium is mostly ulcerated with areas of hemorrhage.
- The underlying connective tissue stroma reveals numerous proliferating **fibroblasts, blood capillaries** and **multiple multinucleated giant cells,** which are scattered throughout the lesion.
- The entire lesion is situated within the sub-epithelial connective tissue of gingiva and is separated from the overlying epithelium by a thin rim of fibrous septa.
- The fibroblasts present in the hypercellular stroma are mostly plump ovoid or spindle shaped and they contain oval shaped nuclei.
- The giant cells are often larger in size and contain only few to several dozens nuclei, (more number of nuclei in individual giant cells as compared to that of true giant cell tumors).
- The nuclei within the giant cells can either be large vesicular in nature or they can be small, pyknotic type of nuclei.

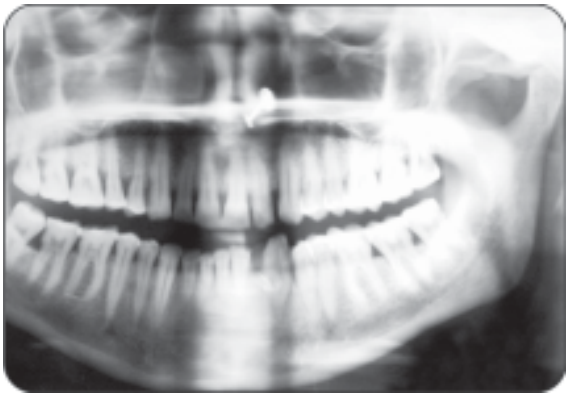

Fig. 2.57: Radiograph of peripheral giant cell granuloma

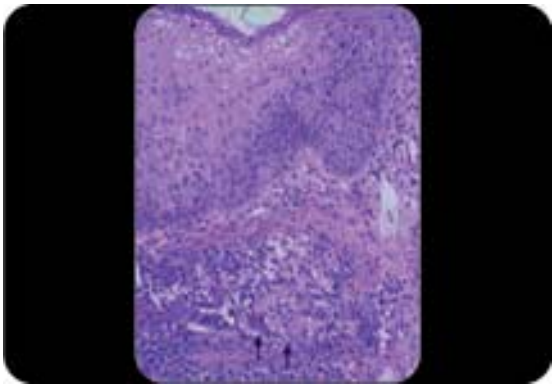

Fig. 2.57A: Photomicrograph of peripheral giant cell granuloma (demonstrated by arrows)

Key points of peripheral giant cell granuloma

- Most common giant cell lesions of the oral cavity arises from the tooth bearing areas of jaw.
- More commonly seen in females and the lesion often presents small, lobulated, purplish-red colored, pedunculated growth with occasional surface ulcerations and bleeding, etc,
- Lesions are exophytic, mostly painless, grow in the gingival area in a typical 'hour glass' pattern, pressure from the growing lesions may create gap between teeth.
- The radiograph reveals "peripheral cuffing" in the bone.
- Histologically, the lesion exhibits overlying thin ulcerated epithelium and the underlying connective tissue shows proliferating, fibroblasts, numerous blood capillaries and multiple multinucleated giant cells, etc.
- The giant cells are large and they tend to group around the blood capillaries.

- Interestingly, the giant cells in this lesion often **tend to aggregate or assemble around the blood capillaries** and in few cases, they can be even found within the lumen of the capillaries.
- The mitotic activity is very high in the mesenchymal cells of the tumor.
- Intercellular edema is sometimes present within the connective tissue stroma and often there is little chronic inflammatory cell infiltration.
- Areas of **hemorrhage and hemosiderin pigments** are often present within the connective tissue stroma.
- Sometimes foci of osteoids or even mature bone tissue may be present within the stroma, especially near the periphery.

DIFFERENTIAL DIAGNOSIS

- Pyogenic granuloma
- Fibroepithelial polyp
- Peripheral ossifying fibroma
- Fibroma
- Traumatic neuroma.

Common giant cell lesions of oral cavity

- Peripheral giant cell granuloma
- Central giant cell granuloma
- Brown tumor of hyperparathyroidism
- Giant cell tumor of bone (osteoclastoma)
- Cherubism
- Fibrous dysplasia of bone
- Aneurysmal bone cyst
- Hodgkin's lymphoma
- Fibrous histiocytoma
- Calcifying epithelial odontogenic cyst.

TREATMENT

By surgical excision with curettage.

CENTRAL GIANT CELL GRANULOMA

DEFINITION

Central giant cell granuloma is a relatively common **benign intraosseous destructive giant cell lesion**, which often affects the anterior part of the jawbone.

Lesions similar to central giant cell granulomas can occur in relation to the long bones as well and they often follow an aggressive course. Central giant cell granuloma is often confused with giant cell tumor of bone (osteoclastoma), however, it should be noted that **giant cell granuloma is a reactive lesion**, whereas **giant cell tumor is a neoplastic condition** of the bone. Moreover osteoclastomas are very rarely seen within the jawbones.

CLINICAL FEATURES

Age: This lesion usually occurs among young adults (mostly below the age of 30).

Sex: Female predilection (female to male ratio is 2:1).

Site:

- Central giant cell granulomas affect mandible more often (nearly 70 percent cases) than maxilla. The lesions occur mostly in the body of the mandible anterior to the first molar area (in the zone where previously the deciduous teeth existed).
- Most of the lesions develop in the tooth bearing areas of jaw and some lesions may even cross the midline of the mandibular bone.
- On rare occasions, central giant cell granuloma may develop from the palate or from the mandibular condylar region.

PRESENTATION (Figs 2.58 and 2.59A)

- Most of the central giant cell granulomas are asymptomatic lesions and are discovered incidentally during routine radiographic examinations.
- Other lesions produce small, slow enlarging and bony hard swelling of the jaw, with expansion of the cortical plates.

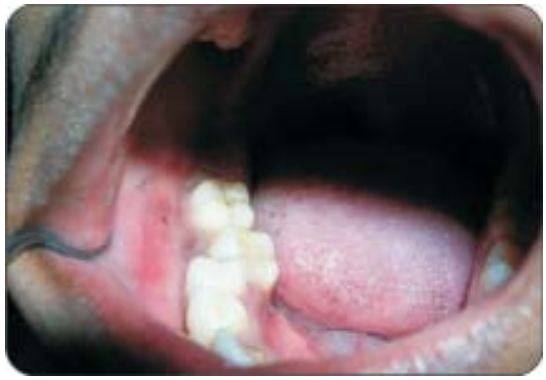

Fig. 2.58: Central giant cell granuloma-I

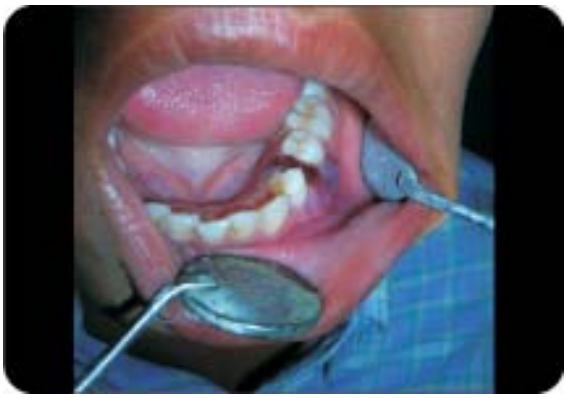

Fig. 2.59: Central giant cell granuloma-II

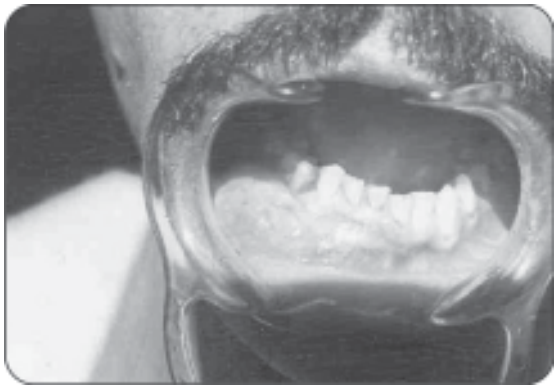

Fig. 2.59A: Central giant cell granuloma of mandible

- Some lesions produce **pain and paresthesia in** the jaw.
- The lesion causes expansion and distortion of both buccal and lingual cortical plates and often there is displacement or mobility of the regional teeth.
- Some lesions **may cause perforation of the cortical plate** and as a result of this, the intra bony lesions may protrude outside jawbone as a **flat-based, dome-shaped, soft, purplish nodule** over the alveolar ridge.
- Central giant cell granulomas sometimes follow an aggressive course and in such cases they produce a fast enlarging, large, painful swelling in the jaw, with anesthesia or paresthesia in the region.
- Larger lesions often cause **loosening or displacement of teeth** in the jaw and **root resorptions**.
- Sometimes, ulceration of the surface epithelium may be seen, especially in larger lesions, and it could be due to either continuous expansion of the underlying tumor or due to trauma from the opposing teeth.
- The teeth in the affected region are always vital.
- On rare occasions, more than one lesion of central giant cell granuloma may develop simultaneously in the jaw.

RADIOLOGICAL FEATURES (Figs 2.60 to 2.62)

- Radiographically the lesion produces a well delineated, multilocular radiolucent area in the jaw, with a '**soap-bubble**' appearance.
- The margin of the lesion is usually **scalloped** and well-demarcated, but it is always non-corticated.
- Sometimes central giant cell granulomas can be unilocular and they produce **"drop-shaped"** radiolucencies in the jawbone and such lesions often resemble cysts.

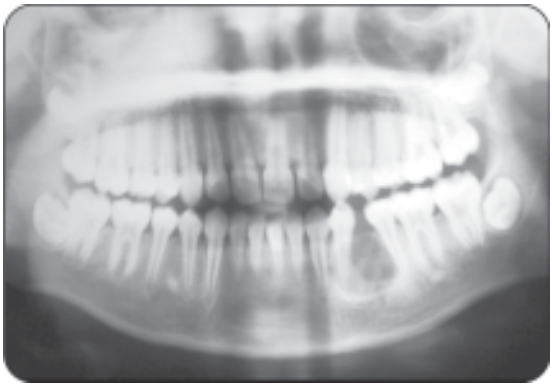

Fig. 2.60: Radiograph of central giant cell granuloma

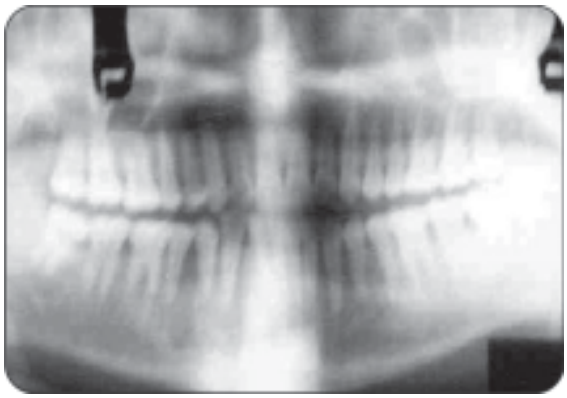

Fig. 2.61: Central giant cell granuloma causing destruction of bone in mandibular Rt. premolar region

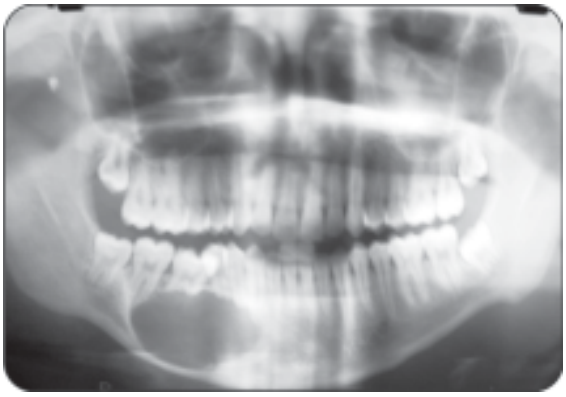

Fig. 2.62: Radiograph of central giant cell granuloma

- Expansion and distortion of the cortical plates are common and in some cases there may be perforation of the cortical plate.
- Resorption of roots of the nearby teeth or divergence of roots is common feature of this lesion.
- Radiographically, the smaller lesions measure about 5 × 5 milimeter in dimension, while the bigger aggressive lesions can be as large as 10 centimeter in diameter.

HISTOPATHOLOGY

- Histologically, central giant cell granuloma exhibits a lobulated mass of fibrovascular connective tissue, consisting of numerous proliferating ovoid or spindle shaped stromal cells and variable amount of interlacing collagen fibers.
- Multiple multinucleated giant cells of varying size are dispersed throughout the fibrous tissue stroma, where numerous small blood capillaries are also found.
- Sometimes giant cells may assamle in great numbers in a focal area of the tumor.
- Several areas of hemorrhage and hemosiderin pigmentation are also evident.
- Giant cells are often found around the blood capillaries or near the areas of hemorrhage.
- In central giant cell granuloma, the small giant cells usually contain about 5 nuclei, however the larger giant cells of the same lesion may contain as many as 20 or mere nuclei.
- The stromal cells are plump and spindle-shaped and these cells often exhibit frequent mitosis.
- Small foci of osteoids or oven normal bone are often found near the periphery of the lesion.

Key points of central giant cell granuloma

- This is a central jaw lesion, which causes bony hard swelling with expansion of the bone.
- The disease is a type of reactive lesion and not a truly neoplastic one.
- Although some lesions are aggressive in nature but it is generally a slow enlarging and painless condition.
- Expansion of the bone occurs with occasional cortical perforation, tooth mobility and root resorptions.
- Radiograph reveals multilocular jaw lesions, generally anterior to the first molar regions, some lesions are typicaly 'drop-shaped'.
- Histologically, the lesion shows proliferating spindle shaped stromal cells in a fibrovascular connective tissue stroma, which characteristically contains multiple multinucleated giant cells.
- Hemorrhage and hemosiderin pigmentations are often seen in tumor.

- There may be little amount of chronic inflammatory cell infiltration in the connective tissue stroma, moreover the older lesions may exhibit considerable degrees of fibrosis in the connective tissue stroma.
- Central giant cell granuloma and giant cell tumor of bone one often confused histologically, but the fact is that in central giant cell granuloma the giant cells are relatively less in number and are very irregularly distributed throughout the lesion.
- Whereas, in giant cell tumor of bone (osteoclastoma), the number of giant cells are more in number and they are evenly distributed throughout the stroma.

PATHOGENESIS

The exact etiopathogenesis of central giant cell granuloma is not known, however few probable causes have been suggested by different investigators which are as follows:

- According to some investigators, **central giant cell granuloma** develops as a **reparative**

process in response to the intrabony hemorrhage or inflammation.
- Some other scientists believe that central giant cell granuloma is a truly neoplastic condition.
- According to other investigators, the lesion occurs as a developmental anomaly and its pathogenesis is similar to that of aneurysmal bone cyst.

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis of central giant cell granuloma following lesions should be included:
- Brown tumor of hyperparathyroidism
- Giant cell tumor of bone
- Ameloblastoma
- Aneurysmal bone cyst
- Central odontogenic fibroma
- Fibrous dysplasia
- Cherubism
- Odontogenic keratocyst
- Calcifying epithelial odontogenic cyst
- Osteoblastoma.
- Myxoma.

N.B. It is often difficult to differentiate between central giant cell granuloma and brown tumor of hyperparathyroidism on the basis of clinical, radiological and histopathological features. For this reason biochemical analysis of blood is always necessary. Normally the raised serum calcium and serum alkalyne phosphatase level along with depressed serum phosphate levels confirm the diagnosis of hyperparathyroidism. However, in cases of central giant cell granuloma the above mentioned biochemical changes in the blood is not observed.

TREATMENT

Surgical excision and thorough curettage.

BENIGN FIBROUS HISTIOCYTOMA

DEFINITION

Benign fibrous histiocytoma is a locally aggressive benign neoplasm of fibroblasts with a propensity to differentiate into histiocytes. These tumors actually arise from the facultative fibroblasts, which are mesenchymal cells that have potential to differentiate into both fibroblasts and histiocytes.

CLINICAL FEATURES

Age: These tumors usually arise in the middle aged and older adults.

Sex: Male people are more prove to develop this lesion as compared to females.

Site: Oral soft tissues like—tongue, buccal mucosa, vestibule, palate and jawbones, etc.

CLINICAL PRESENTATION

- Benign fibrous histiocytoma clinically produces a nodular, soft or firm, nontendered swelling of varying size (Fig. 2.63).
- Intrabony lesions produce expansile swelling with displacement of the regional teeth.
- The size of the tumor varies between few millimeters to several centimeters in size.
- The superficial lesions are generally smaller in size, while the deep tissue lesions tend to be larger in size.

RADIOGRAPHIC FINDING

Bony lesions produce unilocular or multilocular radiolucent areas with ill-defined border (Fig. 2.64).

MACROSCOPY

Macroscopically benign fibrous histiocytoma presents a lobulated, fleshy mass, which is firm in consistency.

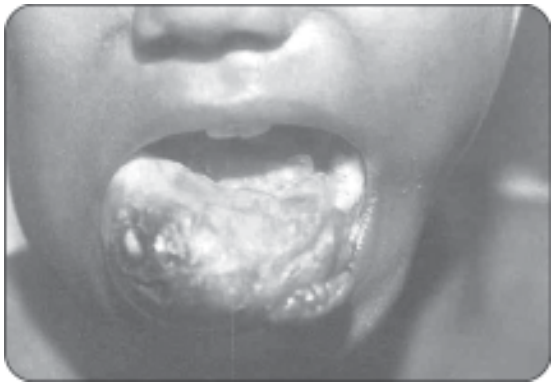

Fig. 2.63: Benign fibrous histiocytoma of mandible

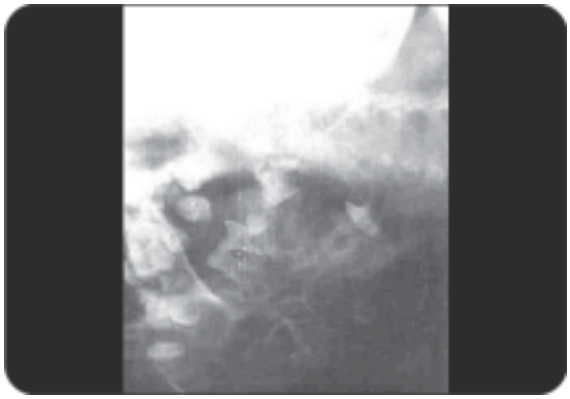

Fig. 2.64: Benign fibrous histiocytoma showing multilocular radiolucency in mandible

HISTOPATHOLOGY

- Histologically, the tumor presents actively proliferating fibroblasts and histiocytes, which are often arranged in **short interlacing fascicles**.
- The fibroblasts are elongated and spindle-shaped with vesicular nuclei, and these cells synthesize mature collagens.
- The histiocytes are large cells with oval nuclei and have a very thin cytoplasm.
- The tumor cells often exhibit a characteristic **`storiform'** pattern of arrangement, as it resembles the irregular, whorled appearance of a typical **'straw-mat'**.
- Lipid containing xanthoma cells and few lymphocytes may also be present in the tumor.
- Mitotic figures are uncommon in the tumor cells, however there may be presence of few multinucleated giant cells.
- The connective tissue stroma sometimes exhibits the presence of myxoid or hyalinized areas.

TREATMENT

Local excision.

MYXOMA

DEFINITION

Myxomas are true neoplasms, which are made-up of tissues that often resemble **primitive mesenchyme (Fig. 2.65)**.

CLINICAL FEATURES

Age: It can occur at any age.

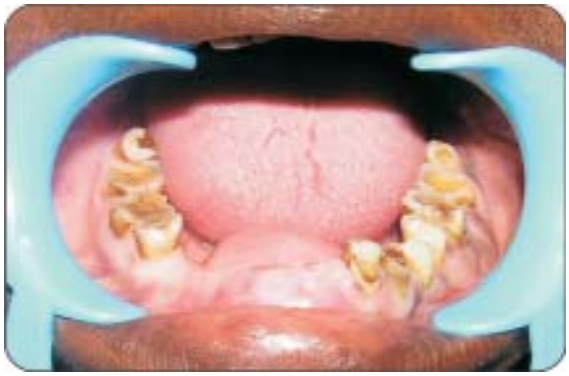

Fig. 2.65: Myxoma

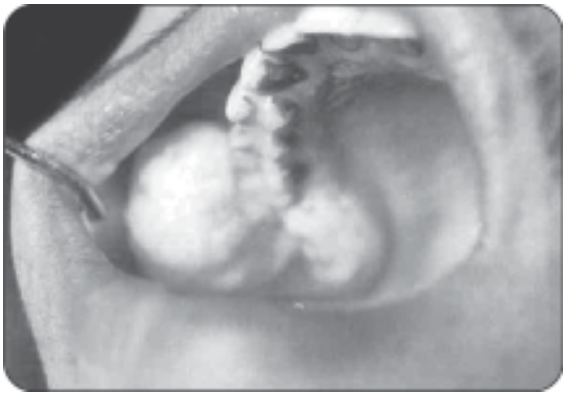

Fig. 2.66: Myxoma involving maxilla

Sex: There is no definite sex predilection.

Site: Oral submucosal area, salivary gland and jawbones.

PRESENTATION

Soft tissue myxomas are rare lesion and they usually produce a nondescript, firm, nodular growth of varying size (Figs 2.65 to 2.68).

HISTOPATHOLOGY (FIGS 2.69 TO 2.71)

- The lesion is composed of a loose textured tissue containing delicate reticulin fibers and **mucoid material**.
- Within the loosely arranged tissue, stellate-shaped cells are sparsely distributed.
- The tumor is not encapsulated and can invade into the surrounding tissues.

TREATMENT

Since myxomas are locally aggressive neoplasms, radical surgery is often recommended for their treatment.

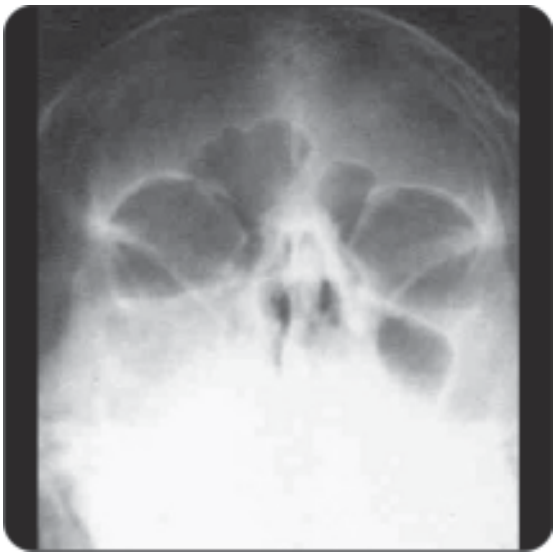

Fig. 2.67: Radiopacity of the Rt. maxillary antrum in myxoma

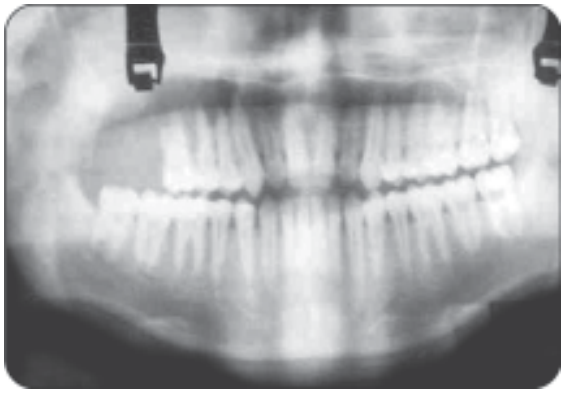

Fig. 2.68: Myxoma causing destruction of the interdental bone in Rt. upper molar region

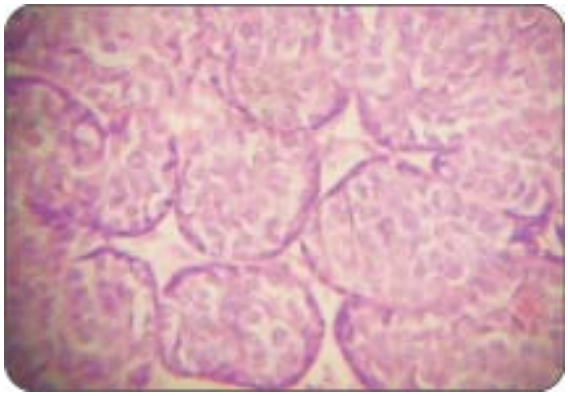

Fig. 2.69: Photomicrograph of myxoma-I

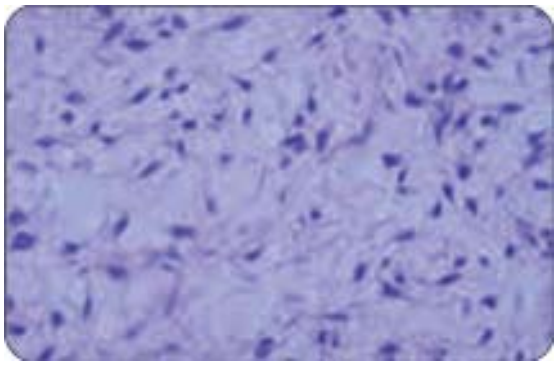

Fig. 2.70: Photomicrograph of myxoma-II

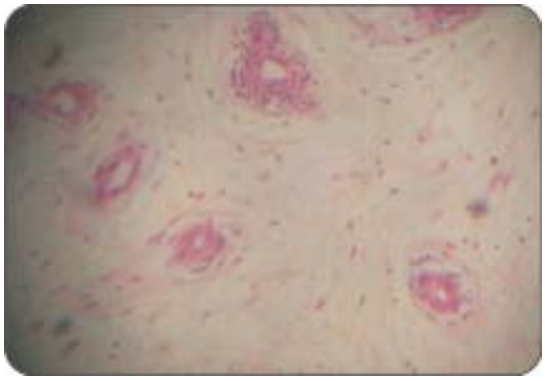

Fig. 2.71: Photomicrograph of myxoma-III

NODULAR FASCITIS

DEFINITION

Nodular or **pseudosarcomatous fascitis** is a localized benign lesion, which is composed of fibroblasts and myofibroblasts and is **often clinically mistaken for malignancy**.

CLINICAL FEATURES

This lesion occurs more commonly in the extremities. About 15% to 20% lesions appear in the head and neck region including the oral cavity.

Age: Third, forth and fifth decade of life.

Sex: Both sexes can be affected, but there is a male predominance.

Site: Buccal mucosa, skin of the face, tongue, alveolar mucosa, parotid gland and submucosa overlying the mandible and zygoma.

PRESENTATION

- Clinically, nodular fasciitis presents a **rapidly growing, firm, submucosal mass**, the rate of growth is sometimes so fast that clinically malignancy is often suspected.
- The lesion is usually measuring less than 5 cm in diameter and it can be partially encapsulated.
- Most of the lesions produce **pain and tenderness** upon palpation.
- Although the onset is very rapid, however the growth potential of this neoplasm is limited.
- These are benign lesions and if left untreated they regress spontaneously.

HISTOPATHOLOGY

- Microscopically nodular fascitis exhibits spindle or stellate shaped cells with vesicular nuclei, which are arranged in a **fascicular or swirled pattern**.
- Hypercellularity, cellular pleomorphism and multiple mitotic activities are often seen.
- Tissue spaces are often **filled with extracellular mucin**, which have a myxoid appearance.
- Multiple multinucleated giant cells may be present in some lesions, these giant cells originate either from the adjacent muscle cells or from fusion of the macrophages.
- Chronic inflammatory cell infiltration and areas of hemorrhage is often seen in the connective tissue stroma.
- Nodular fascitis is **often histologically confused with fibrosarcoma and** this could be due to its typical features like cellular pleomorphism and hypercellularity, etc.
- However, despite increased cellularity in nodular fasciitis, the individual cell nuclei are monomorphic and uniform in appearance, thereby indicates a nonmalignant condition.

DIFFERENTIAL DIAGNOSIS

- Fibrous histiocytoma
- Fibromatosis
- Neurofibroma
- Fibrosarcoma

TREATMENT

Local excision. Recurrence is uncommon.

BENIGN NEOPLASM OF ADIPOSE TISSUE ORIGIN

LIPOMA

DEFINITION

Lipoma is a benign neoplasm of adipose tissue origin and is composed of mature fat cells.

CLINICAL FEATURES

Age: Most of the lesions occur in adults above 40 years of age and are rarely seen in children.

Sex: Both sexes are almost equally affected.

Site: Intraoral lipomas generally arise from the superficial connective tissue and few lesions develop within the deep tissues of cheek and buccal vestibule. Tongue, lips, floor of the mouth and salivary glands are also sometimes affected.

Lipomas often occur in the neck, mostly along the sternocleidomastoid muscle.

PRESENTATION

- Clinically, lipoma presents a relatively well defined, **very soft, frequently movable lump**, within the underlying connective tissue.
- Lipomas are smooth surfaced, nodular, pedunculated or sessile lesions.
- These are painless lesions and on palpation often there is a **cyst-like feeling**.
- The **superficial lipomas** usually appear **yellow** in color and they exhibit a smooth overlying surface. However the **deep lesions** of lipoma often appear **pink** in color.
- Lipomas are mostly asymptomatic lesions and they measure about below 3 centimeter in diameter in most instances.

MACROSCOPIC APPEARANCE

Macroscopically lipoma appears as a soft, yellow, lobulated mass, which floats in aqueous solutions such as formalin fixatives.

HISTOPATHOLOGY

- Histologically, lipomas present well-circumscribed areas of proliferating **mature fat cells** (**adipocytes**) within a loose areolar tissue stroma.

- The tumor cells exhibit a **round, vacuolated, clear cytoplasm with centrally placed nuclei.**
- In most of the lesions, lobules of fat cells are often separated at places by fibrous tissue septa.
- Lipoma is a well-defined lesion, although, it does not display any surrounding capsule. However, in some cases a fibrous capsule may be present.
- Occasionally, lipomas may contain benign lipoblasts; these are multinucleated cells with nuclei arranged in a **'floret'** pattern. These cells often produce a **'soap-bubble'** appearance due to the presence of intra-cytoplasmic vacuoles.
- In some lipomas, myxomatous, osseous or cartilagenous tissues may be present in addition to the fat cells, these cells develp as a result of metaplastic change in the tumor cells of lipoma.

TREATMENT

Simple surgical excision.

BENIGN NEOPLASM OF VASCULAR TISSUE ORIGIN

HEMANGIOMA

DEFINITION

Hemangiomas are relatively common benign proliferative lesions of **vascular tissue origin**, which may be present either at birth or may arise during early childhood.

Most investigators believe that hemangiomas are congenital developmental anomalies and are not true neoplasms.

CLINICAL FEATURES

Age: Being the commonest neoplasm of **infancy**, most hemangiomas are present either at birth or they arise at an early age.

Sex: It is seen more commonly among females.

Site: About 60 percent lesions occur in the head and neck region. Intraorally hemangiomas frequently occur over the **facial skin**, **tongue, lips, buccal mucosa and palate**, etc. It can also develop within the **jaw bones as a central lesion.** Hemangiomas sometimes develop **intra-muscularly** or within the salivary glands.

GROWTH PATTERN

Hemangiomas appear as pale macules with a thread-like telangiectasia over the skin and mucous membrane. During the first few weeks of life, there is rapid growth of the lesion and these are fully recognizable at about 8 weeks of life.

Hemangiomas of Skin and Mucous Membrane (Figs 2.72 to 2.74)

- Hemangiomas of the oral mucosa are usually raised, localized, multinodular or flat lesions. The deeper lesions appear as slightly raised mass with only a **bluish hue**.
- The color of the lesion ranges from distinctly **red to blue or to purple colors**. Sometimes, the

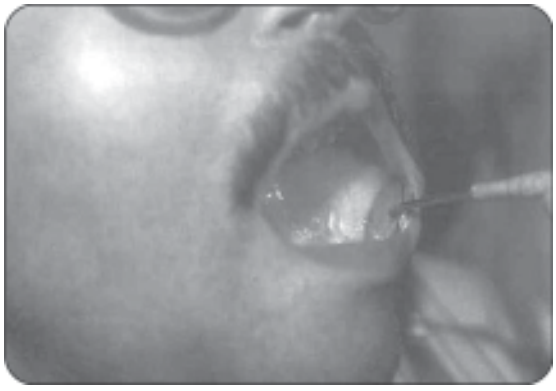

Fig. 2.72: Hemangioma of the Lt. cheek

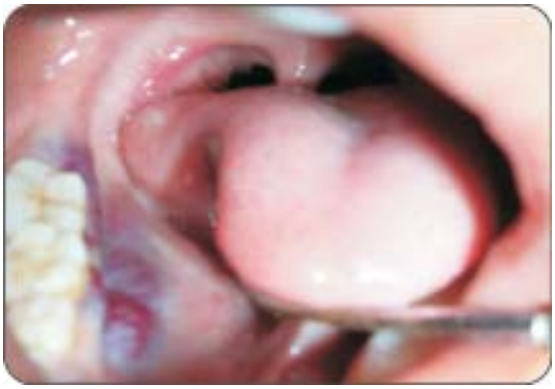

Fig. 2.73: Hemangioma-I

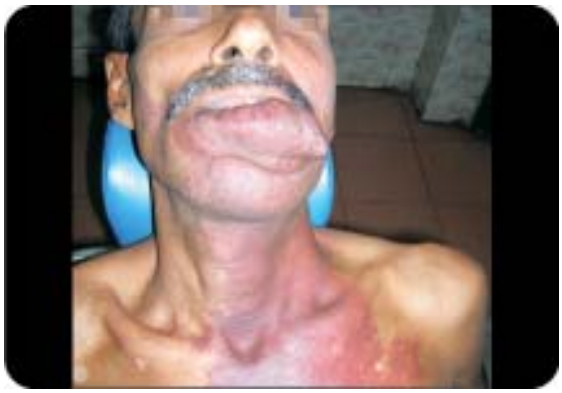

Fig. 2.74: Hemangioma-II

bright red bosselated lesions of the skin occur which are called "**strawberry hemangiomas**".

- After the initial development some of these lesions enlarge continuously while others become static and make no further progress. The mature lesions generally appear **dull purple** in color.
- Moreover, some lesions of hemangiomas can even resolve slowly and finally disappear completely. After such spontaneous regression of hemangiomas, normal skin color is often restored, however in few cases the skin of the affected site appears atrophic, scarred, wrinkled or telangiectatic.
- When a hemangioma lesion is compressed with the help of a glass microscopic slide, it blanches (reddish color disappears) because the erythrocytes are pushed out of the vascular channels due to pressure. However, once the pressure is released, its reddish appearance returns back due to refilling of the tumor vessels with blood.
- When a hemangioma is connected with a large blood vessel, **"bruits"** can be heard during **auscultation** with a stethoscope.
- On palpation hemangioma is always soft, compressible and pulsatile.
- Trauma or laceration to the covering skin or mucosa often causes excessive uncontrolled bleeding from the lesion.
- Larger lesions in the neck and laryngeal region may cause airway obstructions.
- Trauma to the lesion may cause surface ulceration with or without secondary infections.

Intramuscular Hemangioma

- Hemangiomas can frequently occur within skeletal muscles and in the orofacial region, masseter and orbicularis oris muscles are often affected.
- Muscular hemangiomas commonly produce diffuse, pulsatile swelling with occasional pain.
- Size of the lesion and its consistency varies from time to time especially on contraction of the involved muscle.
- Intramuscular hemangioma causes distortion of the area and it has a spongy feeling on palpation.
- When the lesions are deep seated, the surface is often of normal color.
- During examination, the **lesion can be moved across the long axis of the muscle**, but it can not be moved along it.

Port-wine Stain (Figs 2.75 and 2.76)

- Port-wine stain is a unique type of hemangioma (mostly capillary type), which is often encountered over the face.
- The lesion is characterized by a **diffuse, purplish macule** with irregular borders and is **sharply demarcated** from the normal skin.
- Although, these are mostly macular lesions, port-wine stains sometime exhibit nodular elevations as used.
- The lesion is unilateral in distribution and it often appears to follow the course of the first, second or the third divisions of the trigeminal nerve.

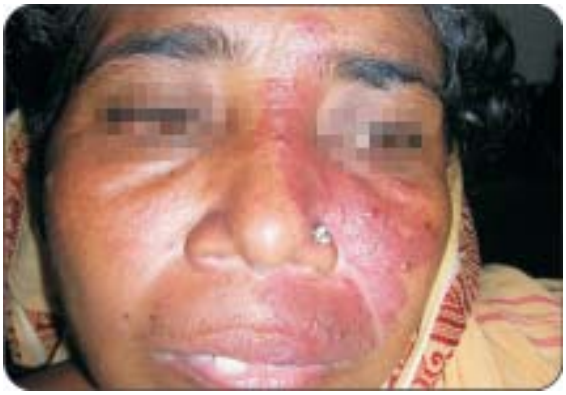

Fig. 2.75: Port wine stain

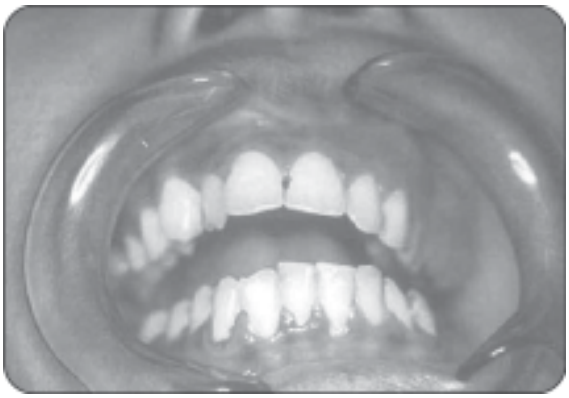

Fig. 2.76: Port-wine stain causing gingival swelling with bleeding tendency

- A specific syndrome called **"Sturge-Weber"** syndrome is sometimes identified, which includes unilateral port-wine stain of the face, intracranial hemangiomas and epilepsy.
- Intracranial hemangiomas may produce calcifications within the walls of the meningial vessels, which lead to an unique radiographic appearance of parallel radiopaque lines and this have been termed as "**tram-line" calcifications**.

Central Hemangiomas (Intraosseous)

Central hemangiomas represent benign vascular proliferation within the bone, these lesions can be either capillary or cavernous type and are identical to the ordinary hemangiomas of the soft tissue.

- Some lesions may be completely asymptomatic and are detected only during routine radiographic examinations.
- Central hemangiomas most commonly affect the vertebrae and skull. Among the jawbones, mandible is affected more often than maxilla.
- These lesions usually occur in the second decade of life and females are affected about 2 to 3 times more frequently than males.
- Clinically central hemangioma often presents a **slow enlarging**, occasionally painful, non-tendered, **expansile jaw swelling**.
- Long standing lesions may cause severe erosion in the bone and thereby make the affected bone pulsatile, thin and compressible.
- There can be considerable amount of expansion of the affected bone, however bruits are not usually detected in these lesions.
- **Loosening of teeth** and sometimes **spontaneous bleeding** from the gingival crevice of the regional teeth can accur.
- Central hemangiomas may produce a throbbing pain in the bone and anesthesia or paresthesia of the affected part of the jaw.

Radiographic Appearance of Central Hemangiomas

- Radiographically hemangiomas of the jaw bone usually present **multi-locular** radiolucent area, with a typical "**soap-bubble**" appearance.
- Sometimes the pattern of bone destruction is ill-defined, irregular and often extensive.
- Larger lesions often cause severe thinning and expansion of the cortical plates in the affected area with occasional **'sun-burst'** appearance.
- Smaller lesions of intraosseous hemangioma may produce tiny areas of radiolucency in the bone. Whenever such lesions are present near the root apex of any tooth, they may resemble periapical cysts.

MACROSCOPIC FINDINGS

- Macroscopically hemangiomas can be either diffuse or circumscribed lesions. The teeth in the affected areas may be loose and often there is bleeding from the gingival crevices of these teeth.
- Although the teeth are mobile, their extraction may result in severe hemorrhage.

HISTOPATHOLOGY

There are several histologic types of hemangiomas found in the oral cavity, among them two very common types are: (a) capillary hemangioma and (b) cavernous hemangioma.

Capillary Hemangioma

- Capillary hemangiomas are histologically characterized by numerous, minute, small, endothelial-lined capillaries in the lesion, which are densely packed with erythrocytes.
- The cells of the endothelial lining are usually single layered and are supported by a connective tissue stroma.

- These cells (endothelial) are well formed, spindle shaped or slightly elongated and plump.
- Although, well formed capillaries are mainly present throughout the lesion, there may be some foci of proliferating endothelial cells, which form small aggregates or rosettes and these cells often lack in their attempt at vessel formation.
- The fibrous connective tissue stroma is not well formed and is loosely arranged.
- Capillary hemangioma often histologically resembles pyogenic granuloma, however, presence of certain features like—intercellular edema and chronic inflammatory cell infiltration, etc. are very common in pyogenic granuloma but are rare in case of capillary hemangioma.

Cavernous Hemangiomas

- Cavernous hemangiomas **histologically reveal large**, irregularly shaped, **dilated, 'endothelial-lined sinuses'**, which contain large aggregates of erythrocytes (Figs 2.77 and 2.78).
- These blood-pooled sinuses are often **inter-communicating** with one another.

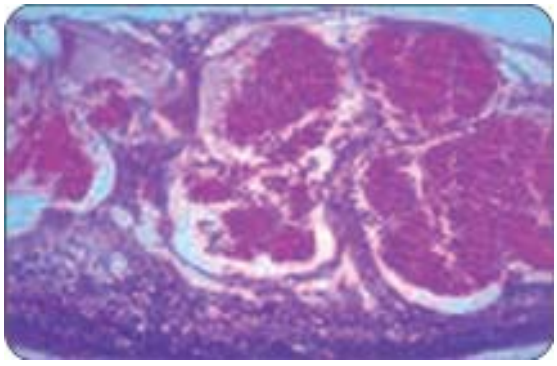

Fig. 2.77: Photomicrograph of cavernous hemangioma

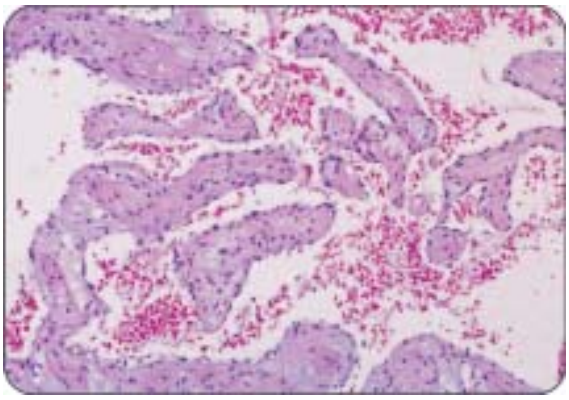

Fig. 2.78: Photomicrograph of hemangioma

Key points of hemangioma

- Hemangiomas are benign vascular tissue neoplasms arising from the vascular tissue which generally occur during infancy.
- These are commonly seen over the face, tongue, palate, cheek, muscles and bones including the jawbones.
- Lesion of the soft tissue presents painless, soft, fluctuant swelling with a typical red or blue or purple color.
- Soft tissue lesions are characteristically pulsatile and 'bruits' can be heard during auscultation with a stethoscope, if the lesion is associated with a large vessel.
- Hemangiomas sometimes produce 'port-wine stain' lesions over the facial skin, which are diffuse, purple, macules with irregular borders and are sharply demarcated from the normal skin.
- Moreover strawberry hemangiomas also develop on the facial skin, which are bright red, bosselated lesions.
- Intramuscular lesions of hemangioma produce diffuse, firm, movable swelling with occasional history of pain.
- Intraosseous lesions cause slow enlarging, painless, bony hard swelling of the jaw with loosening of teeth. They produce multilocular radioluceny in the bone with a typical 'soap-bibble' appearance on radiograph.
- Hemangiomas have two main histological patterns: **capillary type**—which exhibits numerous, proliferating young blood capillaries, lined by single layer of spindle shaped endothelial cells. The other important type is cavernous hemangioma, which exhibits few large, dialated, blood filled sinuses of irregular size, lined by a single layer of flat endothelial cells.
- Treatment of hemangioma is difficult and is done by local excision for smaller lesions; however larger lesios are excised surgically after pretreatment with sclerosing agents.

- A single layer of flattened endothelial cell lines each sinus.
- These sinuses are of variable caliber and they usually lack a muscular coat on their walls.
- A mature fibrous connective tissue stroma often separates one sinus from the other.
- Large areas of hemorrhage and hemosiderin pigmentation are often seen within the cavernous hemangioma lesions.
- However, inflammatory cell infiltration is very rare unless the lesion is secondarily infected or traumatized.

HISTOLOGY OF OTHER FORMS OF HEMANGIOMAS

Port-wine Stain

- The 'port-wine stain' lesions are composed of numerous, microvascular channels, similar to capillary hemangiomas.
- However, these vessels are often separated from one another by a mature fibrous tissue stroma.

Central Hemangiomas

- Central hemangiomas are histologically similar to the cavernous type, although tumors of capillary variety may also occur.
- The vascular spaces are usually few and far between and there is presence of a relatively thick connective tissue stroma.
- Sometimes areas of osteoid or mature oven bone formation can also be seen in the lesion.

DIFFERENTIAL DIAGNOSIS

- Pyogenic granuloma
- Mucoceles
- Kaposi's sarcoma
- Salivary gland neoplasm
- Inflammatory hyperplasia of the tissue.

TREATMENT

- Local excision is the treatment of choice in small lesions.
- Larger lesions are treated by excision after pretreatment of the lesion with sclerosing agents to reduce their size.
- Hemangiomas in children may be left untreated until puberty, anticipating their spontaneous regression.

BENIGN NEOPLASM OF LYMPHATIC VESSELS

LYMPHANGIOMA

DEFINITION

Lymphangiomas are uncommon benign hematogenous neoplasms, characterized by excessive proliferation of the lymphatic vessels. They may occur either as a focal superficial lesion within the oral cavityor as a massive, diffuse lesion of the neck (cystic hygroma).

Types of lymphangioma

Capillary lymphangioma	Containing numerous small lymphatic capillaries.
Cavernous lymphangioma	Containing large dialated lymphatic vessels.
Cystic hygroma	Massive diffuse lesion of neck, containing macroscopic cyst like spaces of lymphatic vessels.

CLINICAL FEATURES

Age: Most of the lesions are present at birth or they can arise during childhood (90 percent lesions occur within 2 years of age).

Outline of diagnosis in hemangiomas

A. From clinical point of view	• Color of the lesion—bright red or bluish-red. • Pulsation—often present. • Auscultation—bruits can be heard during auscultation of the lesion with a stethoscope.
B. Radiography	Intraosseous or central hemangiomas present multi-locular radiolucency with 'soap-bubble' appearance.
C. Imaging	Doppler angiography. Contrast time-lapse angiography.
D. Histopathology	Capillary and cavernous types.

Sex: There is no sex predilection.

Site: About 50 to 75 percent lesions develop in the head and neck region, intraoral lesions predominantly affect the **tongue** and besides this, they can sometimes occur in relation to the palate, buccal mucosa, gingiva and lip, etc.

Lymphagiomas of the neck usually develop from the lateral neck and these lesions are often massive in size and are referred to as '**cystic hygromas**'.

PRESENTATION (FIGS 2.79 TO 2.81)

- Intraoral superficial lymphangiomas usually present a painless, flat or nodular or '**vesicle-like' translucent swelling** over the oral mucosa.
- The surface of the lesion is pebbly and often resembles '**frog-eggs' or 'tapioca-pudding'.**
- These lesions may either regress spontaneously during puberty or they may enlarge in size moderately and become static thereafter without any further growth.
- Some intraoral lymphangiomas produce deep-seated lesions and they often present diffuse, soft, painless, submucosal lumps.
- The color of the lesion is usually **pale** and it is often lighter than the color of the surrounding normal mucosa, however on few occasions lymphangiomas may sometimes produce a **'red-blue'** discoloration of the surface.
- Secondary hemorrhage within the tumor may cause a purple color of the lesion with development of a sudden swelling.
- On palpation, lymphangiomas often produce a typical "**crepitate sound**", which occurs due to sudden movement of the intralesional lymphatic fluid from one part of the lesion to the other because of the pressure from palpation.
- Small lesions of lymphangioma sometimes occur on the alveolar ridge of the jawbone, often bilaterally.
- Diffuse and extensive lesions of lymphangioma of the tongue often produce **macroglossia**, the enlarged tongue shows indentations of teeth on the lateral borders.
- A diffuse, painless swelling often develops when the lesion arises from the lip.

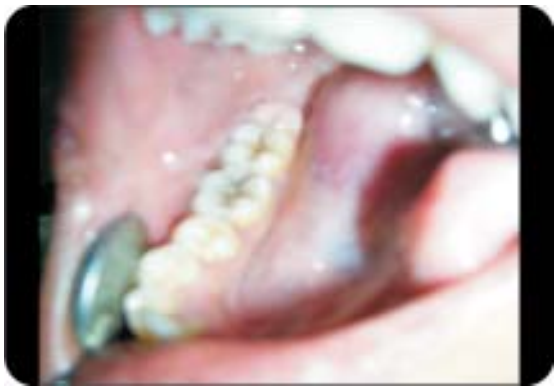

Fig. 2.79: Lymphangioma of floor of the mouth

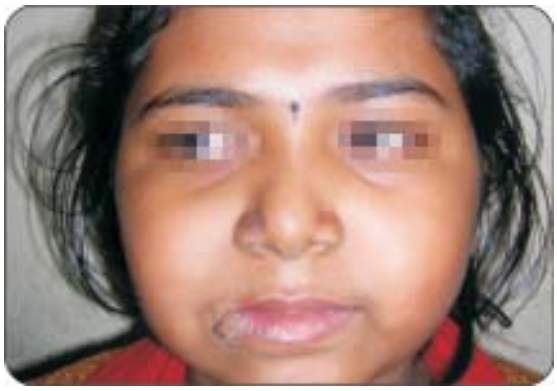

Fig. 2.80: Lymphangioma-I

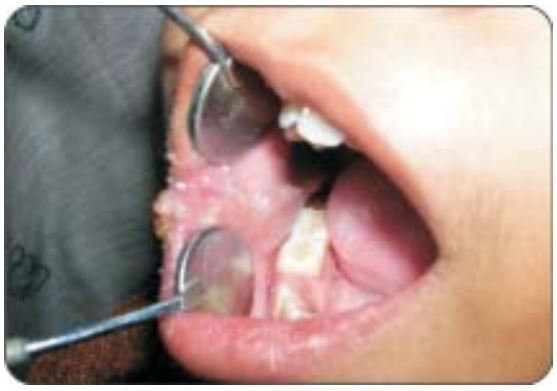

Fig. 2.81: Lymphangioma-II

- Cystic hygromas usually develop in the first or second year of life.
- Cervical lymphangiomas sometimes become so large that they extend into the mediastinum and some lesions may cause **respiratory distress**.
- Clinically these lesions present massive, **'pendulous', fluctuant swelling** on the lateral neck, measuring about several centimeters in diameter.

- Unlike intraoral lymphangiomas, the cystic hygromas do not regress spontaneously during their clinical course.
- Patients with Down's or Turner's syndrome often have a tendency to develop cystic hygromas.

HISTOPATHOLOGY (FIGS 2.82 AND 2.83)

- Histologically, lymphangioma presents numerous proliferating, thin walled, markedly dialated lymphatic vessels, which are lined by plump endothelial cells.
- The lumens of the lymphatic vessels contain an eosinophilic or pinkish proteinaceous coagulum (results from fixation of lymph) with occasional presence of erythrocytes and lymphocytes in it.
- The tongue lesions often exhibit extension of the cavernous lymphatic channels between the rete ridges of the surface epithelium and this can result in multiple papillomatous nodules on the surface.
- The lymphatic channels lie in juxtaposition to one another with little intervening fibrous tissue stroma.
- Moreover, these lymphatic channels also abut the overlying epithelium with no fibrous tissue stroma in between.
- The histologic appearance of cystic hygroma is similar to that of lymphangiomas of the oral cavity, however in cystic hygromas the lymphatic channels are often quite large and dialated (often have a cyst-like appearance).
- These large and dilated channels extend deep into the underlying tissue and traverse between the muscle fibers and fibrous connective tissue.
- Although, clinically cystic hygroma is a massive lesion, histologically the endothelial cells do not show any sign of abnormal cellularity, pleomorphism or hyperchromatism, etc.
- Despite being an infiltrative growth it also does not cause any destruction to the neighboring structures.

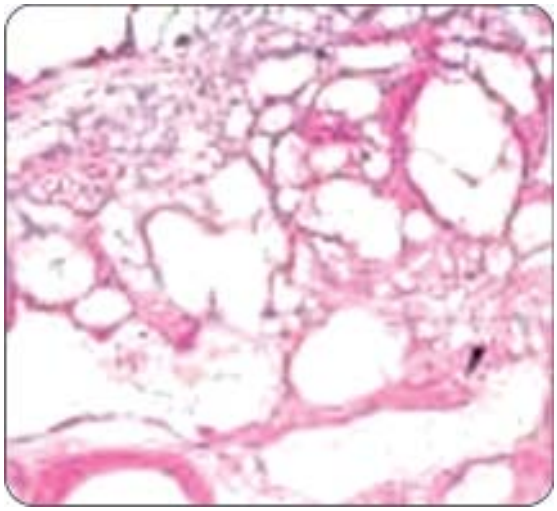

Fig. 2.82: Photomicrograph of lymphangioma-I

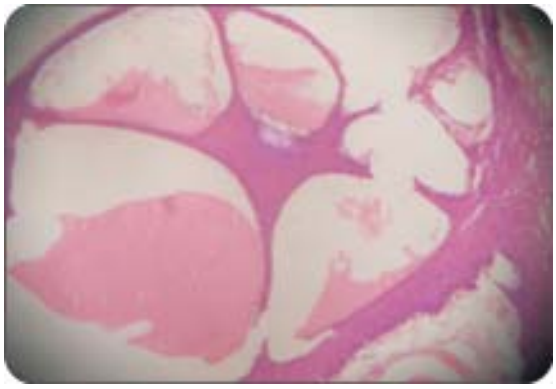

Fig. 2.83: Photomicrograph of lymphangioma-II

DIFFERENTIAL DIAGNOSIS

- Hemangioma
- Mucocele
- Branchial cleft cyst
- Sinus histocytosis
- Lipoma
- Tuberculosis.

SPECIAL INVESTIGATION

In lymphangioma, the neoplastic lymphatic tissue often infiltrates between the muscles and the contagious soft tissues, therefore making it difficult to determine the exact extent of the lesion. For this reason special investigations like—CT scan, MRI (Magnetic Resonance Imaging) and lymphatic scintigraphy, etc. are sometimes useful in determining the peripheral limit of the disease.

TREATMENT

- Many lesions of lymphangioma involute spontaneously during puberty.

- The persistent lesions are treated by surgical excision with careful dissection from the surrounding normal tissue.
- Sometimes, cryosurgery and laser surgery is used with some success.

BENIGN NEOPLASM OF BONE

OSTEOMA

DEFINITION

Osteomas are benign neoplasms of bone (osseous tissue), which are consisting of either mature compact bone or cancellous bone. These neoplasms are almost exclusively found in the craniofacial region.

TYPES

Osteomas are of two types:

Periosteal osteoma: Lesions arising peripherally from the outer surface of the bone.

Endosteal osteoma: Lesions arising centrally within the medullary region of bone.

CLINICAL FEATURES

Age: Second to fifth decade of life.

Sex: More frequent among females.

Site: Osteomas occur either peripherally or centrally in relation to any bone of the cranium and the face, few lesions also develop from within the sinus cavities.

Some lesions may arise from the soft tissues, e.g. tongue or buccal mucosa, etc.

Jawbones are often affected and interestingly osteomas often develop from those areas of the jaw from where tori usually do not arise. Body of the mandible in the molar region (lingual surface) is the most favored location of this tumor.

PRESENTATION

- Osteoma often produces an asymptomatic, slow growing, nodular, exophytic, bony hard growth in the jaw (Fig. 2.84).
- The lesion can be either solitary or multiple and the overlying skin or epithelium appears normal.

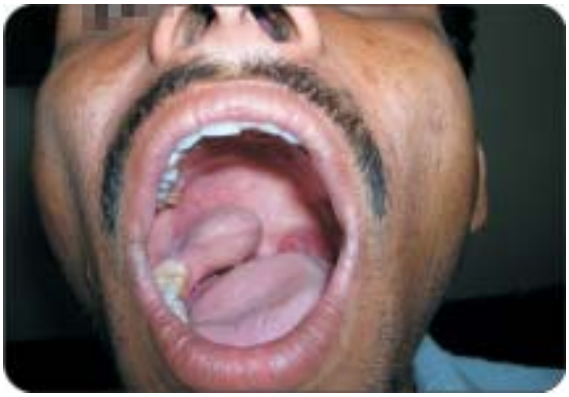

Fig. 2.84: Osteoma of mandible

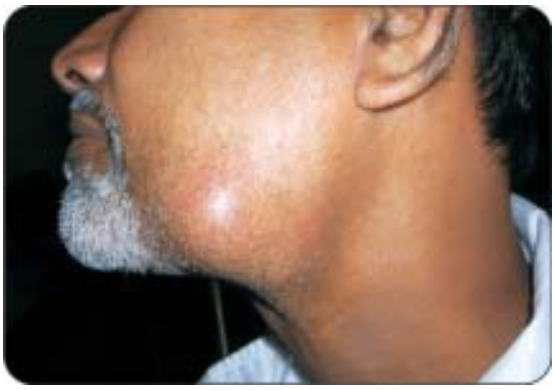

Fig. 2.85: Osteoma

- Larger lesions of osteomas may cause facial deformity, with expansion of the cortical plates of bone and displacement of the regional teeth (Fig. 2. 85).
- Osteomas developing over the condyle of mandible often cause pain, decreased mouth opening, deviation of chin and derangement of occlusion, etc.
- Multiple osteomas often occur in association with **Gardner syndrome**, a hereditary condition with an autosomal dominant pattern.
- The syndrome also consists of multiple intestinal polyps with malignant potential, many unerupted normal or supernumerary teeth, epidermoid cyst and desmoid fibromas of skin.
- Osteomas of the maxillary antrum (Fig. 2.86) may predispose to sinusitis, which produces pain in the maxillary molar area with nasal discharge.

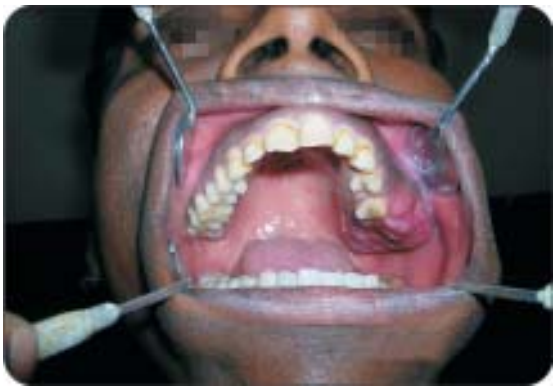

Fig. 2.86: Osteoma of maxilla

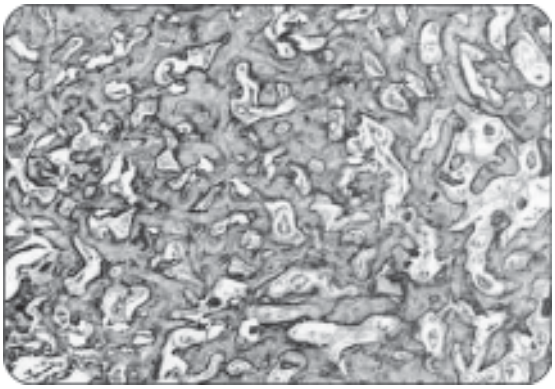

Fig. 2.88: Photomicrograph of osteoma-I

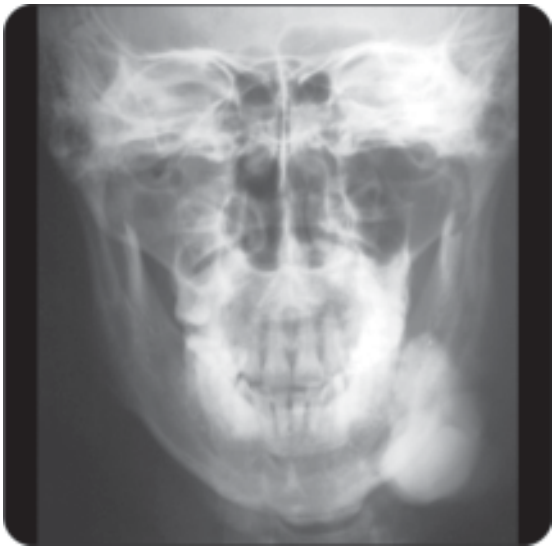

Fig. 2.87: Radiographic view of osteoma

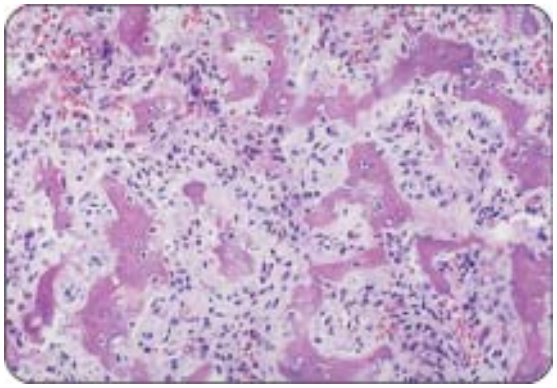

Fig. 2.89: Photomicrograph of osteoma-II

RADIOGRAPHIC FEATURES (FIG. 2.87)

Osteomas radiographically present well-circumscribed, solitary or multiple, round or oval, dense radiopacities in the bone. Larger lesions (endosteal type) cause expansion of the cortical plates and the peripheral outline or the border of the lesion is generally sclerotic.

HISTOPATHOLOGY

Microscopically osteoma presents the following features (Figs 2.88 and 2.89):

- The lesion is composed of dense cortical bone with a distinct lamellar pattern.
- The cortical bone is sclerotic and relatively avascular.
- The medullary bone is denser than normal bone with reduced marrow spaces.
- The marrow spaces are composed of areolar fibrous tissue or adipose tissue.
- The periosteal layer is often more active in case of osteoma than the normal bone.
- When multiple osteomas occur, each discrete ossified mass is separated from one another by a mature fibrous tissue stroma.

DIFFERENTIAL DIAGNOSIS

- Odontomas
- Antrolith
- Exostoses
- Osteoblastoma
- Sclerotic cemental masses
- Focal sclerosing osteomyelitis.

TREATMENT

Surgical excision. Antral lesions are removed by Caldwell-Luc approach.

OSTEOID OSTEOMA/ OSTEOBLASTOMA

DEFINITION

Osteoid osteomas and osteoblastomas are benign intraosseous neoplasms with almost similar clinical, radiographic and histologic features.

These lesions also share many common clinical and histological features with cementoblastoma as well, and therefore, all these lesions are considered to be the variants of a single disease entity.

CLINICAL FEATURES

- Osteoid osteoma usually occurs among young patients, between the age of 10 to 25 years.
- It arises more frequently among males than females.
- These lesions more commonly develop in the long bones and jaw lesions are very rare.
- Osteoid osteoma causes swelling of the bone with expansion of the cortical plates, most lesions measure about 1 cm in diameter.
- The lesion is **almost always painful**, especially when digital pressure is applied on it and the cause of the pain could be either due to the presence of numerous peripheral nerves in the tumor or due to the synthesis of prostaglandins by the tumor cells.
- After growing to the size of about 1 cm in diameter, the osteoid osteomas do not grow any further but it continues to remain painful.
- Osteoblastoma is another bony tumor that often causes expansion and distortion of the cortical plates of the jawbone, however its size is usually much bigger than that of the osteoid osteoma.
- Osteoblastoma clinically differs from osteiod osteoma by the fact that the former one is a progressively expansile lesion with a greater tendency to cause local bony expansion.
- These lesions often develop in mandible in the posterior region, most patients are below 30 years of age and the disease shows definite male predominance.
- The size of osteoblastoma is usually more than 1 cm in diameter (average is 2–4 centimeter) and it is also painful. However, the intensity of pain is much lesser as compared to the osteoid osteoma.
- Like osteoid osteomas, osteoblastomas are also rare lesions of the jawbone.
- Although osteoblastoma is a benign neoplasm, it occasionally shows some tendency to be converted into osteosarcoma.
- Some osteoblastomas can produce very large, locally aggressive and more painful type of lesions, and these are mostly seen in relatively older patients.

RADIOLOGICAL FEATURES

- Radiographically osteoid osteoma presents a small, round or oval, well-defined, radiolucent area that is surrounded by an area of increased radiodensity (reactive sclerosis).
- The central area of radiolucency is often called the **"nidus"**, which may sometimes exhibit some evidence of spotty calcifications.
- Osteoblastoma radiologically presents a well-defined, large, radiolucent area, containing patchy areas of mineralizations and it has a faint bony margin.
- Cementoblastoma is radiologically similar to osteoblastoma, but the former lesion always occurs in continuity with the root portion of a molar tooth.

HISTOPATHOLOGY (FIG. 2.90)

- Histologically, both osteoid osteoma and osteoblastoma passes through several phases.
- Initially a small area of osteoblastic activity is seen, which is followed by a period of deposition of large osteoids.
- In the more mature stages the osteoids become well calcified.
- In osteoid osteoma, the 'nidus' consists of an interlacing meshwork of bony turbeculae of variable size, within a vascular connective tissue stroma.
- Numerous osteoblasts are present and few osteoclasts are also seen in some areas.
- Osteoblastoma is histologically very similar to the osteoid osteoma, however, the former lesion often exhibits an increased vascularity, a more uniform pattern of distribution of osteoid trabeculae and more number of osteoblast cells in the area.

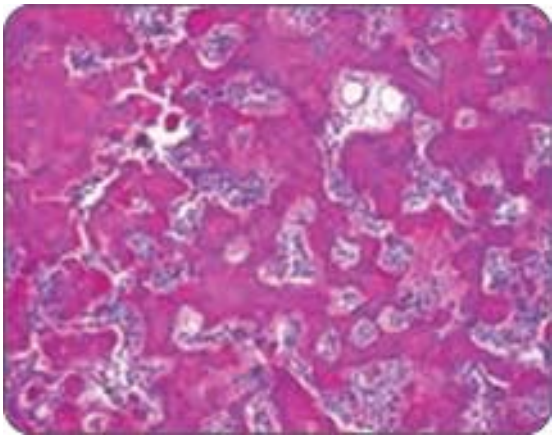

Fig. 2.90: Photomicrograph of osteoblastoma

- Moreover, there is no surrounding zone of reactive bone formation in osteoblastoma.
- Many areas of hemorrhage are seen in this neoplasm as well as few multinucleated giant cells.
- Histologically, osteoid osteoma and osteoblastoma may sometime resemble osteosarcoma.

DIFFERENTIAL DIAGNOSIS

- Chronic nonsuppurartive osteomyelitis
- Chronic selerosing osteomyelitis
- Chronic bone abscess
- Central ossifying fibroma
- Central cemetifying fibroma.

TREATMENT

Osteoid osteomas are often treated by surgical excision or curettage. Osteoblastoma is treated by large surgical enblock resection.

BENIGN NEOPLASM OF CARTILIAGE TISSUE

CHONDROMA

DEFINITION

Chondromas are benign neoplasms of cartilaginous tissue origin and are consisting of mature chondrocytes. These are one of the very common neoplasms of the jawbone.

CLINICAL FEATURES

Age: Chondromas of the jawbone usually occur between the ages of 30 to 60 years. The highest incidence is seen in the forth decade of life.

Sex: Both sexes are almost equally affected.

Site: Chondromas mostly arise from the vestigial cartilaginous rests present in different parts of the jaw. The disease frequently affects the anterior part of maxilla and whenever the mandible is affected, the areas of preference will be the symphysis, premolar-molar area, the condyle and the coronoid process, etc. besides this, the nasal septum is also sometimes affected.

PRESENTATION

- The neoplasm causes a slow enlarging, painless, bony hard swelling of the jawbone.
- In some cases, the lesion shows an aggressive pattern of growth.
- Expansion and distortion of the cortical plates often occur and there can be mobility of the regional teeth.
- The overlying covering epithelium is usually smooth and normal appearing, however on few occasions the epithelium may become ulcerated due to trauma.
- Chondromas are generally solitary tumors, however multiple chondromas can occur on rare occasions in association with some syndromes, e.g. Ollier's syndrome and Maffucci's syndrome, etc.

RADIOGRAPHIC FEATURES

- Radiographic appearance of chondroma is not very pathognomonic. Some lesions produce an ill-defined radiolucency in the jaw bone, containing few irregular foci of radiopacities.
- Most of the lesions cause resorption of roots of the adjacent teeth.

HISTOPATHOLOGY

- The lesion consists of well-defined lobules of hyaline cartilage, containing multiple mature chondrocytes.

- The cells are round or oval in shape with pale cytoplasm and a single nucleus, few tumor cells however have double nuclei.
- An intervening fibrous tissue septa is present, which separates the individual lobules of cartilage from one another.
- There are many areas of calcification within the lesion and moreover, there can be some areas of hemorrhage and tissue necrosis.

DIFFERENTIAL DIAGNOSIS

- Ossifying postsurgical bony defect
- Chronic osteomyelitis
- Osteogenic sarcoma
- Ossifying or centifying fibroma
- Ossifying hematoma.

TREATMENT

Surgical excision.

BENIGN CHONDROBLASTOMA

DEFINITION

Benign chondroblastomas are rare benign neoplasms arising from the epiphyseal ends of the long bones. Rarely these lesions can occur in the oral cavity.

CLINICAL FEATURES

Age: Most of the patients are below the age of 25 years.

Sex: Male people are affected more often than females.

Site: Intraoral benign chondroblastomas are usually rare and whenever they occur, mandibular condyle is the most favored site.

CLINICAL PRESENTATION

- Benign chondroblastomas clinically present a relatively large, bony hard lesion, causing bulging of the jawbones.
- Displacement of the regional teeth often occurs.
- Pain may be present especially during palpation.

RADIOGRAPHIC FEATURES

Radiographically benign chondroblastomas usually present a large radiolucent area in the bone, with ill-defined margins.

There can be presence of few radiopaque foci within the radiolucent zone.

HISTOPATHOLOGY

- Histologically, benign chondroblastomas present a highly cellular structure consisting of numerous round or polyhedral 'chondroblast-like' cells within a thin fibrous tissue stroma.
- Within the fibrous stroma, few areas of calcification are seen, besides this, there can be presence of multiple multinucleated giant cells.

TREATMENT

Surgical excision.

BENIGN NEOPLASM OF SMOOTH MUSCLES

LEIOMYOMA

DEFINITION

Leiomyomas are benign neoplasms of the smooth muscle cells. In the oral cavity they are usually derived from the smooth muscle cells of the blood vessels.

CLINICAL FEATURES

Age: Leiomyomas usually occur among the middle-aged adults.

Sex: Male predilection.

Site: Intraorally, leiomyomas frequently occur in relation to the **tongue**, however other structures like palate, buccal mucosa and lips are also sometimes affected.

In addition to the common source of vascular smooth muscle cells, the pleuripotential mesenchymal cells of the connective tissue may also give rise to these neoplasms.

Intraosseous leiomyomas may occur but are extremely rare and they mostly involve posterior part of mandible.

PRESENTATION

- Clinically leiomyoma appears as a well-delineated, slow growing, painless, sub-mucosal nodule.
- The surface of the lesion is usually smooth and is covered by a normal appearing non-ulcerated epithelium.
- The tumor often has a **yellowish** appearance, although the vascular type of leiomyoma can have a bluish hue.
- On palpation, the lesion feels firm and encapsulated, however the leiomyomas can be painful on rare occasions.
- Sometimes the lesion can be multinodular and whenever the neoplasm arises from the lip or the buccal mucosa, it is usually freely movable.
- The intraosseous leiomyoma of the jaw causes painless, bony hard swelling with expansion of the cortical plates.

RADIOGRAPHIC FEATURE

The intraosseous leiomyoma produces unilocular radiolucency in the jaw with sclerotic margins.

HISTOPATHOLOGY

- Leiomyomas exhibit proliferation of **spindle-shaped smooth muscle cells in solid sheets**, the cells resemble fibroblasts.
- The cells usually evolve from blood vessels and are arranged in fascicles or in a **'stream-like'** fashion.
- The cells contain elongated, blunt-ended, pale nuclei, which often produce a **'cigar-shaped'** appearance.
- These spindle-shaped tumor cells also produce perivascular concentric laminations of parallel fascicles.
- In leiomyoma, the individual tumor cells lack distinct cell margins and because of this, the cytoplasm of one cell appears to be fused to the cytoplasm of the adjacent cells. The cells often reveal the presence of intracytoplasmic myofibrils.
- The lesion is either encapsulated or well-delineated from the surrounding tissue.
- No intervening fibrous tissue is usually evident and only few blood capillaries are found between the tumor cells, these are often known as vascular leiomyomas.
- Some tumors contain epitheloid cells instead of spindle cells and hence are called epitheloid type of leiomyoma.

TYPES

Histologically, leiomyomas are divided into three types:

A. Solid type
B. Vascular type
C. Epitheloid type.

DIFFERENTIAL DIAGNOSIS

- Fibroma
- Neurofibroma
- Myxoma
- Granular cell myoblastoma.

SPECIAL INVESTIGATION

Since the smooth muscle cells and the fibroblast cells both appear **"pink"** with routine hematoxylin and eosin stain, it is normally difficult to differentiate between leiomyoma from neurofibroma or fibroma. For this reason, special investigations are required.

- **MassonTrichome stain** is used to differentiate between these two cells. With this special stain, the smooth muscle cells of leiomyoma appear **'pink'** while the collagenous structures of fibroblasts appear **"blue or green."**
- **Mallory's phosphotungstic acid-hematoxylin stain** helps to demonstrate myofibrils in leiomyoma.
- **Van-Gieson staining** may also be used for this purpose, which stains the collagen fibers "**red**" and the smooth muscle fibers "**yellow**".
- **Immunohistochemical analysis** using the monoclonal antibodies to muscle-specific "actin" may be useful in confirming the diagnosis of leiomyoma.

TREATMENT

Surgical excision including the surrounding normal tissue is the treatment of choice. Recurrence is usually rare.

BENIGN NEOPLASM OF STRIATED MUSCLE

RHABDOMYOMA

DEFINITION

Rhabdomyomas are benign neoplasms of **striated (skeletal) muscles** and these are extremely rare lesions.

CLINICAL FEATURES

Age: Peak age of occurrence is the fifth decade of life, however some cases have been reported at birth or during infancy.

Sex: This lesion occurs more predominantly among males.

Site: Rhabdomyomas of the oral cavity are often develop from base of the tongue, floor of the mouth and soft palate. Some lesions may also develop from the lip, larynx, pharynx and uvula, etc.

PRESENTATION

- The neoplasm clinically presents a slow growing, well-circumscribed, painless mass.
- Some tumors can be 'multinodular' with two or more nodules occurring at the same site.
- Some other lesions can be 'multicentric' in nature and many occur at different locations at a time.
- The lesion is often deep-seated and the overlying tissue appears normal.
- Larger and untreated lesions in the pharyngeal or laryngeal region may sometimes cause airway obstructions.

HISTOPATHOLOGY

- Microscopically, rhabdomyomas appear as sharply outlined, unencapsulated mass; consisting of large, round or oval striated muscle cells.
- These neoplastic cells have a granular eosinophilic cytoplasm and are rich in glycogen and glycoprotein.
- Multiple vacuoles are often present in the cell cytoplasm, which give rise to a spidery appearance to the cell.
- Irregular **cross-striations** are often seen and the cell nuclei are vesicular in nature.
- There can be presence of several multi-nucleated cells.
- Increased and abnormal mitotic activity is usually not seen.

SPECIAL INVESTIGATION

The diagnosis of rhabdomyoma can be confirmed by the electron microscopic demonstration of **'myofibrils'** in the tumor cells.

DIFFERENTIAL DIAGNOSIS

Rhabdomyomas should be differentiated clinically and histologically from the following lesions:

- Leiomyoma
- Granular cell myoblastoma
- Giant cell fibroma
- Neurofibroma.

TREATMENT

Surgical excision is the usually recommended treatment.

GRANULAR CELL MYOBLASTOMA

DEFINITION

Granular cell myoblastomas are benign neoplastic conditions, which are recently being termed as "granular cell tumors" and are commonly seen in the oral cavity and skin.

ORIGIN

The true origin of this lesion is controversial. According to some investigators granular cells myoblastomas arise from the striated muscle cells as a degenerative disease process. However other investigators believe that this neoplasm is of neural tissue (Schwann cell) origin as S-100 protein can be demonstrated from these tumor cells.

CLINICAL FEATURES

Age: Granular cell myoblastoma usually arises in the adult people between the ages of 30 to 60 years, rare in children.

Sex: Both sexes are affected with almost equal frequency. However, some investigators believe that this lesion has a female predilection.

Site: Intraorally tongue is most frequently affected, the other sites include—lips, floor of the mouth, gingiva, palate and uvula, etc.

The neoplasm can also develop from several extraoral locations, which include—breast, skeletal muscles, skin and subcutaneous tissue, etc.

PRESENTATION

- The lesion clinically presents a slow enlarging, painless, well-circumscribed lump or mass on the dorsum of the tongue, just beneath the covering epithelium.
- The size of the lesion is around 2 centimeter in diameter or less.
- On palpation, the neoplasm reveals a firm, nodular growth, which is nonmovable.
- The overlying covering epithelium usually appears normal and sometimes it exhibits a yellow or orange tinge.
- The covering epithelium at the site of the lesion may be atrophic with loss of papilla and hence it often presents a typical 'leukoplakia-like' appearance.
- Multiple lesions sometimes can develop on the tongue.
- On rare occasions, granular cell myoblastomas could be very large in size and in such cases they are often clinically mistaken as carcinomas.
- Midline lesions of granular cell myoblastoma over the tongue are also sometimes confused with median rhomboid glossitis.

HISTOPATHOLOGY (FIG. 2.91)

- The unencapsulated neoplasm consists of diffuse sheets of large, oval or polygonal cells, with distinct cytoplasmic membrane.
- These neoplastic cells are often seen to be lying in continuity with the muscle fibers in some cases or with the peripheral myelinated nerves in other cases.
- The cell cytoplasms usually contain large number of discrete, punctate, eosinophilic granules.

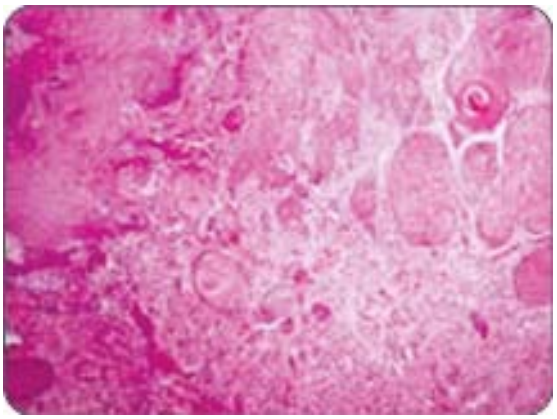

Fig. 2.91: Photomicrograph of granular cells myoblastoma

- The neoplastic cells sometimes also exhibit pale granular cytoplasm, however the nucleus is always small and compact looking.
- The granular cells often extend upwardly toward the epithelium and are present between the rete pegs.
- Due to the presence of these cells, the epithelium sometimes exhibits an unusual proliferative response, which is often referred to as the **'pseudoepitheliomatous hyperplasia'**.
- Pseudoepitheliomatous hyperplasia is characterized by elongated and branched rete pegs of the epithelium resembling the pattern of a neoplastic growth, especially squamous cell carcinoma. The lesion is therefore confused as squamous cell carcinoma on many occasions.
- The cells however are always histologically normal appearing and there is no sign of atypia or dysplasia.
- Inflammatory cell infiltration is usually absent in the connective tissue stroma.

DIFFERENTIAL DIAGNOSIS

- Epidermoid carcinoma
- Neurofibroma
- Neurilemmoma
- Fibroma
- Salivary gland neoplasms.

TREATMENT

Surgical excision.

BENIGN NEOPLASMS OF NEURAL TISSUE

NEURILEMMOMA (SCHWANNOMA)

DEFINITION

Neurilemmomas are benign neoplasms derived from the **Schwann cells**. These cells are neuroectodermal in origin and they envelope the axons of the peripheral nerves in the form of a membrane.

CLINICAL FEATURES

Age: The lesion usually arises before the age of 45 years (mostly seen in young and middle-aged adults).

Sex: Females are affected more often than males.

Site: Neurilemmomas can occur in relation to both the intracranial and the peripheral nerves.

In case of peripheral nerve lesions, head and neck is a common site.

Intraorally dorsum of the tongue is the most favored location. However other sites can be affected, which include palate, floor of the mouth, buccal mucosa, gingiva and lips, etc.

Neurilemmomas often occur as central jaw lesions in relation to the inferior alveolar nerve; at the posterior part of mandible.

PRESENTATION (FIGS 2.92 AND 2.93)

- Neurilemmoma clinically presents a slow enlarging, well-circumscribed, painless, nodule in the oral cavity.
- The lesion is smooth, firm, exophytic and often appears as a movable swelling beneath the mucosa.
- The size of the lesion greately varies, and it ranges between few millimeters to several centimeters in diameter.
- These are painless and asymptomatic in most of the cases, however some lesions can be tendered to palpation.
- Neurilemmoma typically develops in association with a nerve, and as the lesion enlarges the nerve is pushed towards the outer surface of the mass.

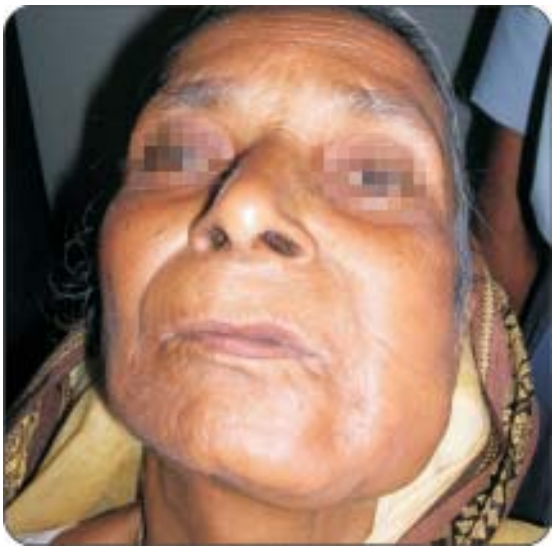

Fig. 2.92: Neurolemmoma-I

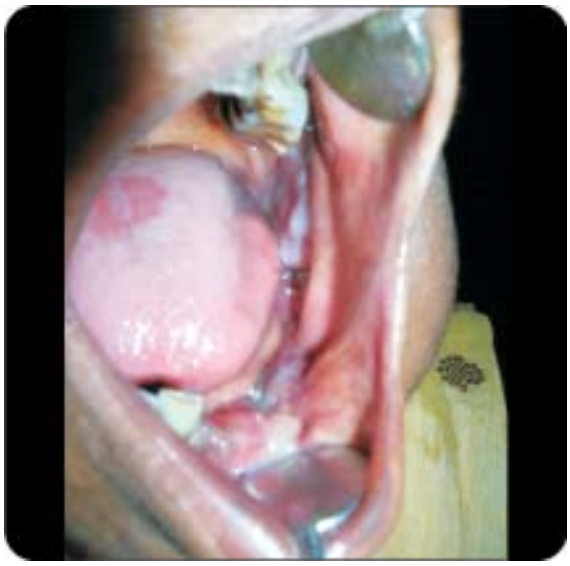

Fig. 2.93: Neurolemmoma-II

- Some lesions may grow at a faster pace with the development of **pain and paresthesia**. The later symptoms are more often associated with the intraosseous lesions.
- Sometimes small, lobulated, firm growths may occur in relation to the gingiva, which simulate the fibrous epulis.
- Central neurilemmoma of the jaw presents a well-demarcated, bony hard lesion that causes

expansion of the cortical plates and sometimes displacement of the regional teeth.
- Intracranical neurilemmoma of the acoustic nerve is commonly referred to as "**acoustic neuroma"** and it often causes hearing loss.
- On rare occasions, these lesions (neurilemmomas) may occur in multiple numbers within the oral cavity.

RADIOGRAPHIC FEATURES (FIG. 2.94)

- Radiographically central neurilemmomas present well-defined, unilocular or **multilocular radiolucent areas** in the jawbone, with expansion and distortion of the cortical plates.
- Large lesions may cause extensive bone destruction with occasional perforation of the cortical plates (Fig. 2.94).
- Lesions developing from the inferior alveolar nerve of mandible often cause enlargement of the mandibular canal.

HISTOPATHOLOGY

Histologically, neurilemmoma presents the following features (Figs 2.95 and 2.96):
- The neoplasm is well demarcated from the surrounding normal tissue by a true capsule or a pseudocapsule of fibrous connective tissue.
- The basic cellular constituents of the lesion are the proliferating spindle-shaped, neoplastic Schwann cells, having elongated nuclei.
- These cells are arranged in two distinct patterns, which are pathgnomonic for the neurilemmomas.
- The first pattern is referred to us the **Antoni A tissue**, which is characterized by parallel rows of palisading nuclei of Schwann cells (regimentation of nuclei).
- The cell cytoplasm cannot be readily delineated since they are blended with the surrounding tissue.
- Often there is presence of two palisaded configurations that are separated from one another by a cell free zone, showing characteristic linear paralleling arrays of collagen fibers.
- The unique configurations of nuclei in 'Antoni-A' tissue are often arranged in organoid swirls and are referred to as **"verocay bodies"**.
- The verocay bodies are eosinophilic acellular areas, consisting of reduplicated basement membrane and cytoplasmic processes.
- The second cellular pattern of neurilemmoma is the **Antoni B tissue**, which exhibits lack

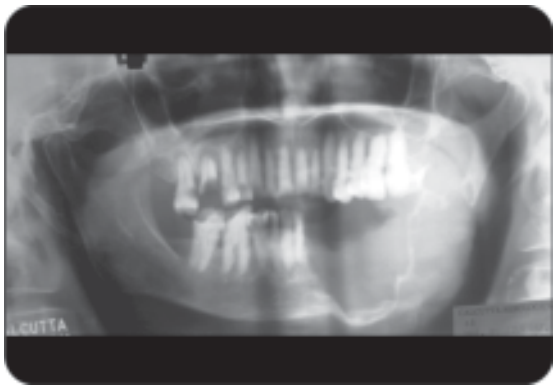

Fig. 2.94: Radiographic view of neurolemmoma

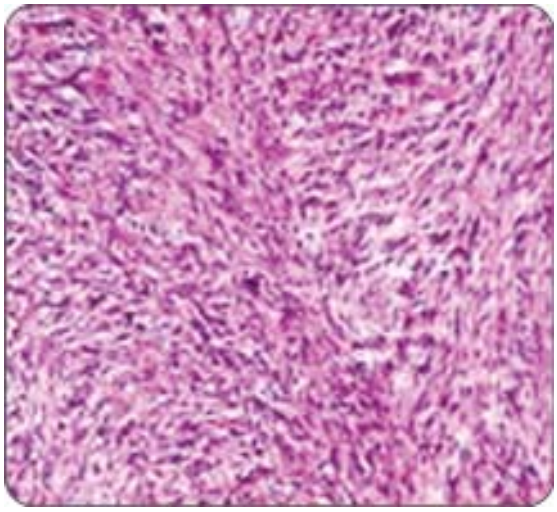

Fig. 2.95: Photomicrograph of neurilemmoma

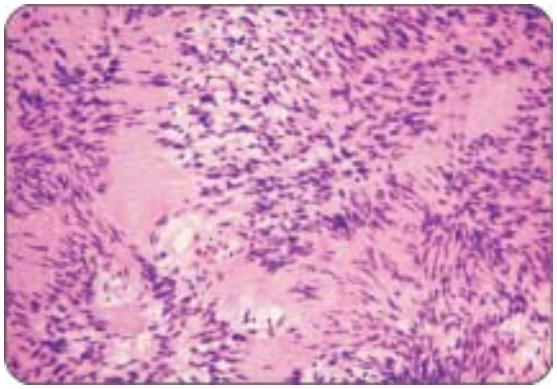

Fig. 2.96: Photomicrograph of neurolemmoma

of typical palisading arrangement of the nuclei.
- The cells in Antoni B tissue exhibit randomly arranged cells with oval nuclei within a loose myxomatous stroma this tissue is typically **less cellular and less organized**.
- Normally in neurilemmoma the 'Antoni A tissue' forms multiple nodules, which are interspersed by Antoni B tissues.
- Sometimes, the cells of the Antoni B tissue are very large and hyperchromatic and hence are often confused with malignancy. However neurilemmomas in general have a very little tendency to undergo malignant transformation.
- Long standing lesions of neurilemmoma often exhibit areas of hemorrhage, inflammation, fibrosis and nuclear atypia, etc.

DIFFERENTIAL DIAGNOSIS

- Neurofibroma
- Fibroma
- Fibroepithelial polyp
- Leiomyoma
- Peripheral giant cell granuloma.

TREATMENT

Surgical excision.

NEUROFIBROMA

DEFINITION

Neurofibromas are most common benign neural tissue neoplasms arising from the perineural **fibroblasts.** They may occur either as solitary lesion in the oral cavity or as multiple lesions in association with neurofibromatosis (Fig. 2.97).

Multiple neurofibromatosis: It is an autosomal dominant hereditary condition characterized by widespread overgrowth of nerve sheaths with formation of multiple neurofibromas on the skin and mucosa, along with 'café-au-lait' pigmentation of the skin.

ORIGIN

Neurofibromas arise from a mixture of cell types that include Schwann cells and the perineural fibroblasts.

CLINICAL FEATURES

***Age*:** Neurofibromas may occur at any age, however most lesions are detected in young adults.

***Sex*:** Both sexes are equally affected.

***Site*:** Intraorally, solitary neurofibromas often arise from the tongue, buccal mucosa, vestibule and lips, etc. These lesions are very commonly seen over the skin surfaces and moreover sometimes they can occur as central jaw lesions as well.

PRESENTATION

- Clinically neurofibromas often present small, asymptomatic, soft or firm, submucosal mass often with a multilobulated surface.
- Lesions are well demarcated, freely movable mass below the skin or mucous membrane, and are almost always painless (Fig. 2.98).
- Neurofibromas may **also occur as central jaw lesions** in relation to the mandible or maxilla and in such cases, they often produce a slow growing, expansile, swelling of the jawbone.
- Pain and paresthesia are rarely present in these lesions.
- In **multiple neurofibromatosis (Figs 2.99A and B)**, the individual neurofibroma lesions are encountered over the skin and as well as the mucosal surfaces. Moreover, neurofibromas in relation to this disease may develop either as nodular lesions or as diffuse lesions.

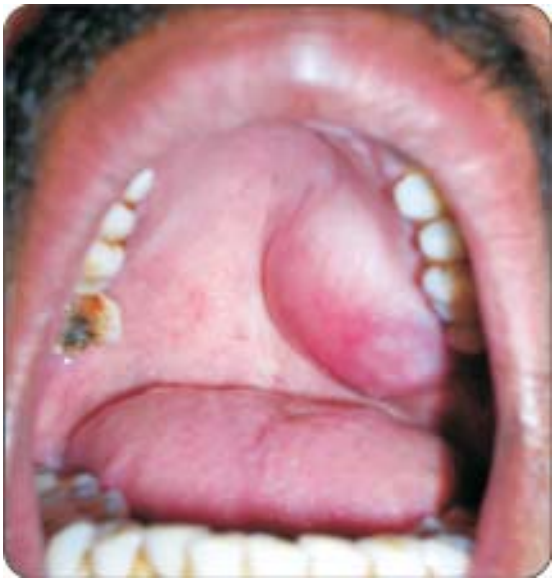

Fig. 2.97: Neurofibroma

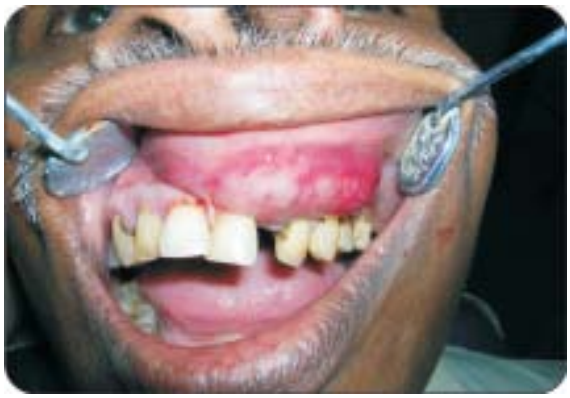

Fig. 2.98: Neurogenic sarcoma

Fig. 2.99A: Neurofibromatosis

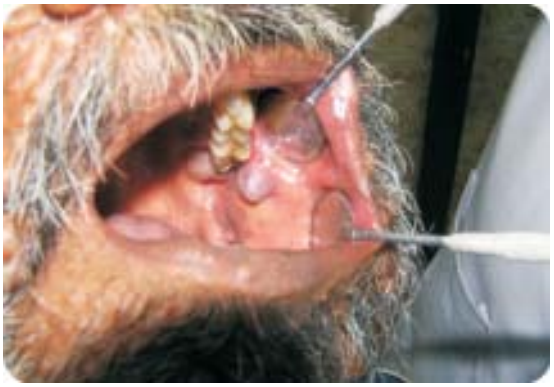

Fig. 2.99B: Neurofibromatosis

- The nodular lesions vary in size from few millimeters to several centimeters in diameter, they are spherical in shape and often produce **multiple, dome-shaped elevations** of the skin.
- Their number varies from only few to several hundreds and in the oral cavity, these lesions produce diffuse soft tissue overgrowths.
- The diffuse lesions can be quite '**grotesque**' with formation of pendulous masses, which may envelope an entire extremity.
- These lesions also produce **massive flabby soft masses**, which emanate from the neck or involve the subcutaneous tissue of the face and scalp.
- Another classic feature of neurofibromatosis is the presence of one or more, large, diffuse, macular brown pigmentations of the skin, which are known as the **'café-au-lait' spots**. Rarely these café-au-lait spots can be visible on the oral mucosa.
- Solitary neurofibromas are mostly innocuous lesions, however, if these lesions are occurring as part of the disease multiple neurofibromatosis, they show a higher tendency for malignant transformation.
- Multiple other diseases can occur in association with neurofibromatosis and they include—hemangiomas and melanomas of the skin, meningeal, cerebral and endocrine neoplasms and disturbance in the growth and development of bone, etc.
- In the oral cavity, neurofibromatosis causes macrognathia, macroglossia and deformity of the mandible, sphenoid bone, and the sigmoid notch, etc.

RADIOGRAPHIC FEATURES

Radiographically nurofibroma of the jawbone usually produces a relatively well-demarcated, unilocular or multilocular radiolucent area, with expansion of the cortical plates and divergence of roots of the regional teeth (Figs 2.100A and B).

HISTOPATHOLOGY (FIG. 2.101)

- Neurofibromas, whether they are occurring as solitary lesions or as a part of the disease 'multiple neurofibromatosis', histologically they produce similar appearances.
- Histologically, neurofibromas exhibit well circumscribed areas of proliferating spindle-shaped cells, which often resemble fibroblasts (neurofibroblasts).

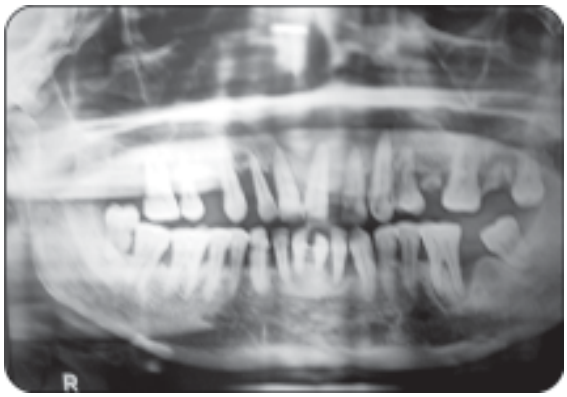

Fig. 2.100A: X-ray neurogenic sarcoma

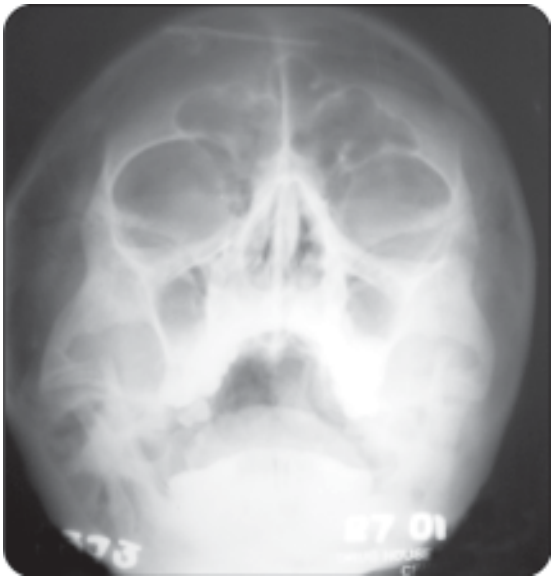

Fig. 2.100B: X-ray of Neurofibroma

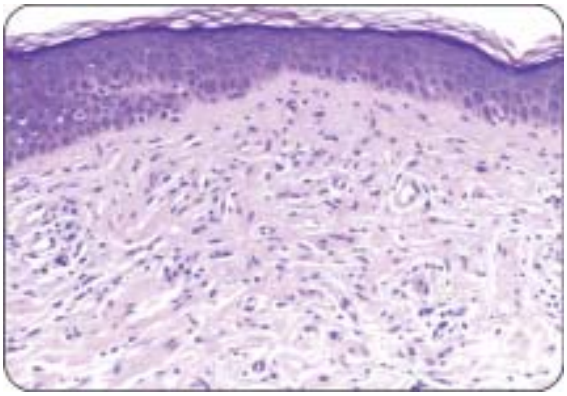

Fig. 2.101: Photomicrograph of neurofibroma

- These cells are often haphazardly arranged in interlacing bundles and the tumor cells have typical wavy nuclei.
- The neoplastic elements in neurofibroma fail to exhibit any specific cellular orientation pattern as seen in neurilemmoma, however, the ground substance sometimes produce a myxoid appearance.
- In some tumors, multiple nodules of fibroblastic tissue are seen and each nodule appears to be surrounded by a pseudocapsule, resembling the perineurium.
- Large numbers of mast cells are sometimes found within the tumor tissue and are of diagnostic importance.
- The 'café-au-lait' pigmentations microscopically reveal basilar melanosis without any proliferation of melanocytes.

TREATMENT

Solitary neurofibromas are treated by surgical excision.

Neurofibromatosis is not treated since surgical intervention may trigger the malignant potential of the individual lesions.

MELANOTIC NEUROECTODERMAL TUMOR OF INFANCY

DEFINITION

Neuroectodermal tumor of infancy is a rare benign, pigmented neoplasm of the jawbone, which is derived from the **primitive neural crest cells**.

CLINICAL FEATURES

Age: The lesion occurs mainly in **infants before the age of 6 months**; some lesions are present at birth (the usual range of age being 1–3 months).

Sex: Both sexes are equally affected.

Site: Majority of the neoplasms arise from the anterior part of maxilla, however mandible is also sometimes affected (about 25% cases).

Rarely the lesion may develop from extraoral sites like—shoulders, scapula, mediastinum and anterior fontanel, etc.

PRESENTATION

- Neuroectodermal tumor of infancy clinically presents a fast enlarging swelling of the

jawbone with expansion and distortion of the cortical plates.
- The swelling often cases elevation of the lip and facial asymmetry.
- Destruction of the underlying bone often causes displacement of developing teeth in the jaw.
- Pain and tenderness is usually not present.
- The surface of the lesion may exhibit a brown or black pigmentation.
- Rate of growth of the lesion often varies, few lesions grow quite rapidly while others may be slow growing.

RADIOGRAPHIC FEATURES

- Radiographically neuroectodermal tumor of infancy often exhibits a well-defined radiolunceny in the jaw that often resembles a cyst.
- The lesion often causes displacement of the developing tooth buds.
- Bone destruction is sometimes associated with bone formation (osteogenesis) and such lesions often radiographically exhibit a typical '**sun-ray**' appearance.
- Sometimes the margin of the lesion may be ill-defined or ragged due to irregular pattern of bone destruction and in such cases the lesion often resembles an invasive tumor.

MACROSCOPIC APPEARANCE

The cut surface of the lesion exhibits a typical **'slate-blue' or 'greyish-black'** appearance. In some cases, there may be presence of some 'greyish-white' streaks in the lesion.

HISTOPATHOLOGY

- The lesion is composed of two types of cells—the **pigmented cells** and the **nonpigmented cells**, both of which are found within a dense connective tissue stroma.
- The neoplastic cells often proliferate in the patterns of nests or tubules or alveolar structures, etc.
- The pigmented cells are large with an open nucleus and a lightly staining cytoplasm, which occasionally contains coarse melanin granules.
- These cells are flattened or cubical in shape with large, pale nuclei and are often arranged in large masses.
- The nonpigmented cells are small with dark, dense nuclei and a scanty cytoplasm and they often resemble lymphocytes.
- These unpigmented cells are arranged in clusters within the connective tissue stroma and sometime these cells are surrounded by the pigmented cells.
- Mitotic activity is rare in the tumor cells.

SPECIAL INVESTIGATIONS

Patients with neuroectodermal tumor of infancy generally have **high urinary levels of vanillyl-mandelic acid** and this observation is suggestive of the neuroectodermal origin of the neoplasm.

TREATMENT

Surgical excision with thorough curettage.

MALIGNANT NEOPLASMS OF MESENCHYMAL TISSUE

FIBROSARCOMA

DEFINITION

Fibrosarcomas are malignant neoplasms of the fibroblast cells, which often exhibit an aggressive and destructive behavior.

CLINICAL FEATURES

Age: The neoplasm can occur at any age, but most commonly affects the young adults and children.
Sex: Both sexes are almost equally affected.

Site:
- Intraorally fibrosarcomas commonly arise from the cheek, tongue, gingiva, palate, floor of the mouth, maxillary sinus and other paranasal sinuses and the pharynx, etc.
- Intraosseous lesions, which occur either periosteally, or endosteally, frequently involve the jawbones.
- Among the jaw lesions, mandible is affected far more commonly than maxilla (Figs 2.102 and 2.103).
- Occasionally, fibrosarcomas may develop following radiotherapy in a pre-existing bony lesion, e.g. fibrous dysplasia of bone.

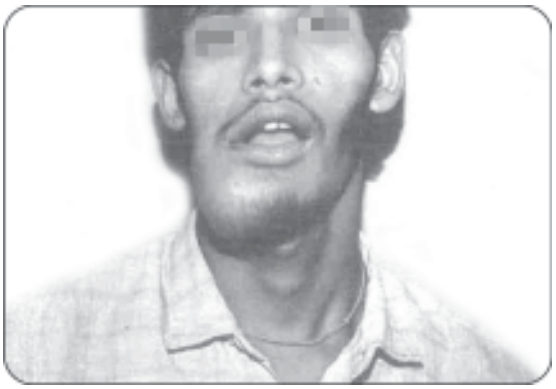

Fig. 2.102: Fibrosarcoma developing in mandible

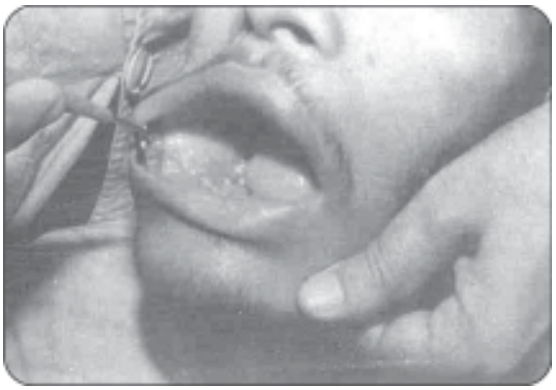

Fig. 2.103: Intraoral view of the same patient

CLINICAL PRESENTATION (FIGS 2.104 AND 2.105)

- In the initial stages, fibrosarcoma mostly remains symptomatic and the condition often resembles a benign fibrous overgrowth.
- In the later stages, the lesion becomes fast enlarging and within a short span of time, it gives rise to a large, painful, bulky, lobulated **"fleshy"** mass.
- The surface of the lesion is smooth and it often becomes ulcerated due to trauma.
- Pain and secondary infections are also common.
- The neoplasm is usually firm in consistency and it is often indurated with the surrounding normal tissue.
- Intrabony lesions of fibrosarcoma often produce **severe swelling and destruction of the affected bone with loosening and exfoliation of the regional teeth.**
- Pain, anesthesia or paresthesia in the affected region is often present.
- Fibrosarcomas are nonencapsulated tumors and they can be fixed to the underlying structures.

Fig. 2.104: Fibrosarcoma-I

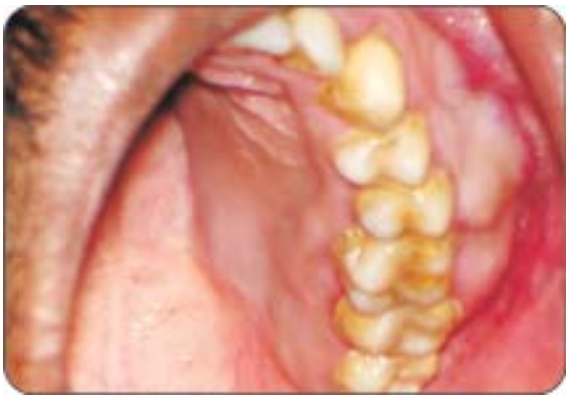

Fig. 2.105: Fibrosarcoma-II

- Lesions developing in the maxillary sinus or other paranasal sinus regions often produce obstructive symptoms and epistaxis.
- The patients are usually severely ill and exhibit marked deterioration of their general health.

RADIOGRAPHIC FEATURES

- Fibrosarcoma of the jawbone radiographically produces a sharply defined radiolucent area with severe destruction of bone (Figs 2.106 and 2.107).
- Expansion and marked thinning of cortical bone, displacement of teeth and resorption of roots, etc. are common.

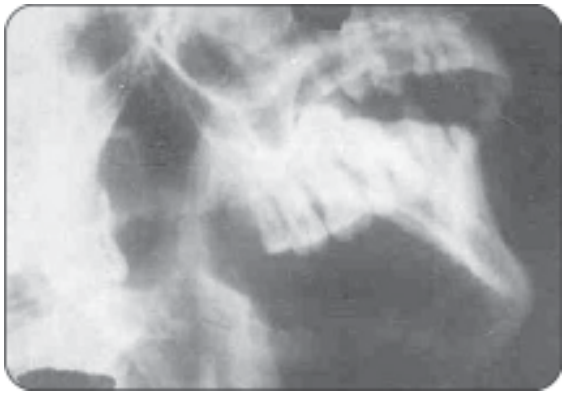

Fig. 2.106: Fibrosarcoma causing extensive bone destruction in mandible

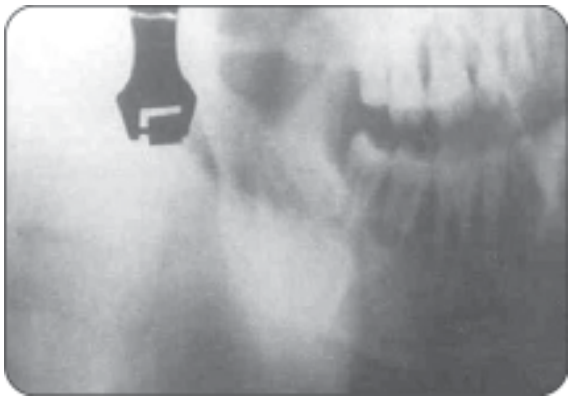

Fig. 2.107: Radiograph showing interradicular bone destruction

HISTOPATHOLOGY (FIG. 2.108)

Microscopically, fibrosarcoma reveals the following features:

- Active proliferation of numerous spindle shaped, malignant fibroblast cells within the connective tissue stroma.
- The malignant fibroblast cells often have a **`tad pole' like appearance** and most of the cells in fibrosarcoma are well differentiated.
- Each malignant tumor cell contains a large, uniformly stained, elongated hyperchromatic nucleus and a thin scanty cytoplasm.
- Normally there is a **'streaming fashion'** of proliferation of the malignant fibroblast cells in the connective tissue.
- Synthesis of collagen is very minimum and often the collagen bundles are arranged in a typical **"Herringbone"** pattern.
- Increased mitotic activity, hypercellularity, cellular pleomorphism and nuclear hyperchromatism, etc. often distinguishes fibrosarcoma from other benign fibroblastic neoplasms.

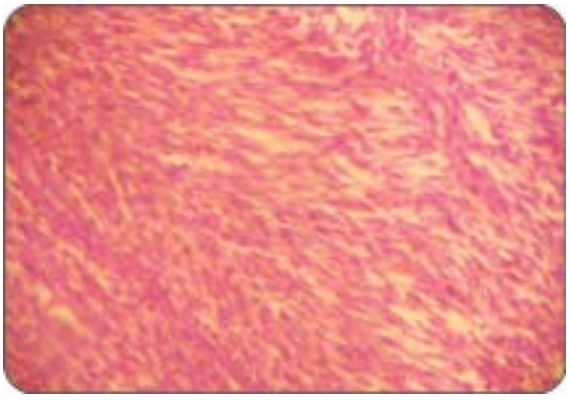

Fig. 2.108: Photomicrograph of fibrosarcoma

- The mitotic activity is very minimum in the 'well-differentiated' lesions of fibrosarcoma, however the rate of mitotic activity gradually increases with more and more poorly differentiated lesions.
- In poorly differentiated fibrosarcomas, the individual malignant fibroblast cells appear large, plump, round or oval, and these cells synthesize very little collagen.
- In many cases, the tumor cells exhibit abnormal mitotic activity in the form of **"bi-radiate"** or **"tri-radiate"** mitosis, etc.
- In the anaplastic form of fibrosarcoma, the tumor cellularity is markedly increased, mitotic figures become numerous and there can be even presence of few malignant giant cells.
- Distant metastasis is rare but local infiltration to the adjacent tissues is very common in fibrosarcoma.

DIFFERENTIAL DIAGNOSIS

The following lesions are to be included in the differential diagnosis of fibrosarcoma:

- Malignant fibrous histiocytoma
- Rhabdomyosarcoma
- Liposarcoma
- Neurogenic sarcoma
- Nodular fascisitis.

TREATMENT

Radical surgical excision and chemotherapy is the treatment of choice. Radiotherapy is not

effective. Prognosis is good because metastasis occurs only in few cases.

MALIGNANT FIBROUS HISTIOCYTOMA

DEFINITION

Malignant fibrous histiocytomas are a group of aggressive malignant neoplasms, arising from the undifferentiated mesenchymal cells that differentiate along both **fibroblastic and histiocytic** pathways. This is probably the most common soft tissue sarcoma of the adults.

CLINICAL FEATURES

Age: The disease predominantly affects the people of relatively older age group.

Sex: Both sexes are almost equally affected.

Site: Malignant fibrous histiocytomas are slightly uncommon neoplasm in the oral cavity. Whenever, they occur intraorally, they can be found in the maxillary antrum, tongue, buccal mucosa and maxillary or the mandibular bones, etc.

PRESENTATION

- The neoplasm clinically presents a fast expanding, exophytic, lobulated and ulcerated growth in the oral cavity.
- Malignant fibrous histiocytomas often have a **"fleshy"** appearance and thus they clinically resemble the fibrosarcomas.
- Pain and surface ulceration may or may not be present.
- Pain, hemorrhage, anesthesia or paresthesia of the neighboring structures is commonly seen.
- Intraosseous lesions often produce large, painful, expansile growth in the jawbone with mobility or spontaneous exfoliation of the regional teeth.
- Facial asymmetry or gross facial disfigurement is often associated with this lesion (Fig. 2.109).
- Tumors developing in the nasal cavity or paranasal sinuses may cause obstructive symptoms and epistaxis.
- Secondary infections in the lesion or pathological fracture of the affected bone may sometimes occur.

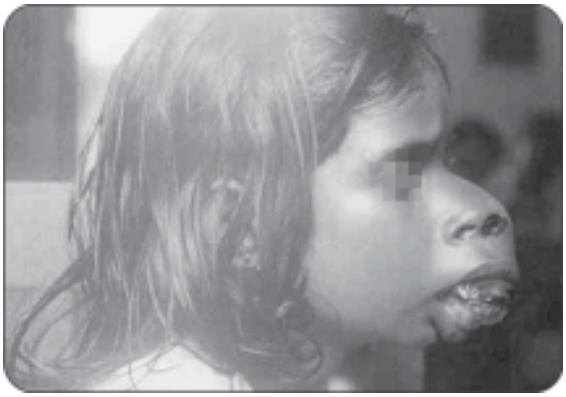

Fig. 2.109: Malignant fibrous histiocytoma causing massive swelling of the maxilla

RADIOGRAPHIC FEATURES

- Malignant fibrous histiocytoma radiographically presents a large, multilocular radiolucent area in the jawbone, with severe expansion and distortion of the cortical plates.
- Destruction of inter-radicular bone and perforation of the cortical plates occur quite frequently.
- On rare occasions, pathological fractures of the bone can be seen.
- Radiographically, the teeth in the affected area are often seen to be 'floating' within the radiolucent zone.

HISTOPATHOLOGY (FIG. 2.110)

- Histologically, the neoplasm reveals actively proliferating, numerous polyhedral or oval shaped malignant histiocytes and many spindle-shaped malignant fibroblast cells.
- Short fascicles of malignant cells are often arranged in a typical **"cart-wheel"** or "**storiform**" pattern.

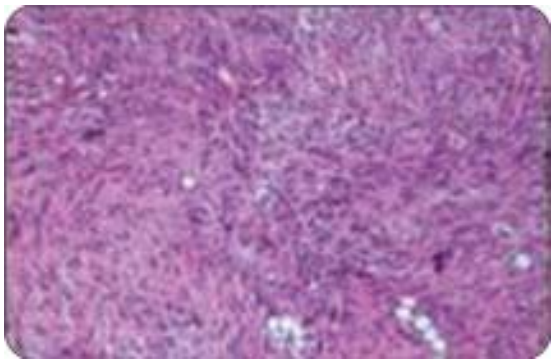

Fig. 2.110: Photomicrograph of malignant fibrous histiocytoma

- Increased mitotic activity, cellular pleomorphism and nuclear hyperchromatism are often seen in these tumor cells.
- In many cases, there can be presence of multiple multinucleated giant cells and in addition to these, few large foam cells are also found.
- Some of the tumors are extremely cellular and they produce copious amount of collagen.
- Malignant fibrous histiocytoma is usually non-encapsulated and it often exhibit focal areas of chronic inflammatory cell infiltration in the connective tissue.

TREATMENT

Wide surgical excision coupled with radiotherapy and chemotherapy.

LIPOSARCOMA

DEFINITION

Liposarcomas are malignant neoplasms derived from cells that differentiate along adipose tissue lines and show some evidence of fat synthesis. This is the second most common soft tissue sarcoma of the adults.

CLINICAL FEATURES

***Age*:** The peak age of occurrence is between 40 to 60 years.

***Sex*:** Male people are affected more often than females.

Site: In the oral cavity, the lesions frequently develop from the cheek or buccal mucosa, the other common sites include the soft palate, floor of the mouth and the maxilla or the mandible, etc.

PRESENTATION

- These are externally rare neoplasms especially in the oral cavity. In the head and neck region, they are more often encountered in the deep tissues of the neck.
- Clinically liposarcomas produce relatively slow growing, occasionally painful, submucosal masses.
- Lesions are mostly poorly demarcated and lobulated in nature, and are soft or firm in consistency.
- The overlying epithelium may be either normal or yellow in color.
- These neoplasms are sometimes so soft and fluctuant that they can be clinically mistaken for a large cyst.
- Liposarcomas more often arise as 'de novo' lesions rather than through malignant transformation of a pre-existing lipoma.

HISTOPATHOLOGY

- Histologically, liposarcomas are more cellular lesions than lipomas and they consist of multiple numbers of **foamy and 'fat-containing' malignant lipoblast cells.**
- Many cells with **'signet-ring'** appearance (vacuolated cytoplasms) are also found in these neoplasms.
- The nuclei in the tumor cells are prominently displaced to the side of a large vacuole.
- Some liposarcomas are composed of poorly-differentiated round cells, with only focal evidence of cytoplasmic vacuolization.
- In some cases, there can be presence of irregularly shaped giant cells having foamy cytoplasms.
- In liposarcoma, the malignant lipoblast cells often produce large amount of fat within the tumor and this often leads to a myxoid appearance of the lesion.
- Liposarcomas can metastasize to distant sites in the body like- lungs, bone and brain, etc.
- There are five histologic types of liposarcomas—namely the myxoid type, round cell type, well-differentiated type, de-differentiated type and the pleomorphic type.

TREATMENT

Radical surgery and radiotherapy.

HEMANGIOENDOTHELIOMA

DEFINITION

Hemangioendothelioma is a malignant angiomatous neoplasm of mesenchymal tissue origin, which is derived from the **endothelial cells** of the blood vessels or lymphatic vessels.

There are in fact three distinct neoplasms, which are categorized as angiosarcomas and these are named as hemangioendothelioma, hemangiopericytoma and the Kaposi's sarcoma.

The hemangioendothelioma and hemangiopericytoma are **'quasi-malignant'** neoplasms of vascular endothelium and vascular pericytes respectively.

These neoplasms are extremely cellular and represent proliferations of the individual component cells of the blood vessels, rather than entire blood channels per se, as seen in hemangiomas.

CLINICAL FEATURES

Age: Hemangioendotheliomas are more commonly seen in children and young adults.

Sex: Females are affected more often than males with a ratio of about (2:1).

Sites: Hemangioendotheliomas are more commonly found in the skin and the subcutaneous tissues.

Oral lesions are rare and they may arise from the lips, palate, gingiva and tongue, etc.

The neoplasm can also occur as central jaw lesions in relation to either maxilla or mandible.

PRESENTATION

- Hemangioendothelioma clinically presents a fast enlarging, localized, painful, nodular swelling (Fig. 2.111).
- The lesion often shows surface ulceration, moreover, paresthesia or anesthesia of the affected area is also common.

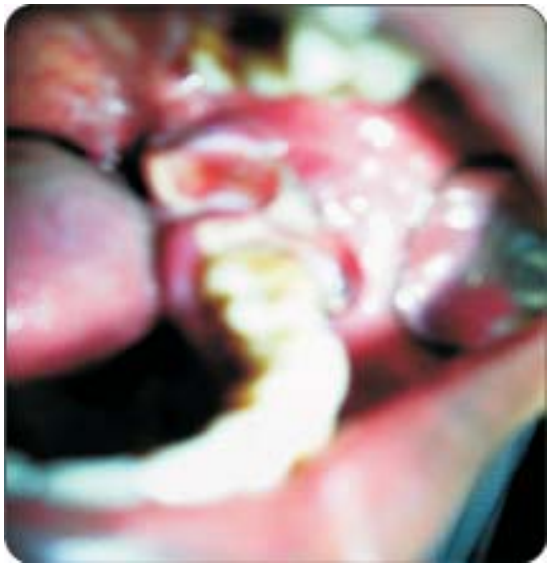

Fig. 2.111: Hemangioendothelioma

- Hemangioendothelioma sometimes clinically exhibit hemangioma-like appearance and in such cases the neoplasm appears as flat or slightly raised lesion, with a dark-red or bluish-red surface.
- Mobility of the regional teeth and bleeding upon slight trauma are common.
- The central jaw lesions usually produce expansile, destructive growths with swelling, pain and cortical expansion, etc.

HISTOPATHOLOGY

- Hemangioendothelioma microscopically presents neoplastic proliferation of **malignant** endothelial cells with variable degrees of individual cell differentiation.
- The cells are pleomorphic, large, polyhedral or slightly flattened with a faint cytoplasmic outline.
- The nuclei are hyperchromatic, round and contain several minute nucleoli.
- In most areas, the neoplastic cells proliferate as a single layer but in some cases there may be proliferation of cells in large masses, which fills up the entire lumen of the involved vessel.
- An increased abnormal mitosis may be seen but not in all cases.
- The neoplasm is not encapsulated and the cells often tend to invade into the surrounding tissue.
- In silver-reticulin stain, the tumor cells of hemangioendothelioma lie within the delicate reticulin sheath encircling the blood vessel.

TREATMENT

Surgical excision and radiotherapy.

HEMANGIOPERICYTOMA

DEFINITION

Hemangiopericytomas are malignant neoplasms arising from the pericytes around the blood vessels (these are contractile cells that along with their interlacing processes form a network around the outer aspect of the capillary walls).

In every blood vessels or lymphatic vessels, the endothelial cells lie on the inner aspect of the basement membrane, while the network of pericytes embraces the capillaries from outside. These pericytes usually help in the process of contraction and dilatation of the vessels.

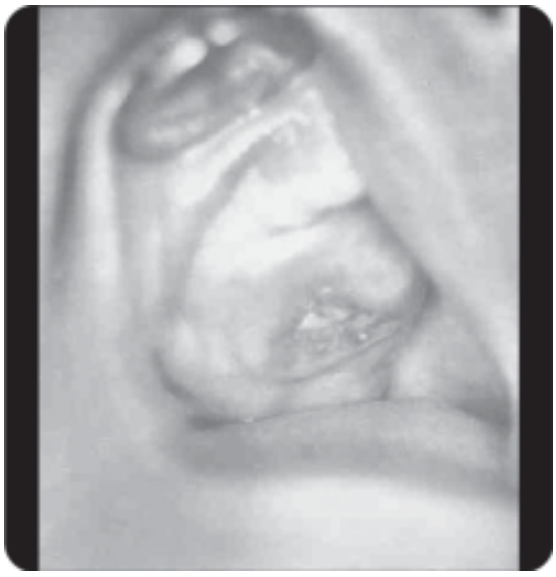

Fig. 2.112: Hemangiopericytoma of the palate

CLINICAL FEATURES

Age: The neoplasm can occur at any age, however majority of the lesions arise before the age of 50 years.

Sex: Both sexes are affected with almost equal frequency.

Site: Oral lesions of hemangiopericytoma generally arise from the tongue, lips, floor of the mouth, gingiva and jawbones, etc (Fig. 2.112).

PRESENTATION

- Hemangiopericytoma clinically presents a slow enlarging, painless, well-circumscribed growth (Figs 2.113 to 2.115).
- It is often firm in consistency and the surface is usually nodular.
- There may or may not be any reddish appearance in the lesion, which could be indicative of its vascular origin. However the superficial lesions may have vascular prominence and pigmentations.
- Some neoplasms can be fast enlarging and they produce large, painful, nodular swellings with surface ulceration.
- Central jaw lesions may produce large, expansile, painful growths of the jawbone with mobility or exfoliation of the regional teeth.

HISTOPATHOLOGY

Histologically, the neoplasm reveals the following features:

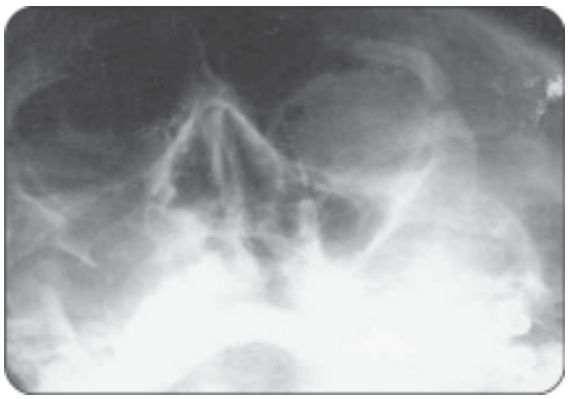

Fig. 2.113: Hemangiopericytoma causing invasion into the Lt. Maxillary antrum

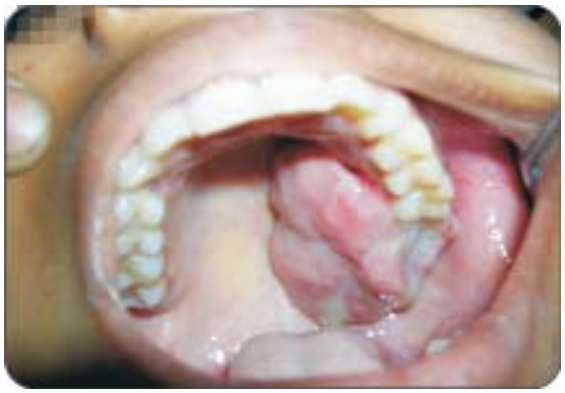

Fig. 2.114: Hemangiopericytoma-I

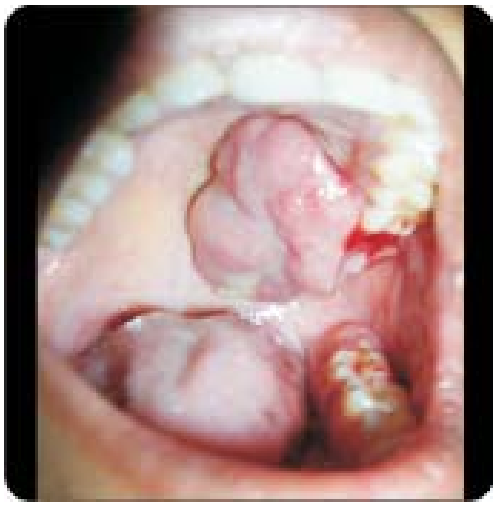

Fig. 2.115: Hemangiopericytoma-II

- There will be multiple number of normal appearing, **'capillary-like' tubules** lined by a single layer of flattened endothelial cells.
- The capillary-like tubules are bordered on their outer aspect by some densely or loosely packed

cells, which are showing plump nuclei and indistinct cytoplasm.
- These cells at the periphery of the capillaries are malignant pericytes and they often exhibit cellular pleomorphism, nuclear hyperchromatism and increased abnormal mitotic activity, etc.
- The malignant pericytes are often spindle shaped and these cells are often haphazardly arrangd within the tumor.
- The blood vessels often exhibit irregular branching and therefore produce a typical 'stag-horn' or 'antler-like' appearance.
- The demonstration of capillary basement membrane by silver-reticulin stain reveals that these malignant pericytes are present outside the basement membrane and these cells are sharply demarcated from endothelial cells by the 'peri-endothelial ring' of reticulin fibers.

DIFFERENTIAL DIAGNOSIS

- Hemangioma
- Kaposi's sarcoma
- Glomus tumor.

TREATMENT

Surgical excision is the treatment of choice, the lesion is radioresistant.

KAPOSI'S SARCOMA

DEFINITION (FIGS 2.116 AND 2.117)

Kaposi's sarcoma is a malignant neoplasm **arising from the endothelial cells** of the blood capillaries and it is considered to be the commonest sarcoma of the **angiomatous tissue**.

ENDEMIC KAPOSI'S SARCOMA

Kaposi's sarcoma was first reported by **Moritz Kaposi in 1872** and it was described as a rare endemic disease among elderly persons of Central European or Mediterranean origin. The endemic form of the disease is also seen among the children and young black Africans.

The endemic Kaposi's sarcoma usually affects the skin and the lymph nodes; and it rarely affects the viscera.

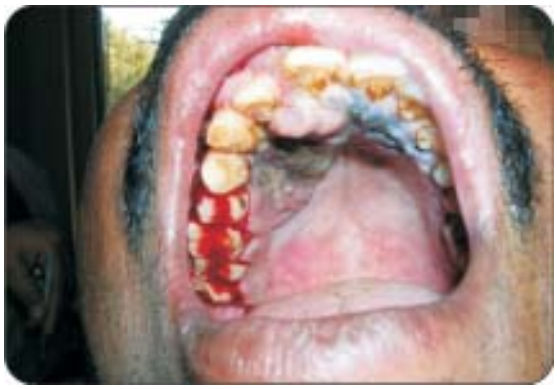

Fig. 2.116: Kaposi's sarcoma-I

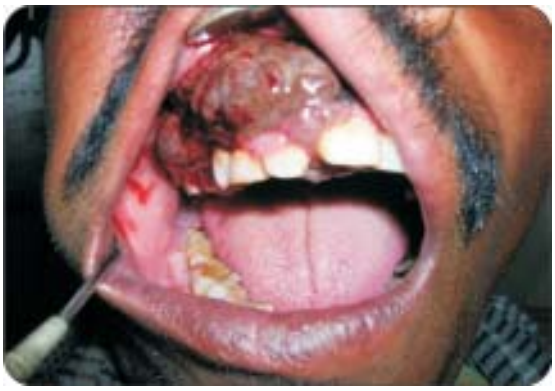

Fig. 2.117: Kaposi's sarcoma-II

EPIDEMIC KAPOSI'S SARCOMA

- Kaposi's sarcoma has really become an epidemic since 1981, as large numbers of cases are being reported in association with patients suffering from AIDS.
- The AIDS-associated Kaposi's sarcomas are multicentric angiosarcomatous lesions that affect skin, lymph nodes, bone and viscera (especially the GI tract), etc.
- AIDS patients with history of homosexuality develop Kaposi's sarcoma very frequently.
- In AIDS related Kaposi's sarcoma, it is not clearly known whether the disease occurs as a result of direct infection from human immunodeficiency virus or due to immunosuppression.
- According to some investigators, Kaposi's sarcoma occurs in association with cytomegalovirus infection as well.

ETIOLOGY

The following factors are believed to 'triggers' the initiation of Kaposi's sarcoma:

- Genetic predisposition
- Infection by human immunodeficiency virus (HIV) or cytomegalovirus (CMV)
- Immunosuppression
- Environmental factors.

CLINICAL FEATURES

In Kaposi's sarcoma, oral lesions are seen in about 10% cases and these are mostly seen in the palate. Other intraoral sites, which may be involved, are the maxillary gingiva and tongue, etc.

Kaposi's sarcoma is usually present in three different clinical stages, namely—(A) the patch stage, (B) the plaque stage and (C) the nodular stage.

Patch stage: Patch stage is the initial stage of the disease and during this a **pink, red or purple macule** appears over the oral mucosa.

Plaque stage: Patch stage is actually continued into the plaque stage with time and during this stage, the lesion appears as a **large, raised, violaceous plaque**.

Nodular stage: It is the last stage of the disease and is characterized by the occurrence of **multiple nodular lesions** on the skin or the mucosa.

HISTOPATHOLOGY (FIG. 2.118)

The microscopic features of Kaposi's sarcoma vary depending upon the clinical stage of the disease:

Patch Stage

During the "Patch Stage", Kaposi's sarcoma histologically shows multiple dilated, irregular blood vessels, which are lined by normal appearing endothelial cells. Few chronic inflammatory cells infiltration in the connective tissue stroma are also evident.

Plaque Stage

The "Plaque stage" histologically shows many **dilated, jagged, vascular channels**, lined by **'spindle-type' cells**. Similar looking cells are also present as perivascular aggregates.

In between the vascular structures, RBCs, macrophages, plasma cells, lymphocytes and hemosiderine pigments, etc. are often present.

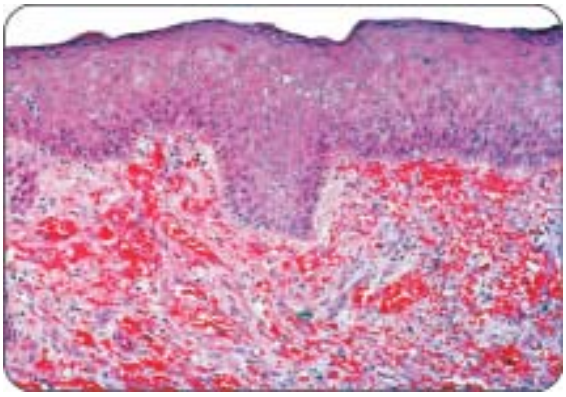

Fig. 2.118: Photomicrograph Kaposi's sarcoma

Nodular Stage

Microscopically, nodular lesion of Kaposi's sarcoma consists of **sheets of spindle-shaped cells** in a background of scattered blood vessels and 'slit-like' spaces containing RBC.

Marked hemorrhage, hemosiderin pigmentation, lymphocyte and macrophage infiltrations are also commonly seen.

DIFFERENTIAL DIAGNOSIS

- Pyogenic granuloma
- Hemangioma
- Angiosarcoma.

TREATMENT

Kaposi's sarcomas are treated by radiotherapy and chemotherapy, surgery is a difficult proposition since the disease is often multicentric.

EWING'S SARCOMA

DEFINITION

Ewing's sarcoma is a **highly malignant distinctive primary mesenchymal neoplasm of bone,** which was first reported in 1921 by James Ewing. It is the third most common primary malignant neoplasm of bone after osteosarcoma and chondrosarcoma.

HISTOGENESIS

The exact cell of origin of Ewing's sarcoma is not known, however it is generally believed that the lesion arises from either the endothelial cells of the blood vessels within the bone or from the

undifferentiated reticuloendothelial cells. Recent investigators believe that Ewing's sarcoma is neuroectodermal in origin and also given another name to this tumor as '**Peripheral Primitive Neuroectodermal Tumors' (PNET).**

CLINICAL FEATURES

Incidence: Ewing's sarcomas constitute about 10% of all the malignant bone tumors.

Age: The neoplasm usually occurs in children and young adults, between the ages of 5 to 25 years. 80 percent patients are below 20 years of age.

Race: Majority of the people are whites; black people are rarely affected.

Sex: There is a slight male predominance seen in the disease (M:F ratio 60:40)

Site: The disease is mostly encountered in the long bones of the lower extremity, e.g. femur and pelvic bones, etc. Among the jaw lesions, mandible is affected more often than the maxilla.

Jaw lesions of Kaposi's sarcoma are sometimes metastatic in origin and in such cases long bones are the primary sites of the neoplasm.

PRESENTATION

- The tumor causes rapid swelling in the affected part of the bone, which is often associated with severe pain.
- The **initial symptoms** of Ewing's sarcoma are very similar to that of osteomyelitis and care should be taken in this regard while making the diagnosis.
- Expansion of the jawbone with **paresthesia or anesthesia** of the area can be frequently seen.
- Sometimes, the tumor perforates the cortical plate of the bone and protrudes as a soft tissue mass overlying the affected area of bone.
- **Unexplained loosening of the tooth** is a very common feature of Ewing's sarcoma.
- In the later stages, the neoplasm develops surface ulceration.
- Patients with Ewing's sarcoma may develop moderate **fewer, leukocytosis, anemia and raised ESR**, etc. These symptoms often indicate a poor prognosis of the disease.

RADIOGRAPHIC FEATURES

- Radiographically Ewing's sarcoma usually presents a radiolucent area in the bone with ill-defined margins.
- Expansion and distortion of the cortical bones often occur along with widespread destruction of the alveolar bone.
- In this disease, the periosteum of the bone characteristically exhibits lamellar layering (an osteophytic reaction), which is known as **onion-skin appearance**.

HISTOPATHOLOGY

- Microscopically, Ewing's sarcoma presents numerous, proliferating, closely packed, small round cells, which have monotonous looking round or oval nuclei.
- The neoplastic cells of Ewing's sarcoma often resemble the lymphocytes.
- These hyperchromatic malignant cells are arranged either in diffuse sheets or in loosely arranged lobules.
- The sheets or lobules of neoplastic cells are often separated from one another by a thin fibrous band, containing small blood vessels and chronic inflammatory cells.
- The individual malignant cells may be of two types: small round cells with darkly staining nuclei and well-delineated cytoplasms.
- The other cells are larger with finely granular nuclei and ill-defined, faint cytoplasms.
- Increased mitotic activity with areas of tissue necrosis and hemorrhage are also commonly observed in Ewing's sarcoma.

DIFFERENTIAL DIAGNOSIS

- Neuroectodermal tumor of infancy
- Embryonal rhabdomyosarcoma
- Garre's osteomyelitis
- Lymphoma
- Metastatic carcinoma
- Neuroblastoma
- Leukemia
- Myeloma
- Mesenchymal chondrosarcoma
- Small cell osteosarcoma.

TREATMENT

Radiotherapy and multidrug chemotherapy; surgery is occasionally attempted, 5 years survival rate is only 10%.

CHONDROSARCOMA

DEFINITION

Chondrosarcomas are malignant neoplasms of bone, in which the neoplastic cells exclusively produce abnormal cartilage tissue but no osteoids or bone.

HISTOGENESIS

Chondrosarcomas may be of two types:

- ***Primary chondrosarcoma:*** Lesion arising directly from the bone as a malignant neoplasm.
- ***Secondary chondrosarcomas:*** Lesion arising from the pre-existing benign cartilaginous neoplasms such as chondromas or osteochondromas, etc.
- Besides this, chondrosarcomas may also arise from other pre-existing bony diseases like—Paget's disease of bone, Ollier's disease (multiple enchondromatosis) and Maffucci syndrome (multiple enchondromatosis, hemangiomas and fibromas).
- In the jawbone, nearly all chondrosarcomas arise as **'de novo'** malignant lesions, without the pre-existence of any benign chondroma.
- It is also important to note that **malignant cartilaginous tissue neoplasms are far more common in the jaw bones, as compared to their benign counterparts.**

CLINICAL FEATURES

Age: Peak age of occurrence of chondrosarcomas is between 30 to 40 years.

Sex: It is more commonly seen among males (M:F ratio-2:1).

***Site*:** Chondrosarcomas develop less frequently in maxilla as compared to the osteosarcomas and these are mostly confined to the anterior part, where pre-exiting nasal cartilage is present.

In the mandible, the disease mostly occurs in the posterior region, at the site of the embryonically derived Meckel's cartilage. Besides this, mandibular lesions may also develop from the symphysis, coronoid or the condylar processes. Few lesions may occur in relation to the nasal septum and the paranasal sinuses.

PRESENTATION

- During the initial stages chondrosarcomas produce a painless swelling of the jaw with facial asymmetry (Fig. 2.119).
- With further enlargement of the lesion, the disease produces pain, tenderness, anesthesia or paresthesia in the region.
- Chondrosarcomas are often very fast enlarging neoplasms and although metastasis does not occur during the initial period, many patients may die of extensive local tissue destruction.
- The jaw swelling progresses rapidly, causing severe expansion of the bone and loosening of teeth.
- The edentulous patients may feel poor fitting of the artificial dentures due to swelling of the jaw caused by the tumor.
- Chondrosarcomas occurring in the anterior maxilla may produce nasal obstruction, epistaxis, photophobia, visual loss and breathing difficulties, etc.
- Distant metastasis occurs in about 10 percent cases, mostly to the lung and other bones.

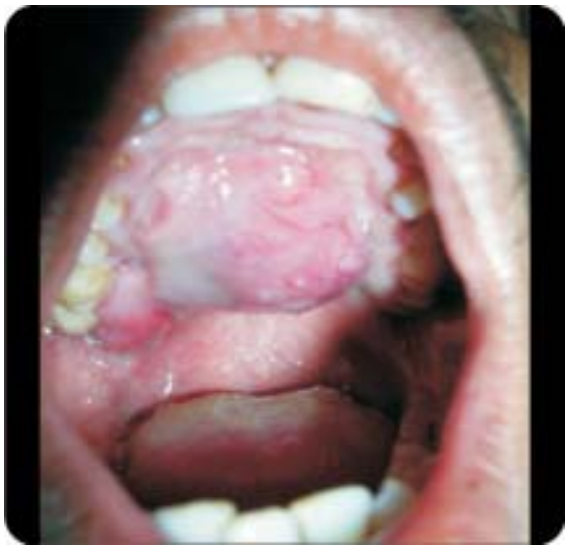

Fig. 2.119: Chondrosarcoma

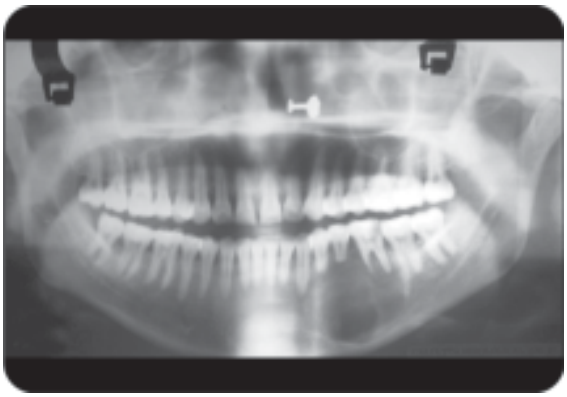

Fig. 2.120: Radiograph of chondrosarcoma

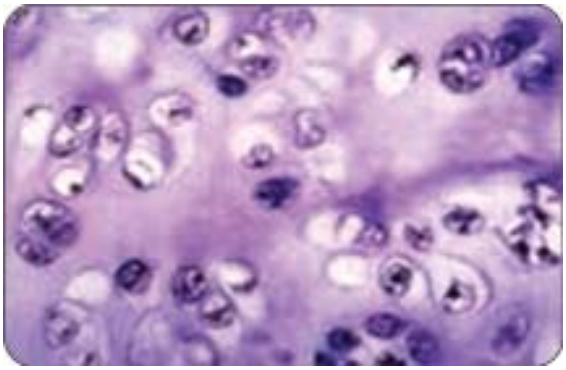

Fig. 2.121: Photomicrograph of chondrosarcoma-I

RADIOGRAPHIC FEATURES (FIG. 2.120)

- Radiographically chondrosarcoma appears as an expansile, **"moth-eaten"** radiolucent area in the bone with ill-defined borders.
- Within the area of radioluency, **multiple flecks or blotchy areas of radiopacities** are found. These are caused by calcification or ossification of the cartilage matrix. In some tumors the calcification can be dense and extensive.
- Widening of the periodontal ligament space of the adjoining teeth may be present with occasional root resorptions.
- Penetration of the cortex with peripheral osteogenic reaction may sometimes produce the typical 'sun-ray' appearance, as often seen in osteosarcomas.

HISTOPATHOLOGY (FIGS 2.121 AND 2.122)

The microscopic appearance of chondrosarcoma is highly variable.

- Some lesions are well-differentiated and resemble benign cartilaginous neoplasms, whereas, other lesions could be anaplastic in nature and are composed of spindle-shaped malignant cells, with little or no evidence of cartilage formation.
- In well-differentiated lesions, typical lacuna formation is seen within the chondroid matrix.
- The neoplastic cells of chondrosarcoma are pleomorphic and hyperchromatic, and many of them contain multiple nuclei. (Binuclear cells are very common).
- Most of the neoplastic cells in these highly cellular malignant lesions tend to surround an abnormal cartilage.
- Calcification and ossification often occur within the cartilage matrix.
- Mitotic activity in the neoplastic cells is rare in grade I and grade II lesions, but it is common in grade III lesions.
- Some lesions of chondrosarcomas exhibit formation bone instead of cartilage and such lesions often histologically resemble osteosarcoma.
- Sometimes many clear cells (cells with abundant clear cytoplasm) may be present in the tumor.
- Grade II and grade III lesions may have areas of myxoid tissue and or areas of cystic degeneration within the lesion.

Histological gradings of chondrosarcoma

Grade I	This variant is characterized by the presence of chondroid matrix and chondroblasts with only little variation from normal cartilage, there is increased calcification and ossification, and little or no mitosis. The tumor often resembles a 'chondroma'.
Grade II	The grade II variant shows increased cellularity and the tumor cells exhibit moderate sized nuclei. The cartilage matrix is myxoid in nature.
Grade III	This variant of chondrosarcoma is highly cellular in nature with little or no sign of calcification, the rate of mitotic activity is high.

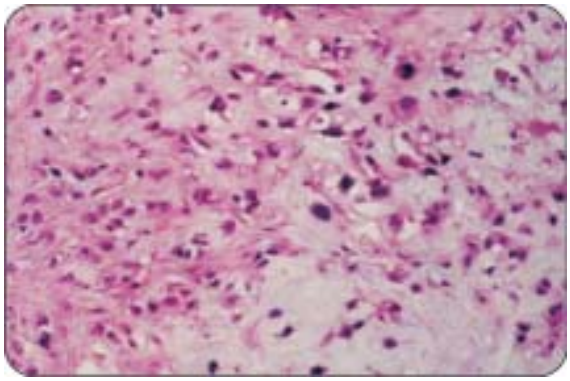

Fig. 2.122: Photomicrograph of chondrosarcoma-II

TREATMENT

Wide surgical excision is the only viable treatment. Radiotherapy and chemotherapy are not effective. Prognosis of chondrosarcoma is poorer as compared to the osteosarcoma. Moreover, prognosis of jaw chondrosarcomas is particularly worse than the lesions occurring elsewhere in the body.

MESENCHYMAL CHONDROSARCOMA

DEFINITION

Mesenchymal chondrosarcoma is a **highly malignant variant** of the conventional chondrosarcoma and it occurs more commonly from the jawbone and extra skeletal soft tissues.

CLINICAL FEATURES

Age: This lesion often affects the younger people, usually in the second and third decade of life.

Sex: Males and females are almost equally affected.

***Site*:** Unlike the conventional chondrosarcomas, these lesions affect the jawbones more frequently. 25 to 30 percent tumors occur in relation to the soft tissues rather than bone.

PRESENTATION

Mesenchymal chondrosarcomas present rapidly developing swelling and pain in the affected area of bone. The clinical nature of the tumor is much aggressive than that of the conventional chondrosarcoma (Figs 2.123 and 2.124).

Fig. 2.123: Mesenchymal chondrosarcoma-I

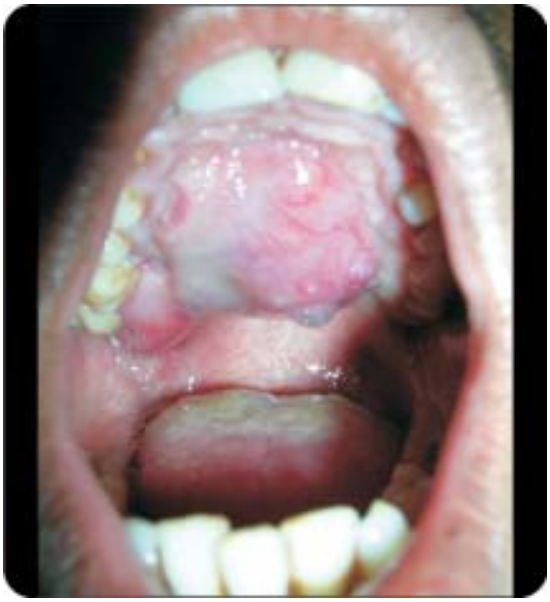

Fig. 2.124: Mesenchymal chondrosarcoma-II

RADIOLOGICAL FINDINGS

Radiographically, the tumor presents well-circumscribed radiolucency with ill-defined borders, foci of calcification may be seen within the lesion.

HISTOPATHOLOGY

- Microscopically mesenchymal chondrosarcoma shows sheets of proliferating round or

oval shaped malignant chondrocytes, interspersed by small islands of well-differentiated cartilages.
- Increased abnormal mitosis and cellular pleomorphism, etc. are rare.
- Sometimes, the cartilage tissue within the tumor shows calcification and metaplastic bone formation.
- A typical branching vascular pattern is seen in the soft tissue variant of the disease.

DIFFERENTIAL DIAGNOSIS

- Ewing's sarcoma
- Lymphoma
- Hemangiopericytoma
- Metastatic small cell carcinoma.

TREATMENT

Surgery is the best treatment. Prognosis is usually poor.

OSTEOSARCOMA

DEFINITION

Osteosarcoma is a common **highly malignant primary neoplasm arising from the bone** and beside plasma cell myeloma, it is the most common primary bone tumor. The neoplastic cells in osteosarcoma characteristically exhibit the ability to produce osteoids or immature bone within the tumor.

ETIOLOGY

The exact etiology is not known, many patients give a history of previous trauma to the particular area of bone wherefrom the tumor has developed later. In many cases, radiotherapy to pre-existing bony diseases may cause development of this tumor and such bony lesions are as follows:

- Paget's disease of bone
- Fibrous dysplasia
- Giant cell tumor of bone
- Osteochondroma
- Bone infarct
- Chronic osteomyelitis
- Osteogenesis imperfecta.

TYPES OF OSTEOSARCOMA

The osteosarcomas may be of various types and these are as follows.

According to Location of the Lesion:

- Medullary osteosarcoma
- Periosteal osteosarcoma
- Parosteal osteosarcoma (arising from the external surface of bone)
- Soft tissue osteosarcoma (extra skeletal).

According to the Radiological Characteristics:

- Osteolytic type of osteosarcoma
- Osteoblastic type of osteosarcoma
- Mixed type.

According to the Tumor Histology:

- Osteoblastic type of osteosarcoma
- Chondroblastic type of osteosarcoma
- Fibroblastic type of osteosarcoma
- Telangiectatic type of osteosarcoma.

CLINICAL FEATURES OF OSTEOSARCOMA

Osteosarcomas account for about 20 percent of all sarcomatous lesions occurring in the body and about 5 percent of them occur in the jawbones.

***Age*:** The tumor has bimodal age distribution (i.e. the maximum number of cases occur between 10–20 years of age and above 50 years of age). However the jaw lesions particularly occur at the mean age of about 34 years (1 – 2 decades later than the other skeletal osteosarcomas).

***Sex*:** Males are affected more frequently than females.

***Site*:** The tumor most commonly involves the long bones, e.g. lower end of the femur, upper end of the tibia, humerous and fibula, etc.

In the jawbones, maxilla is slightly more commonly affected than mandible. The lesions of the upper jaw frequently involve the alveolar ridge area, the antrum and sometimes the palate.

The mandibular lesions on the other hand commonly involve the symphysis, the angle and the ramus area, as well as the temporomandibular joint.

Extra skeletal (soft tissue) osteosarcomas occur rarely in the oral cavity and they may involve the tongue and the lip.

CLINICAL PRESENTATION (FIGS 2.125 AND 2.126)

Clinically, osteosarcomas may present the following features.

- A very fast enlarging, firm, painful swelling of the jaw, causing expansion and distortion of the cortical plates (Fig. 2.127).

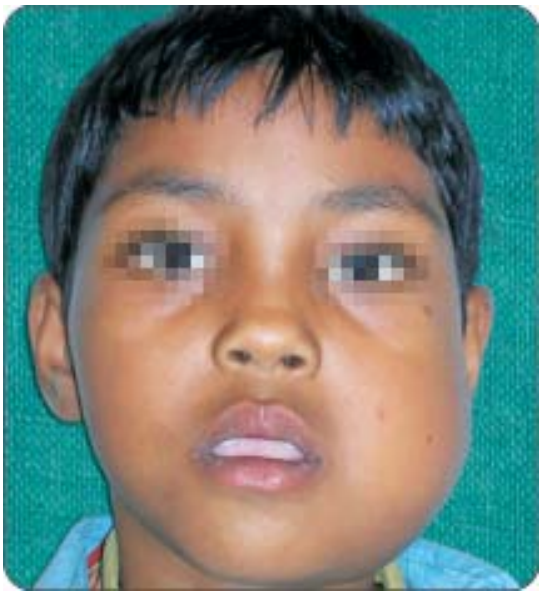

Fig. 2.125: Osteosarcoma-I

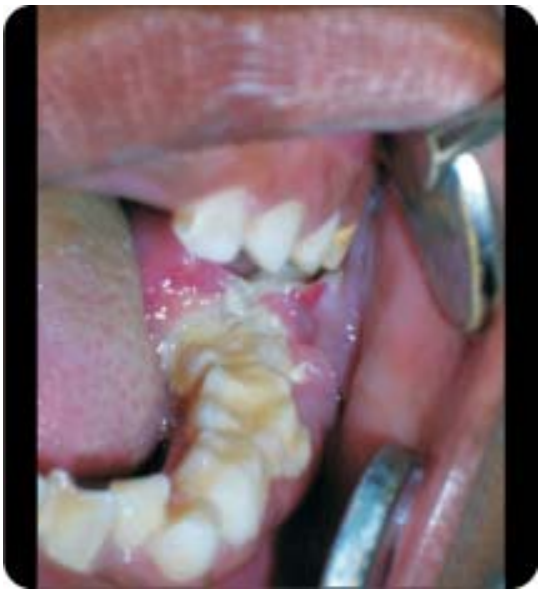

Fig. 2.126: Osteosarcoma-II

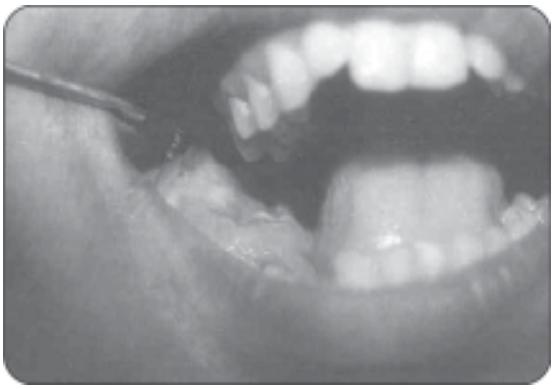

Fig. 2.127: Osteosarcoma of the mandible causing extensive swelling

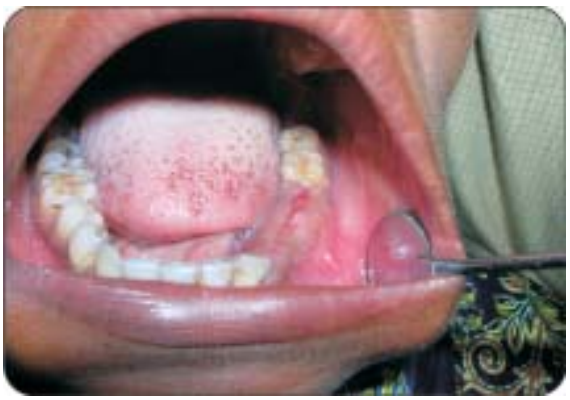

Fig. 2.128: Osteosarcoma of mandible

- Severe facial deformity and difficulty in taking food due to restricted jaw movements.
- Displacement and loosening of the regional teeth are often seen and sometimes the pain arising from the tumor can mimic toothache.
- The mandibular tumors (Fig. 2.128) frequently cause paresthesia or numbness of the lower lip and the chin regions, which may be due to the involvement of inferior alveolar and mental nerves.
- The maxillary lesions cause paresthesia of the infraorbital nerve, epistaxis, nasal obstruction, loosening of teeth and pressure sensation in the eyes, etc.
- The overlying skin or mucosa often appears red and inflamed, and careful examination may reveal a vascular prominence in the area.
- Ulceration, hemorrhage, pathological fracture of bone, etc. are the commonly associated features.
- Jaw lesions are usually not associated with any past history of trauma or any pre-existing bony diseases.

- Some lesions of osteosarcomas are slow growing and are present for long durations before diagnosis.

RADIOLOGICAL FEATURES (FIGS 2.129 TO 2.131)

The radiological features of the osteosarcomas are highly variable.

- In osteolytic type of osteosarcoma, the lesion commonly presents a large, irregular, radiolucent area in the bone with a typical **"moth-eaten"** appearance.
- The border of the lesion is often ill-defined or indistinct.
- Expansion, destruction and perforation of the cortical plates are also commonly seen and in most of the cases, the lesion does not produce any new bone at the periosteal front (Fig. 2.130).
- Few lesions cause resorption of roots of the teeth in the affected areas of the jaw, interestingly the resorption often causes tapered narrowing of the teeth and hence, it is called **'spiking resorption'**.
- The osteoblastic type of osteosarcomas commonly exhibit **multiple, irregular foci of** radiopacities within the large radiolucent zone. This typical appearance may be due to the deposition of newly formed bony trabeculae with in the tumor.
- In osteoblastic type of osteosarcoma, there may be deposition of new bone on the surface of the lesion in a **'radiating fashion'** and on radiographs it may produce a typical **"sun-ray"** or a **"sunburst"** appearance at the periphery (best seen in standard occlusal radiographs).
- At the margin of the tumor, there is lifting of the periosteum and new bone formation, this phenomenon is often known as **'Codman's triangle'**.
- Early osteosarcomas are characterized by localized, symmetric widening of the periodontal ligament space around the regional teeth. This phenomenon occurs as a result of invasion of the tumor cells into the periodontal ligament space and subsequent destruction of the supporting alveolar bone.
- Loss of supporting bone often causes displacement of the regional teeth from their normal position in the jaw.
- Many lesions osteosarcoma radiologically present the evidence of pathological fractures.
- In contrast to the conventional radiographic pictures, few larger lesions of osteosarcomas may produce only little radiographic changes in the affected part of bone.
- Chest **radiographs** are mandatory since early lung metastasis is common in case of osteosarcoma.

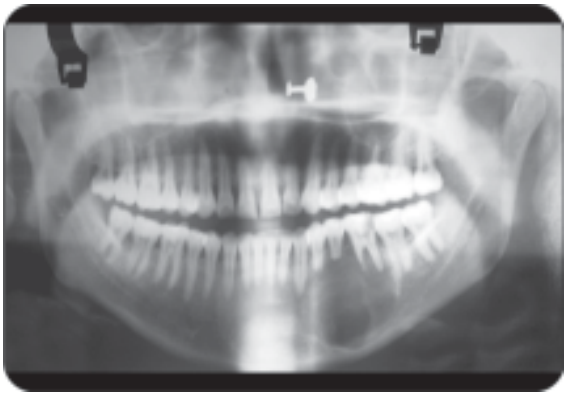

Fig. 2.129: Radiograph of osteosarcoma-I

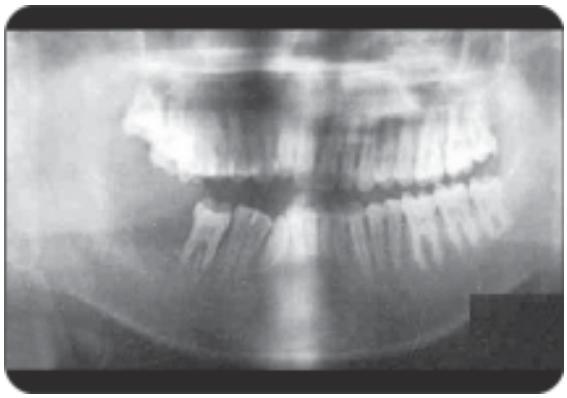

Fig. 2.130: Osteosarcoma causing gross irregular bone destruction in mandible

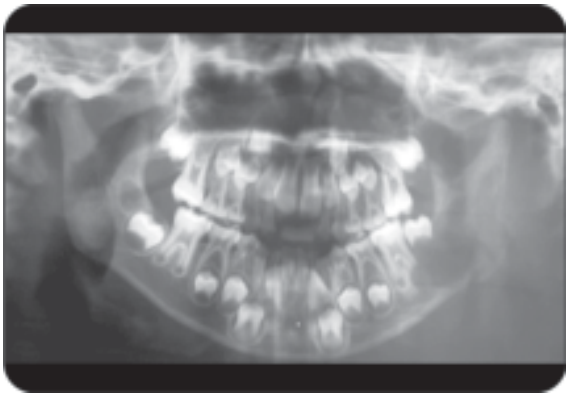

Fig. 2.131: Radiograph of osteosarcoma-II

Key points of osteosarcoma

- It is the common primary malignant neoplasm of bone, with unique clinical, radiological and histological characteristics.
- Predominantly affects children and clinically the disease causes very fast enlarging bony swelling with facial asymmetry.
- Pain, swelling of the jaw, mobility and displacement of teeth are the general complaints. Sometimes, the pain mimics toothache.
- Anesthesia and paresthesia of the affected area are also common.
- Maxillary lesions may cause pain, swelling, pressure sensation in the eye and epistaxis, etc.
- Radiograph reveals 'moth-eaten' radiolucency with multiple small radiopaque foci within it, deposition of new bone on the surface of the lesion in a radiating facion often produces a 'sun-ray' appearance. Besides this, symmetric widening of periodontal ligament space is also commonly seen.
- Microscopically, osteosarcoma reveals neoplastic proliferation of spindle or oval-shaped malignant osteoblast cells with production of osteoids or newly formed bone within the lesion.
- There may be chondroblastic, fibroblastic or telangiectatic variant of osteosarcomas.

HISTOPATHOLOGY

Histologically, osteosarcomas present highly characteristic features, which are as follows (Fig. 2.132):

- There will be presence of numerous, actively proliferating, **spindle-shaped, oval or angular, malignant osteoblast cells** within a cellular stroma.
- The tumor cells in osteosarcoma can be either small, uniformly round in shape or they may be large pleomorphic type with bizarre hyperchromatic nuclei.
- The malignant osteoblast cells often exhibit cellular pleomorphism, increased abnormal mitosis and nuclear hyperchromatism, etc. Moreover, these cells are often larger than the normal osteoblasts.
- Multiple areas of **newly formed bone or osteoid tissues** are often present within the fibrous stroma and it is an extremely important characteristic of osteosarcoma.
- The osteoid areas or structures are always bordered at the periphery by the malignant tumor cells.
- Increased mitotic activity may be seen in few lesions, making the tumor an extremely cellular one, with minimum or no tumor bone formations. Histologically, this form of osteosarcoma often resembles the fibrosarcoma.
- In the chondroblastic variants of osteosarcoma, the malignant tumor cells produce large amount of cartilaginous tissues within the tumor, with little or no bone tissue formation. These variants are commonly seen in the oral cavity and they often have a better prognosis.
- Osteosarcomas in few cases may be extremely vascular in nature and exhibit multiple numbers of large, poorly formed, blood vessels within stroma. These types of lesions are known as telangiectatic type of osteosarcomas.
- Well differentiated osteosarcomas often exhibit minimum cellular atypia with abundant bone formations, such lesions are sometimes confused with fibrous dysplasia of bone.
- On rare occasions, there may be presence of giant cells in osteosarcoma.

DIFFERENTIAL DIAGNOSIS

- Chondrosarcoma
- Fibrosarcoma
- Fracture callus
- Organized hematoma
- Garre's osteomyelitis
- Osteoblastoma
- Eosinophilic granuloma.

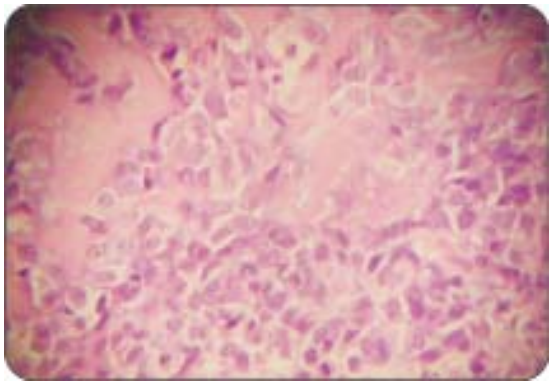

Fig. 2.132: Photomicrograph of osteosarcoma

Laboratory investigations: In osteosarcoma, both the tissue and the serum alkaline phosphatase levels may be raised considerably.

TREATMENT

The combination of surgery, radiotherapy and chemotherapy are usually recommended in the treatment of osteosarcoma. Prognosis is usually poor due to early metastasis of the tumor cells to the lung, brain and other areas. The average five-year survival rate is only 10 to 20 percent.

Majority of the patients in osteosarcoma die of uncontrolled local spread of the tumor cells.

Parosteal Osteosarcoma

This uncommon variant of osteosarcoma **develops from the external surface of bone**, the lesion produces a lobulated nodule attached to the cortex by a stalk. There is no elevation of the periosteum and no peripheral bone formation or regeneration. The tumor microscopically presents many well-formed bony trabaculae in a fibrocellular stroma. This tumor does not show the same degree of cellular pleomorphism as seen in case of the endosteal variety. It grows slowly and metastasizes late, and thereby has a much better prognosis.

Periosteal Osteosarcoma

Periosteal osteosarcomas are sessile lesions, **which arise from the cortex of the affected bone** and cause elevation of the overlying periosteum. There are also significant periosteal new bone formations.

LYMPHOMAS

DEFINITION

Lymphomas are malignant neoplasms of the cells native to the lymphoid tissue (i.e. lymphocytes, histiocytes and their precursors and derivatives). Unlike leukemias lymphomas are solid tumors, although lymphocytic lymphomas can be accompanied by lymphocytic leukemias as well. Lymphomas arise from T-lymphocytes, B-lymphocytes and occasionally from the histiocytes, however majority of the lesions arise from B cells.

Two broad groups of lymphomas have been recognized: (A) Hodgkin's lymphoma, and (B) non-Hodgkin's lymphoma. Although, diseases arise from the lymphoid tissue, the Hodgkin's lymphoma differs from the non-Hodgkin's lymphoma by the presence of Reed-Sternberg giant cells and an increased number of non-neoplastic inflammatory cells which frequently outnumber the neoplastic cells (Reed-Sternberg giant cells) in the former lesion.

RISK FACTORS FOR THE DEVELOPMENT OF LYMPHOMA

- Age—although the disease occurs both in children and adults, but it is more common abobe 60 years of age.
- Primary deficiency—makes the person more susceptible to lymphomas.
- Family history—several members of the same family can be affected.
- Immunosuppressive treatment.
- Infections such as HIV/AIDS, Epstein Barr virus infection, Hepatitis C and *Helicobacter pylori* infections.
- Radiation therapy
- Cytotoxic drug therapy
- Rheumatoid arthritis
- Sjogren's syndrome
- Benign lymphoepithelial lesions.

CLASSIFICATION OF LYMPHOMAS

The **WHO Classification**, published in 2001 and updated in 2008 is the latest classification of lymphoma and is based upon the foundations laid within the "Revised European-American Lymphoma Classification" (REAL). This system attempts to group lymphomas by cell type (i.e. the normal cell type that most resembles the tumor). There are three large groups: the B cell, T cell, and natural killer cell tumors.

NON-HODGKIN'S LYMPHOMA (NHL)

Non-Hodgkin's lymphomas are a diverse and complex group of malignancies arising from the lymphoreticular system. The disease occurs more frequently in the oral cavity as compared to the Hodgkin's lymphomas and the oral NHL lesions

WHO classification of lymphomas	
Mature B cell neoplasms	• Chronic lymphocytic leukemia/Small lymphocytic lymphoma • B-cell prolymphocytic leukemia • Lymphoplasmacytic lymphoma (such as Waldenström macroglobulinemia). • Splenic marginal zone lymphoma • Plasma cell neoplasms: – Plasma cell myeloma – Plasmacytoma – Monoclonal immunoglobulin deposition diseases – Heavy chain diseases • Extranodal marginal zone B cell lymphoma, also called MALT lymphoma • Nodal marginal zone B cell lymphoma (NMZL) • Follicular lymphoma • Mantle cell lymphoma • Diffuse large B cell lymphoma • Mediastinal (thymic) large B cell lymphoma • Intravascular large B cell lymphoma • Primary effusion lymphoma • Burkitt lymphoma/leukemia.
Mature T cell and natural killer (NK) cell neoplasms	• T cell prolymphocytic leukemia • T cell large granular lymphocytic leukemia • Aggressive NK cell leukemia • Adult T cell leukemia/lymphoma • Extranodal NK/T cell lymphoma, nasal type • Enteropathy-type T cell lymphoma • Hepatosplenic T cell lymphoma • Blastic NK cell lymphoma • Mycosis fungoides /Sezary syndrome • Primary cutaneous CD30-positive T cell lymphoproliferative disorders – Primary cutaneous anaplastic large cell lymphoma – Lymphomatoid papulosis • Angioimmunoblastic T cell lymphoma • Peripheral T cell lymphoma, unspecified • Anaplastic large cell lymphoma.
Hodgkin lymphoma	• Classical Hodgkin lymphomas: – Nodular sclerosis – Mixed cellularity – Lymphocyte-rich – Lymphocyte depleted or not depleted • Nodular lymphocyte-predominant Hodgkin lymphoma.

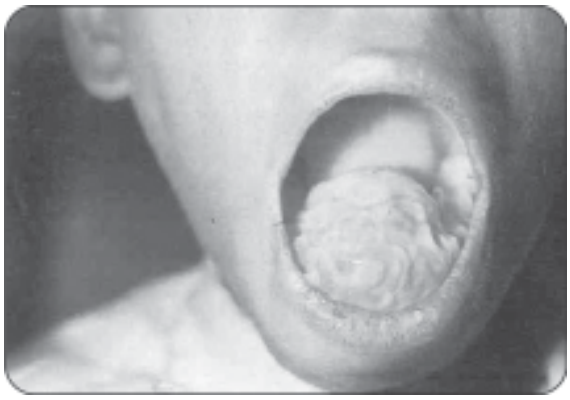

Fig. 2.133: Non-Hodgkin's lymphoma of mandible

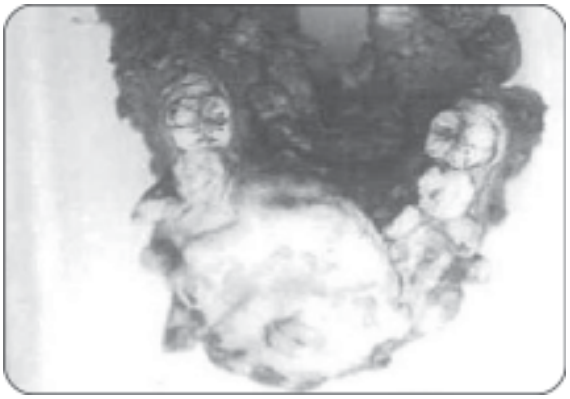

Fig. 2.134: The specimen after jaw resection

frequently exhibit involvement of the extranodal tissues (Fig. 2.133). Recent literatures also suggest a high incidence of these tumors among AIDS patients.

CLINICAL FEATURES OF NON-HODGKIN'S LYMPHOMA

***Age*:** Middle-aged or elderly persons are commonly affected.

Sex: Slightly more common among males.

***Site*:** In the head and neck region the most common site for non-Hodgkin's lymphoma is the lymphoid tissue of Waldeyer's ring.

The other common intraoral sites are the hard palate, buccal vestibule, tongue, floor of the mouth, gingival, retromolar areas and maxillary or mandiblular bones (Fig. 2.134).

CLINICAL PRESENTATION

Clinically, NHL presents the usual features of a sarcomatous lesion.

- The patients may develop some constitutional symptoms like fever of unknown origin, fatigue, night sweats, pruritus, malaise, anorexia, dyspnea and weight loss, etc. along with generalized lymphadenopathy and abdominal pain, etc.
- Oral non-Hodgkin's lymphomas frequently occur in association with HIV/AIDS.
- The nodal lesions produce slow enlarging, non-tendered, freely movable swellings of long duration (6 months or above) and as the disease progresses more and more number of lymph nodes get involved.
- The affected lymph nodes become firm or rubbery in consistency and they often get fixed or matted together, and gradually the lesion invades directly into the adjacent tissue structures.
- In the oral cavity, the soft tissue lesions are characterized by fast enlarging, diffuse, exophytic, non-tendered, soft or firm swellings with boggy consistency (Figs 2.135 to 2.137).
- Misfitting dentures are common complaints for older individuals and it occurs due to gradual expansion of the jawbone due to the disease.
- The overlying surface epithelium appears red or purplish and inflamed, and extensive tissue necrosis often causes ulceration, bleeding and superadded candidal infections, etc.
- In the later stages of the disease, multiple lymph node groups are enlarged, e.g. meningeal and axillary, etc. along with hepatosplenomegaly.
- Nasopharyngeal lymphoma is a multifocal destructive disease, which frequently produces swelling and ulceration of the palate.
- Non-Hodgkin's lymphomas are the second most common malignancy in AIDS patients after Kaposi's sarcoma.
- Intrabony lesion of the jaw initially produces vague pain and discomfort which mimics toothache, with further progression of the disease a large, expansile swelling develops in the jaw with pain, paresthesia and mobility of the regional teeth.
- Swelling of the gingiva and palate are common, and pathological fracture of the involved bone is also seen in some cases.
- The jaw lesions of the NHL occur either as central jaw lesions (called the primary

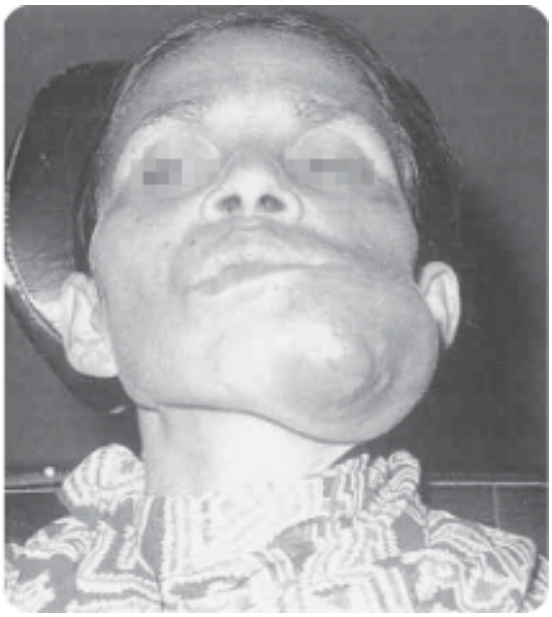

Fig. 2.135: Non-Hodgkin's lymphoma of mandible causing massive swelling

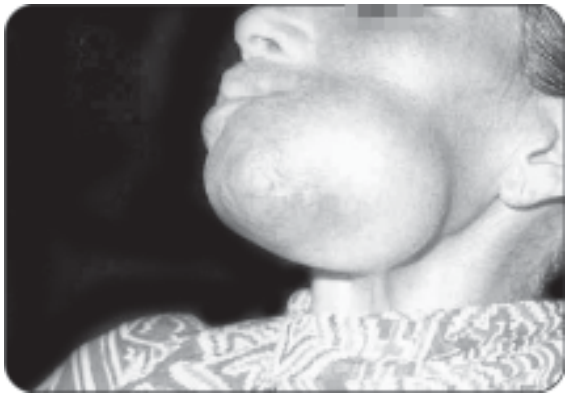

Fig. 2.136: Closer view of the photograph showing erythematous change in the skin

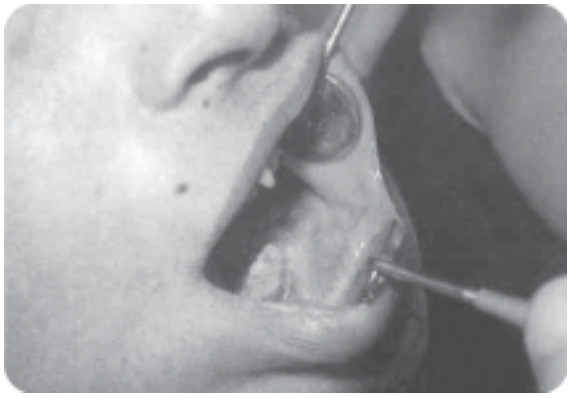

Fig. 2.137: Intraoral view of the same patient

lymphoma of bone) or they involve the jawbones secondarily as an extension from the nearby soft tissue lesions.

- The untreated central jaw lesions may cause perforation of the cortical plates and protrude outside the bone as a nontendered, lobulated soft tissue lump.

RADIOLOGY (FIG. 2.138)

Radiographically non-Hodgkin's lymphoma of bone reveals the presence of a diffuse, large, irregular or **'ragged' area** of radiolucency with expansion and destruction of the cortical bone. The regional teeth appear to be **'floating'** inside the radiolucent zone.

However, in the early stages of the disease there can be only little or subtle radiographic changes in the bone.

HISTOPATHOLOGY

- Histologically, NHL is characterized by monotonous proliferation of malignant lymphocytes with varying degrees of differentiation.
- The cells are relatively uniform in size and they proliferate in broad sheets, generally there is no evidence of tissue necrosis or hemorrhage in the tumor

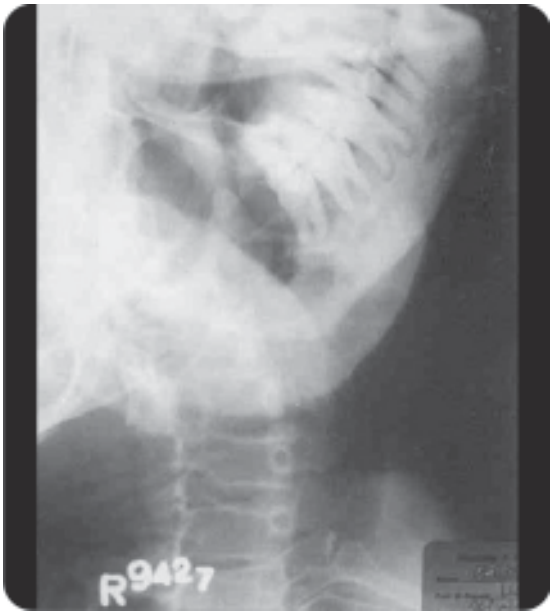

Fig. 2.138: Non-Hodgkin's lymphoma causing irregular bone destruction in mandible

Key points of non-Hodgkin's lymphoma

- Non-Hodgkin's lymphoma is a relatively commom malignant neoplasm of the lymphoreticular system.
- It occurs in the oral cavity more often than the Hodgkin's lymphoma, the other important variant of lymphoma.
- It also commonly occurs in AIDS patients.
- Non-Hodgkin's lymphomas affect the lymph nodes as well as the extranodal sites, the orofacial structures commonly affected include palate, cheek, tongue and jaws, etc.
- The nodal lesons produce slow enlarging swelling of the affected node with fixation.
- The extranodal lesions often produce fast enlarging, gross painful swelling with ulceration and superadded candidal infection, etc.
- Whenever the jaw bone is involved, it radiographically shows multilocular radiolucency with irregular border and displacement of teeth.
- Histologically, non-Hodgkin's lymphoma presents neoplastic proliferations of uniform looking lymphocytes in diffuse sheets with minimum intervening connective tissue stroma.
- Sometimes the neoplastic cells, which resemble lymphocytes or histiocyte, tend to aggregate in large clusters.
- Special investigations like immunohistochemistry and DNA-hybridization, etc. are often done for confirmation of diagnosis of these lesions.
- Chemotherapy provides the best result in the treatment of non-Hodgkin's lymphoma.

- Cellular pleomorphism and nuclear hyperchromatism may be observed in few cells, with minimum amount of intervening connective tissue stroma.
- The malignant cells in NHL may be small in size and uniform in shape, and they can be readily recognized as lymphocytes. In other instances, the tumor cells may be very large and immature in appearance and they often resemble histiocytes.
- These malignant cells, whether large or small, are mostly arranged in two distinct patterns: (A) **nodular pattern**, and (B) **diffuse pattern**.
  - In the nodular pattern, the tumor cells (large or small) tend to aggregate in large clusters, which are separated from one another by very thin connective tissue septa.
  - The diffuse pattern of NHL is characterized by monotonous proliferation of tumor cells (large or small) within the connective tissue, with no evidence of cluster formation.
- Special staining with the help of reticulin stain helps in the differentiation between nodular and diffuse type of NHLs.
- In the oral cavity, the diffuse large cell type is the most common form of NHL.

SPECIAL INVESTIGATIONS

- DNA-hybridization study reveals-Epstein Barr virus DNA in the malignant B-lymphocytes.
- Bone marrow biopsy
- Liver biopsy
- Laparotomy
- Bone scan
- Liver scan
- Blood picture
- CT-scan
- Bone marrow biopsy
- Immunohistochemistry- monoclonal nature of the malignant lymphocytes can be recognized by the production of kappa and lamda light chains only.

TREATMENT

Chemotherapy is the most successful treatment modality in lymphomas. However, radical surgery and radiotherapy are also commonly done. The overall five-year survival rate is about 30 percent.

BURKITT'S LYMPHOMA

DEFINITION

Burkitt's lymphoma is an uncommon, highly aggressive form non-Hodgkin's lymphoma (B lymphocytic origin), which occurs commonly among the African children. This tumor is believed to be caused by the Epstein-Barr virus and the disease frequently occurs in areas of malaria endemic. The tumor was first reported by Denis Burkitt (a surgeon) in 1958.

CLINICAL FEATURES

Age: Burkitt's lymphoma occurs commonly at the age of about 1 to 3 years.

Sex: More commonly seen among male children.

Site: The tumor predominantly involves the extra nodal areas. Maxilla and mandible are the most frequently affected sites in the head and neck region, however maxilla is more frequently affected than mandible. The lesion can also develop from the other visceral organs like ovary, kidney, liver and endocrine glands, etc.

Pathogenesis: It has been observed that Burkitt's lymphomas occur commonly in the geographic areas, where the malarial infections are very common.

The most accepted explanation for this phenomenon is that acute malarial infections cause reactive lymphoid hyperplasia and as a result body's control over the proliferation of "Epstein-Barr virus specific B lymphocytes" is lost. This results in an increased abnormal neoplastic proliferation of B lymphocytes, leading to the development of Burkitt's lymphoma.

Chromosomal abnormality is believed to be the most important factor in the development of Burkitt's lymphoma. In this neoplasm, translocation of a portion of chromosome 8 to chromosome 2, 14 and 22 is often observed, which results in over expression of the *C-myc oncogene*. Over expression of *C-myc oncogene*, which is a DNA-binding transcription protein results in the activation of cell cycling in B lymphocytes.

TYPES OF BURKITT'S LYMPHOMA

Burkitt's lymphoma is generally divided into three forms:

Endemic form (African type): This is the most common type and is seen in children in equatorial Africa, where the incidence rate is highest and where malaria is also very prevalent.

Non-endemic or sporadic (non-African) form: Burkitt's lymphoma is very uncommon outside Africa, hence it is called the sporadic form, but otherwise it is same as the African form.

Immunodeficiency associated form: Occurs in adults with HIV infection or organ transplant patients undergoing immunosuppressive drug therapy.

According to **WHO** Burkitt's lymphomas are classified into three types:

- **Classic Burkitt's lymphoma**
- **Burkitt's lymphoma with plasmacytoid proliferations**
- **A typical Burkitt's/Burkitt-like lymphoma.**

CLINICAL FEATURES OF BURKITT'S LYMPHOMA

- The earliest sign of the disease is characterized by rapid painless expansile swelling of the jaws with loosening of teeth, it starts from the posterior part of the jaw and gradually moves to the anterior area.
- Within a short span of time the lesion produces gross deformity of the face and proptosis of the eyeball.
- The nature of the swelling is usually massive, painless and uniform, and it often causes facial asymmetry.
- The mucosa overlying the tumor is often ulcerated and there can be areas of hemorrhage.
- Toothache itself is a frequent complaint among these patients (especially adults), which occurs due to the invasion and damage of dental pulp by tumor cells.
- The tumor cells frequently involve the mental and the infraorbital nerves, damage to these nerves often leads to paresthesia or anesthesia of the related structures. Paraplegia in the facial region is also common
- Peripheral lymphadenopathy is uncommon in Burkitt's lymphomas.
- Advanced lesions of Burkitt's lymphoma produce massive expansion of the jaw with displacement of teeth, derangement of the dental arch and malocclusion, etc.
- As the tumor mass increases in size, it causes massive enlargement of the gingiva or the alveolar process in the jaw, as a result many deciduous or even permanent teeth are pushed out of their socket and some of which may exfoliate prematurely.
- Sometimes, the tumor is so large that it may fill up the entire oral cavity, in such cases a large tumor mass often protrudes outside the mouth, which contains many rootless teeth.

- Maxillary tumors besides causing massive bony expansions also produce bilateral, soft and spongy swellings of the buccal and the palatal mucosa.
- Although the tumor is solitary, there can be more than one individual tumor affecting different jaw quadrants.
- Some tumors cause perforation of the cortical plates of jawbone and in such cases, a soft tissue lump often protrudes from these perforated openings.
- Abdominal swelling is also common in Burkitt's lymphomas and the tumor cells frequently invade the kidney and the ovary, etc.
- In AIDS patients, Burkitt's lymphoma often produces a soft nodular mass in the palate, which has severe hemorrhagic tendency. Such lesions frequently resemble the Kaposi's sarcoma.
- Involvement of the maxillary antrum is common and these patients often have epistaxis and pressure in the eyeball.
- Burkitt's lymphoma is a multifocal tumor and besides the face, it simultaneously affects multiple organs in the body.

RADIOLOGICAL FEATURES

- Radiographically, Burkitt's lymphoma presents a large, irregular radiolucent area in the bone with a ragged **'moth-eaten'** appearance.
- In the initial stages of the disease, there are multiple small radiolucent foci seen in the jaw, these small lesions coalesce together with time to form a large, massive defect in the bone.
- The earliest sign of the disease is the loss of lamina dura and enlargement of the crypt of the developing tooth, which occur due to involvement of the dental papilla by the tumor cells.
- Tooth displacement and root resorption are common.
- Some lesions cause blurring of the shadow of maxillary antrum.
- Widening of the periodontal ligament space occurs due to invasion of the tumor cells in the area.
- Pathological fracture of the bone is seen in few cases.

Key points of Burkitt's lymphoma

- Burkitt's lymphoma is an uncommon, highly aggressive form non-Hodgkin's lymphoma of B lymphocytes origin.
- It occurs commonly among the African children, moreover jawbones are very frequent sites for the occurrence of this tumor.
- This tumor is believed to be caused by the Epstein-Barr virus and the disease frequently occurs in areas of malaria endemic.
- Clinically the lesion produces rapid painless expansile swelling of the jaws with loosening of teeth.
- Maxilla is affected more often than mandible and the swelling starts from the posterior part of the jaw and gradually extends to the anterior area.
- Massive enlargement of the gingiva or the alveolar process may result in many deciduous or even permanent teeth being pushed out of their socket and many of which may exfoliate prematurely.
- Sometimes the tumor is so large that it may fill up the entire oral cavity.
- Burkitt's lymphoma radiographically presents a large, irregular radiolucent area in the bone with a ragged 'moth-eaten' appearance.
- Histologically, Burkitt's lymphoma is exhibits monotonous proliferation of small, non-cleaved B-lymphocytes in diffuse sheets.
- These cells along with macrophages produce a characteristic **"starry-sky"** appearance in the tumor.
- Chemotherapy is the best treatment in Burkitt's lymphoma.

HISTOPATHOLOGY (FIG. 2.139)

- Histologically, Burkitt's lymphoma is characterized by monotonous proliferation of small, non-cleaved B-lymphocytes in diffuse sheets.
- These malignant lymphocytes often have large round nuclei with prominent nuclear membrane, moreover they also exhibit stippled nucleoplasm, prominent nucleoli and minimal cytoplasm.
- Each nucleus is surrounded by a cytoplasm, which gives the sheets of neoplastic cells a syncytial appearance.

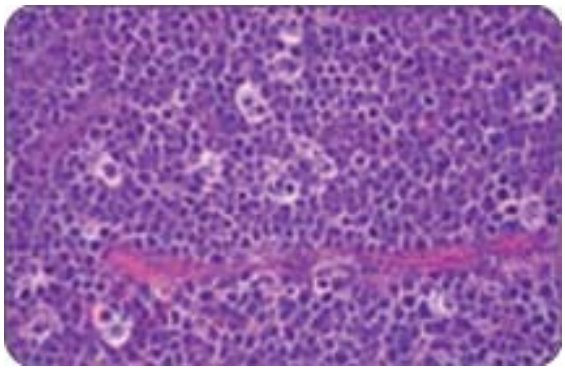

Fig. 2.139: Photomicrograph of Burkitt's lymphoma

- The mitotic activity is abundant and this tumor probably shows the fastest rate of cell multiplication among all malignant lesions (each cell doubles itself in just 24 hours).
- Numerous macrophages with abundant clear cytoplasm containing cellular debris are usually found scattered uniformly throughout the tumor and this often gives rise to a very characteristic **"starry-sky"** appearance.
- The starry-sky appearance occurs because in Burkitt's lymphoma the macrophages have abundant cytoplasm but are less intensely stained, therefore these cells stand out as **'stars'** set against the **'night sky'** of deeply hyperchromatic malignant lymphocytes.
- The malignant cells often invade into the periodontal ligament tissue and some cells can even invade into the dental pulp.
- Few multinucleated giant cells may also be seen within the tumors.

TREATMENT

Chemotherapy gives the best response in Burkitt's lymphoma, of course surgery and radiotherapy are the other therapeutic options.

HODGKIN'S LYMPHOMA

DEFINITION

Hodgkin's lymphoma (HL) is an extremely rare lymphoproliferative disorder characterized by the presence of **'Reed Sternberg' giant cells in the tissue**. The disease seldom affects the oral cavity and in most of the cases, oral structures are involved secondarily due to the extension of the cervical lymph node tumors.

CLINICAL FEATURES

Age: The disease commonly occurs between the age of 15 and 35 years, although it can occur at a higher frequency in the later part of life (beyond 55 years).

Sex: Slight male predilection is seen.

Site: The tumor occurs more commonly from the lymphoid tissues of the cervical chain of lymph nodes and the tonsils, extranodal areas in the oral cavity like the submucosa, maxilla and mandible, etc. are also affected in few cases. Axillary and inguinal nodes may also be involved.

CLINICAL PRESENTATION

- **Persistent generalized lymphadenopathy** is the most important feature of Hodgkin's lymphoma (HL) and the enlarged lymph nodes are nontendered, firm and rubbery in consistency.
- In the initial stages of the disease, the affected lymph nodes are freely movable, however as the disease progresses, the nodes become matted and fixed to the surrounding tissues.
- Generalized weakness, pain in the abdomen and back, weight loss, low grade episodic fever and night sweats are the initial systemic complaints.
- Patients also have persistent cough, dyspnea due to pressure in the trachea, anorexia, itching of the skin (pruritus).
- Edema of the extremities due to progressive venous obstructions, obstructive jaundice, plural or pericardial effusion and hemoptysis or melena, etc. are the other constitutional symptoms.
- In untreated cases, the disease spreads from one lymph node to the other and eventually spreads to several **vital organs such as spleen, liver, lung and bone marrow,** etc.
- As the disease involves the liver and spleen, **hepatosplenomegaly** soon develops, and it is a common feature of Hodgkin's lymphoma.
- Oral lesions of Hodgkin's lymphoma are rare and mostly present large submucosal swellings with ulceration, pain, paresthesia, etc.
- Although, primary oral lesions do occur in Hodgkin's lymphoma but in most of the cases oral lesions in this disease develop as a result of dissemination of the tumor cells into the oral soft tissues or jaw bones from the cervical areas.

Key points of Hodgkin's lymphoma

- Hodgkin's lymphoma (HL) is an extremely rare malignant neoplasm of lymphoid tissue characterized by the presence of 'Reed Sternberg' giant cells in the tumor.
- The disease causes persistent generalized lymphadenopathy and the involved nodes are nontendered, firm and rubbery in consistency.
- The constitutional symptoms are very significant in this disease and they include generalized weakness, pain in the abdomen and back, weight loss, generalized pruritus (itching), low grade episodic fever and night sweats, etc.
- Histologically, Hodgkin's lymphoma is characterized by the proliferation of malignant lymphoid cells and non-neoplastic inflammatory cells, including lymphocytes, macrophages, plasma cells and eosinophils, etc.
- **"Reed-Sternberg giant cells"** (RS cells) with two mirror image nuclei, that often creates an '**owl eye'** appearance are are the chief malignant cells of the tumor.
- Radiotherapy and chemotherapy are the common modes of treatment, prognosis is often poor.

HISTOPATHOLOGY (FIG. 2.140)

- In Hodgkin's lymphoma, the involved lymph nodes are histologically characterized by the presence of **malignant lymphoid cells** and **non-neoplastic inflammatory cells**, including lymphocytes, macrophages, plasma cells and eosinophils, etc.
- The chief malignant cells of this tumor are the **"Reed-Sternberg giant cells" (RS cells)**. These cells are characterized by two mirror image nuclei, each containing a large acidophilic nucleolus and surrounded by a distinctive clear zone, together they impart an '**owl-eye**' appearance.

HISTOLOGICAL TYPES OF HODGKIN'S LYMPHOMA

There are four recognized histologic types of Hodgkin's disease.

Lymhocyte predominant: Characterized by abundant lymphocytes, few plasma cells with occasional RS cells. This type carries the most favorable prognosis.

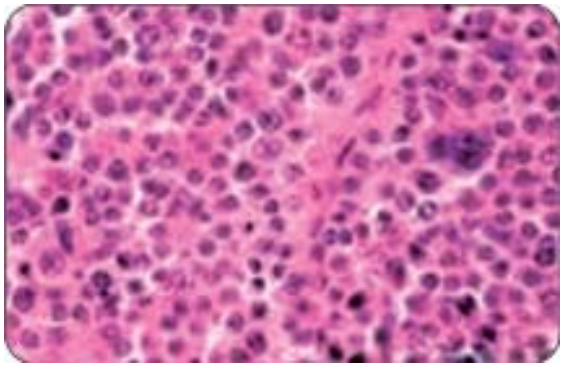

Fig. 2.140: Photomicrograph of Hodgkin's lymphoma

Mixed cellularity: Characterized by lympho-cytes, plasma cells, eosinophils and easily identifiable RS cells.

Lymphocytes depletion: This type shows sparse lymphocytes and stromal cells, with areas of fibrosis and highly malignant bizarre RS cells. This type carries the poorest prognosis.

Nodular sclerosis: Characterized by bands of collagen, subdividing the tumor cells into many small islands within the lymph node.

LABORATORY INVESTIGATIONS

- Biopsy of the lymph nodes to see the characteristic histopathologic findings.
- Complete blood count.
- Chest X-ray and tomography.
- Radiographic skeletal survey.
- Technetium bone scans.
- Liver function test and scan.
- Bone marrow biopsy.
- Lymphangiogram to see the size of the node.
- Laparotomy to see the extent of the disease.

TREATMENT

By chemotherapy and radiotherapy. The overall prognosis is good and 5 years survival rate is about 80 percent.

MULTIPLE MYELOMA

DEFINITION

Multiple myelomas represent a group of **malignant diseases of plasma cells**, which infiltrates

the bone and soft tissues, and are consisting of **terminally differentiated B lymphocytes or plasma cells.** The manifestations the multiple myelomas produce are due to either uncontrolled proliferation of neoplastic plasma cells or due to the **production of abnormal immunoglobulins** (monoclonal) by these neoplastic plasma cells.

CLINICAL FEATURES OF MULTIPLE MYELOMA

Age: 40 to 70 years.

Sex: Both sexes are equally affected.

Race: Blacks peoples are affected twice as often as whites.

***Site*:** Bones anywhere in the skeleton can be affected and among the jawbones, mandible is more frequently affected than maxilla.

Mandibular lesions are often multiple and they commonly occur over the molar-ramus region or the angle. In some cases, the lesion can occur in relation to the gingival tissue.

CLINICAL PRESENTATION

- Severe deep bone pain and tenderness are the most common and characteristic early symptoms, these symptoms often increase as then patient moves.
- When the disease affects the mandibular bone it causes **early development of numbness** in the lips or chin.
- Patients suffer from gradual weight loss and increased susceptibility to infection due to **severe neutropenia** and **decreased production of normal immunoglobulins**.
- Patients also suffer from nausea, vomiting and marked anemia, etc.
- **Increased bleeding tendency with petechial hemorrhage** in the skin and mucous membrane due to severe fall in the number of platelets.
- There are also increased chances of **renal complications** as the kidney is overburdened by the excess and abnormal protein production in the body by the neoplastic plasma cells.
- In multiple myeloma, jaw lesions occur in about 15 percent cases, initially these jaw lesions produce pain that often simulates toothache.
- In the early stages of the disease, the jaw swellings are unremarkable, since the tumor cells occupy only the marrow spaces during this period.
- The jaw lesions in advanced stages, however produce fast enlarging, painful swelling, with expansion and destruction of the bone.
- Severe bone destruction may lead to the "**egg-shell cracking" or pathological fractures**.
- The regional teeth in the jaw are usually mobile due to weakness of the bone and as a result malocclusion often develops.
- Perforation of the bony cortex by the neoplastic cells often causes protrusion of the lesion outside the bone as an ulcerated, fleshly lump.
- Extraction of teeth in these patients usually causes **severe uncontrolled hemorrhage** and **delayed wound healing**.
- Multiple myelomas sometimes cause immunosuppression and thereby increase the risk of secondary infection, in the oral cavity; this often results in **candidiasis and oral hairy leukoplakia.**
- Production of abnormal proteins such as amyloids occur in multiple myeloma, deposition of amyloids in the form of nodular swellings may occur in various parts of the body as well as the oral cavity; in the tongue such deposits often cause macroglossia.
- Metastatic calcification of the oral and other soft tissues may occur **due to hypercalcemia** secondary to tumor related osteolysis.

RADIOLOGICAL FEATURES

In multiple myeloma, the radiograph shows numerous well-defined, **punched-out** radiolucencies with no peripheral bone reaction. The lesions commonly involve the skull, vertebrae, ribs and jaw bones. Diffuse radiolucency in case of multiple myeloma may be seen occasionally.

HISTOPATHOLOGY (FIG. 2.141)

- The lesion is histologically characterized by **diffuse sheets of closely packed, monotonous, round or oval cells**, which often resemble the typical plasma cells.
- Among these neoplastic plasma cells, some are well-differentiated while the rests are poorly differentiated.

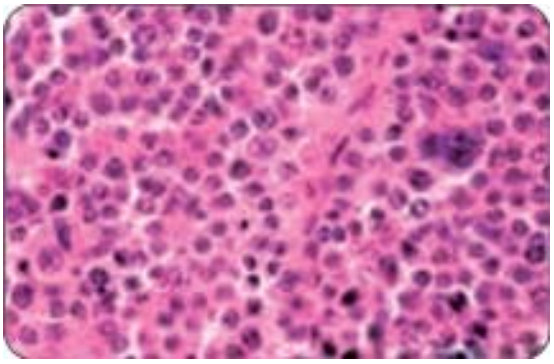

Fig. 2.141: Photomicrograph of multiple myeloma

Laboratory investigations

- Routine hemogram shows anemia, neutropenia, thrombocytopenia and greately raised ESR.
- Most of the multiple myeloma patients exhibit hyperglobulinemia, with reversal of the serum albumin-globulin ratio.
- There will be an abnormal increase in the production of light chain proteins (known as Bence-Jones protein) by the tumor cells as a result the serum protein level may become very high (measuring up to 8–16 gm%).
- Presence of **Bence-Jones protein in urine** is also reported in (30–50 percent) patients of multiple myeloma and it is one of the most important hallmarks in the diagnosis of the disease.
- Serum and urinal protein immunoelectrophoresis is done to detect these abnormal proteins in multiple myeloma.
- The Bence-Jones protein coagulates when the urine is heated to the temperature of 42°C to 60°C, it disappears when the urine is boiled and finally it reappears again as the urine is cooled.
- Occasionally, the Bence-Jones protein in urine can also be present in patients with **polycythemia** or **leukemia**. However, the absence of this protein also does not rule out the presence of multiple myeloma in a patient.
- Biopsy of the bone marrow in multiple myeloma patients exhibits the presence of at least 10 percent atypical plasma cells in the total marrow cell population.

- The cells eccentrically placed nuclei and they often exhibit chromatin clumping in a typical **"cart-wheel"** or a **"checkerboard"** pattern.
- Mitotic figures may be high in few cases, with occasional presence of binucleated or multinucleated cells.
- These neoplastic plasma cells often invade and destroy the normal tissues of the body.
- Deposition of amyloids may be seen in the tissue beneath the plasma cells, which appear as homogenous, eosinophilic acellular areas.

Key points of multiple myeloma

- Multiple myelomas represent a group of malignant diseases of **plasma cells**, which infiltrate the bone and soft tissues.
- The tumor consists of terminally differentiated B lymphocytes or plasma cells.
- **Production of abnormal immunoglobulins** (monoclonal) by these neoplastic plasma cells is also another important feature of the disease.
- Clinically, it presents severe, deep bone pain and tenderness; often there is early development of numbness in the lips or chin.
- Increased bleeding tendency with petechial hemorrhage, occasional uncontrolled hemorrhage and delayed wound healing, etc. are the other important features of the disease.
- Radiograph shows numerous well-defined, **punched-out** radiolucencies in the affected bone. Severe bone destruction may even lead to the **"egg-shell cracking" or pathological fractures**.
- Presence of **Bence-Jones protein** in urine is an important feature of multiple myeloma.
- Histology reveals diffuse sheets of closely packed monotonous, round or oval cells, which often resemble the typical plasma cells.
- Chemotherapy is mostly given but the disease is fatal.

TREATMENT

Chemotherapy is mostly given but the disease is fatal.

SOLITARY PLASMACYTOMA

Solitary plasmacytoma is a single tumor of plasma cell origin and is often located in the soft tissue of the upper air passages. The lesion often represents

a clonal proliferation of plasma cells in an extra nodal site.

CLINICAL FEATURES

Age: Adults are generally affected (average age 55 years).

Sex: More common in males (ratio is 3:1)

Site: Mostly affects the bone, sometimes soft tissue lesions (extramedillary plasmacytomas) occur in the tongue, nasopharynx, parotids and paranasal sinuses, etc.

PRESENTATION (FIG. 2.142)

- Solitary plasmacytomas commonly cause swelling of the affected bone with pain and tenderness.
- Some lesions are asymptomatic and are detected only during routine radiographic examinations in the affected part of bone.
- Soft tissue lesions produce well-circumscribed, painless, soft nodule in the affected organ.
- Systemic complications like anemia or renal failure, etc. are generally absent in solitary plasmacytoma.
- About 50 percent lesions of solitary plasmacytomas turn into multiple myelomas over time.

RADIOGRAPHIC FINDINGS

Radiographically solitary plasmacytoma produces well-defined, unilocular radiolucency

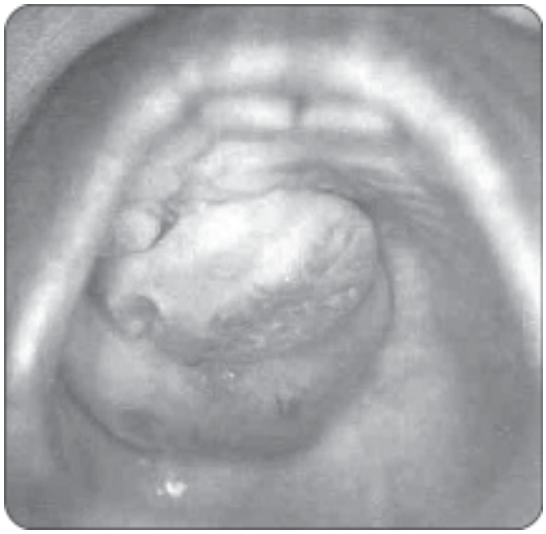

Fig. 2.142: Solitary plasmacytoma of the palate

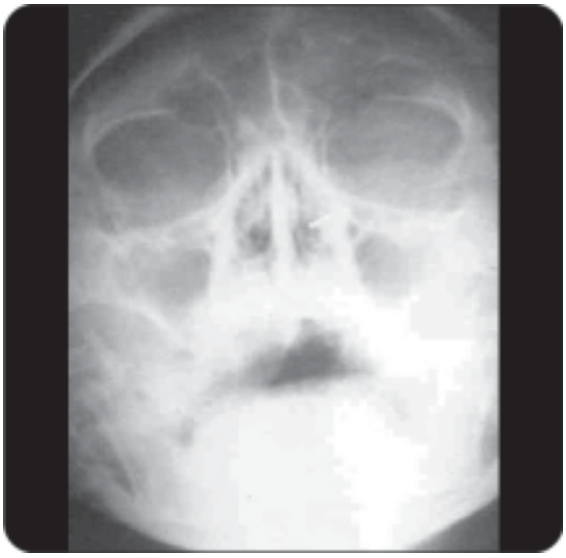

Fig. 2.143: Plasmacytoma causing invasion of the Rt. Maxillary antrum

in the bone with no sclerotic reaction at the margin (Fig. 2.143).

HISTOPATHOLOGY

Histopathologic appearance of solitary plasmacytoma is same as multiple myeloma, it exhibits sheets of proliferating neoplastic plasma cells with varying degrees of differentiation.

LABORATORY INVESTIGATION

- Bence-Jones protein is present but very little in amount as compqred to multiple myelomas.
- Atypical plasma cells are not found in the bone marrow.

TREATMENT

By radiotherapy.

LEIOMYOSARCOMA

Leiomyosarcomas are malignant neoplasms of the smooth muscle cell origin.

CLINICAL FEATURES

Oral lesions of leiomyomas are rare, whenever they occur the lesions involve the jawbones. Clinically the lesions produce fast enlarging swelling of the affected tissue with development of a soft or firm lobulated mass, which can be painful. Secondary

ulceration of on the surface may occur due to trauma.

HISTOPATHOLOGY

Histologically, leiomyomas present neoplastic proliferation of **spindle-shaped malignant smooth muscle cells in fascicles.** The malignant cells often have blunt ended or cigar shaped nuclei and abundant eosinophilic cytoplasm. Some tumor cells are round and somewhat epitheloid in shape. Increased mitotic activity is common.

TREATMENT

Combination of surgery, radiotherapy and chemotherapy.

RHABDOMYOSARCOMA

DEFINITION

It is a malignant neoplasm developing from the striated (skeletal) muscle cells. It is the most common soft tissue sarcoma among children head, and neck area is the most frequent site.

TYPES

Rhabdomyosarcomas are histologically categorized into three variants:

A. ***Embryonal rhabdomyosarcoma (60–70%)***—occurs in children upto 10 years of age.
B. ***Alveolar rhabdomyosarcoma (20–30%)***—occurs between 10 to 25 years of age.
C. ***Pleomorphic rhabdomyosarcoma (5% or less)***—occurs at the age of about 40 years.

ORIGIN

These neoplasms may arise either from the existing skeletal muscle cells or may be from the pleuripotential mesenchymal cells of connective tissue.

CLINICAL FEATURES

Age: Most of these tumors arise during childhood, some lesions occur in teenagers or young adults.

Sex: Both sexes are equally affected.

Site: The embryonal and the alveolar types predominantly affect the head and neck region; and the common sites include—orbit, nasal cavity, nasopharynx, palate, tongue and maxillary sinus, etc. The pleomorphic type mostly affects the extremities.

PRESENTATION

- Rhabdomyosarcomas usually are rapidly growing lesions, which cause swelling, pain and extensive tissue damage.
- These lesions are indurated, fixed and are often ulcerated.
- Some exophytic lesions produce polypoid growths that resemble '**cluster of grapes**'.
- Lesions of the maxillary sinus may often break the sinus wall and invade into the oral cavity.

HISTOPATHOLOGY

Microscopically, rhabdomyosarcomas are composed of malignant rhabdomyoblasts.

- ***Embryonal rhabdomyosarcoma***—Histologically this variant is characterized by small round cells with monotonous looking hyperchromatic nuclei.
- ***Alveolar rhabdomyosarcoma***—Histologically it is characterized by rounds cells, which assume a pattern similar to the lung alveoli.
- ***Pleomorphic rhabdomyosarcoma***—This variant is the more differentiated form and it exhibits primitive muscle fiber formation. The cells are having extremely pleomorphic nuclei and many prominent nucleoli. The cell cytoplasms are brightly eosiniophilic and many of these cells reveal cross-striations.

TREATMENT

Surgery, radiotherapy and chemotherapy. All the variants have a poor prognosis.

NEUROGENIC SARCOMA

DEFINITION

Neurogenic sarcomas are malignant neoplasms of perineural fibroblast or schwann cells with a poor prognosis.

ORIGIN

The disease can occur either from the pre-existing neurofibromatosis lesions or as *de novo* lesions.

CLINICAL FEATURES

- Neurogenic sarcomas mostly occur in young adults, common intraoral sites are mandible, lips and buccal mucosa, etc.
- The disease produces rapidly growing, non-compresible exophytic masses, which cause paresthesia of the lower lip and expansion of the mandible (Figs 2.144 and 2.145).
- Lesions are often painful, indurated and non-movable.
- Intrabony lesions often cause severe expansion and destruction of jaw with mobility of the regional teeth.
- The tumor often occurs inside the mandibular canal, in association with the mandibular nerve.

Fig. 2.144: Neurogenic sarcoma-I

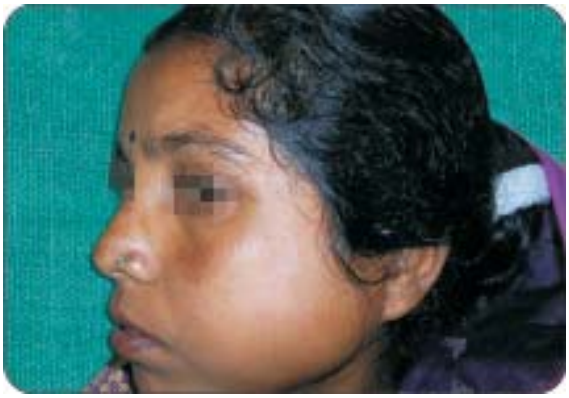

Fig. 2.145: Neurogenic sarcoma-II

RADIOLOGICAL FEATURES (FIGS 2.146 AND 2.147)

Radiologically, neurogenic sarcomas may produce a small area of fusiform widening of the mandibular canal. However, some lesions may even cause large area of bone destruction. Root resorption is uncommon.

HISTOPATHOLOGY

- Histologically the neoplasm exhibits numerous fascicles of spindle-shaped cells with variable number of mitotic figures.
- The tumor cells often resemble to those of fibrosarcoma, however neurogenic sarcoma cells are more irregular in shape and have 'comma' shaped wavy nuclei.
- The nuclei are often pleomorphic and hyper-chromatic.
- The fascicles often exhibit some resemblance to the 'Antoni-A' type of tissue with palisading nuclei.

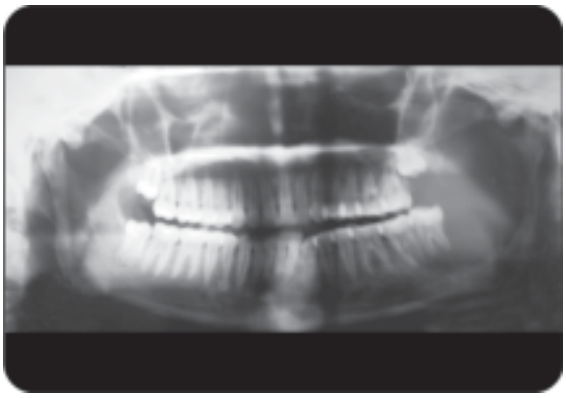

Fig. 2.146: X-ray of neurogenic sarcoma-I

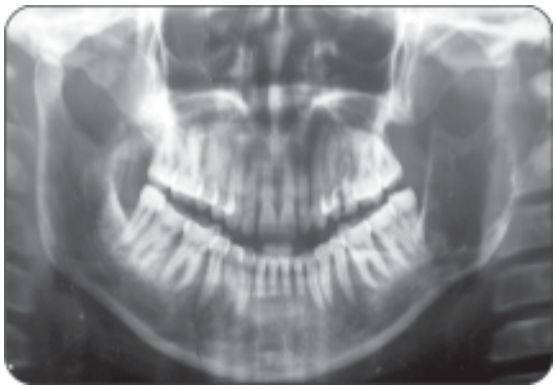

Fig. 2.147: X-ray of neurogenic sarcoma-II

- Neoplastic cells often spread along the course of the involved nerve.

TREATMENT

Surgical excision, radiotherapy and chemotherapy.

METASTATIC TUMORS OF THE JAWS

Metastatic tumors of the jaws are not very uncommon lesions (comprising only 1 percent of all oral malignancies), however the exact incidence rate may be much higher than what is generally appreciated.

CLINICAL FEATURES

- Metastatic tumors can develop from both soft as well as hard tissues of the oral cavity, however the jawbones are particularly targeted more often than the soft tissues.
- Intrestingly, jaw metastasis can be associated with a widely disseminated disease in the entire body.
- Sarcomas of both bone and soft tissue origin can metastasize into the jaws.
- **Metastasis in the orofacial region** predominantly occurs from primary tumors located in the **breast, lung, prostate, thyroid and kidney**, etc.
- More precisely tumors from the breast metastasize into the maxillary or mandibular bones, while the tumors from the lung often metastasize into the oral soft tissues.
- The metastatic tumors develop in the mandible (molar region) four times as often as in the maxilla.
- The metastatic jaw lesion mostly causes pain, swelling, expansion of the cortical plates, paresthesia or anesthesia of the region, loosing of teeth and pathological fractures of the bone, etc.
- Metastatic tumor of mandible with involvement of the inferior alveolar nerve may produce **'numb chin syndrome'**, which is characterized by unexplained loss of sensation in the lower lip and chin.
- Some metastatic lesions are however asymptomatic and are discovered accidentally.
- In about 20 to 30 percent cases, these tumors are the first indication of the disease.

RADIOGRAPHY

- Radiographs often reveal osteolytic or sometimes osteoblastic areas in the jaw with hazy outlines.
- The bony defects may also appear either as a cyst or as a 'moth-eaten' defect, severe loss of alveolar bone results in widening of the periodontal ligament space.
- Metastatic jaw tumors are sometimes discovered during thorough examination of a non-healing extraction socket.

HISTOPATHOLOGY (FIG. 2.148)

- Both carcinomas as well as sarcomas occurring elsewhere in the body can metastasize in the jaws, however adenocarcinomas are the most common histologic type of tumors, which metastasize into the jawbones.
- The metastatic lesions often histologically resemble the primary lesions and these are mostly poorly differentiated in nature.

INVESTIGATIONS

- Total hemogram
- X-ray of the involved area
- Total skeletal survey
- CT scan
- Magnetic resonance imaging (MRI).

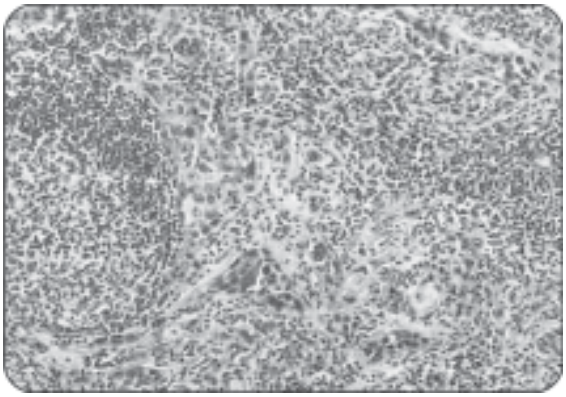

Fig. 2.148: Photomicrograph of metastatic tumor

TREATMENT

Treatment of metastatic as well as the primary tumor (if accessable) is to be done at a time by surgery, radiotherapy or chemotherapy.

Most of the tumors carry a grave prognosis.

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CHAPTER 3

Oral Precancerous Lesions and Conditions

Oral cancers are sometimes preceded by some clinically visible lesions, which are noncancerous to begin with and have therefore been termed as "precancers". However, it is widely understood that neither do all the precancerous lesions progress to cancer, nor all cancers necessarily originate from such lesions.

According to the World Health Organization (WHO), the oral precancerous state is divided into two board groups: (i) precancerous lesions and (ii) precancerous conditions.

PRECANCEROUS LESION

A precancerous lesion is defined as **'a morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart'** -WHO 1978.

- **Leukoplakia, erythroplakia, stomatitis nicotina, chronic candidiasis**, etc. are the common examples of precancerous lesions found in the oral cavity.

PRECANCEROUS CONDITION

A precancerous condition is defined as **'the generalized state of the body, which is associated with a significantly increased risk of cancer'**- WHO 1978

- **Oral submucous fibrosis, sideropenic dysphagia (mucosal atrophy with chronic iron deficiency anemia), syphilis and oral lichen planus,** etc. fall into this category.

Examples of precancerous lesions and conditions

Precancerous lesions:	• Erythroplakia • Stomatitis nicotina • Chronic candidiasis • Leukoplakia
Precancerous conditions:	• Syphilis • Oral lichen planus • Oral submucous fibrosis • Sideropenic dysphagia

It is important to note that all these precancerous lesions and conditions mentioned above, produce a wide variety of clinical and histopathological features, but the most important criteria for evaluating their malignant potential is the microscopic study of "epithelial dysplasia". It has been reported by a large number of investigators that the "dysplastic" lesions carry a risk of malignant transformation, which is nearly 15 times higher than the non dysplastic lesions.

LEUKOPLAKIA

DEFINITION

Leukoplakia can be defined as a **"white patch"** or **"plaque"** in the oral cavity, which cannot be scrapped off or stripped off easily and more over, which cannot be characterized clinically or pathologically as any other disease"- WHO 1978.

This definition was revised five years later at the International Conference and the new definition states that "leukoplakia is a white patch or plaque in the oral cavity, which cannot be scrapped off or stripped off easily and which cannot be characterized clinically or pathologically as any other disease and it is not associated with any physical or chemical agents except the use of tobacco"

PRELEUKOPLAKIA

This is a grayish or grayish-white, slightly lobular lesion of oral mucosa with ill-defined borders.

ETIOLOGY OF LEUKOPLAKIA

The exact etiology of leukoplakia is unknown but a large number of factors have been implicated for their occurrence, which are known as the "predisposing" factors. The common predisposing factors for leukoplakia are tobacco, alcohol,

candidiasis, dietary deficiency, syphilis, viral infections, hormonal imbalance, chronic irritation, galvanism and actinic radiation, etc.

Among these, tobacco is considered to be the single most important factor.

Etiological factors of leukoplakia

- Tobacco (in smoking and smokeless forms)
- Alcohol
- Candidiasis
- Dietary deficiency
- Syphilis
- Viral infections
- Hormonal imbalance
- Chronic irritation
- Actinic radiation
- Galvanism

Tobacco

- It is used by large number of people in various forms, such as smoking of cigarettes, cigars, pipes and beedes (country-made cigarettes), tobacco chewing and snuff dipping, etc.
- All these types of tobacco habits are important for the development of leukoplakia and it has been confirmed that the people those who use tobacco in any form, develop leukoplakia more often than the people those who do not use them.
- Furthermore, the leukoplakic lesions (Fig. 3.1) regress significantly more often when the tobacco habits are discontinued or reduced, as compared to when the habits remain unchanged or continued.
- It is believed that during smoking a significantly large amount of tobacco end products are produced in the oral cavity, these products in association with the heat, (generated during smoking) cause severe irritation to the oral mucous membrane and finally results in the development of leukoplakia.
- An important observation in this regard is the higher rate of occurrence of leukoplakia among the "reserve smokers" (those who keep the burning end of the cigarettes inside the mouth).
- Finally, it is important to note that the risk of development of leukoplakia in a person depends upon the frequency and duration of the tobacco habits, and the age and sex of the person concerned.

Alcohol

Alcohol itself is not an important risk factor for leukoplakia but many people may develop leukoplakia who consume alcohol as well as use tobacco in some form. Therefore, it is believed that the synergistic effect of tobacco and alcohol both, increase the risk of leukoplakia more often than in cases where a single habit is practiced.

Candidiasis

Chronic candidal infections are often associated with leukoplakia, however, it is not very clear whether the fungi are directly responsible for the initiation of the disease or they are only producing secondary infections in a pre-existing leukoplakia. However, it has been observed that the Candida associated leukoplakias develop more epithelial dysplasia than the non candidal lesions.

Dietary Deficiency

Deficiency of Vitamin A causes metaplasia and hyperkeratinization of the epithelium, which may eventually result in the development of leukoplakia. Deficiency of vitamin B complexes may also cause leukoplakic changes in the oral mucosa, but the exact pathogenesis is not clear.

Syphilis

In the older literatures, syphilis was considered to be a very important predisposing factor for the development of leukoplakia, especially the tertiary stage of the disease, which presents mucous patches over the tongue and buccal mucosa. However, recent reports indicate that the syphilitic infections play only a minor role in the causation of leukoplakia.

Viral Infections

Experimental studies indicate that, oral mucosal infections caused by the herpes virus hominis type I (HSV–I) and human papilloma virus (HPV)

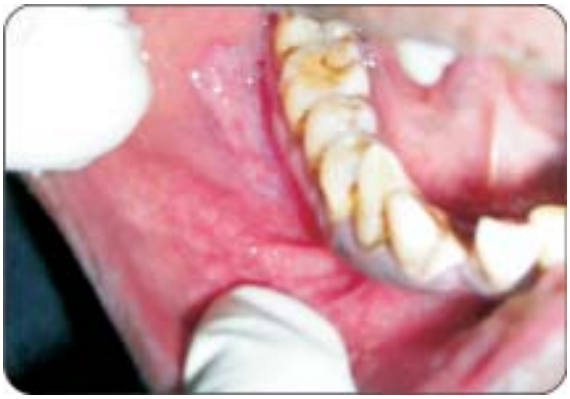

Fig. 3.1: Betel quid lesion

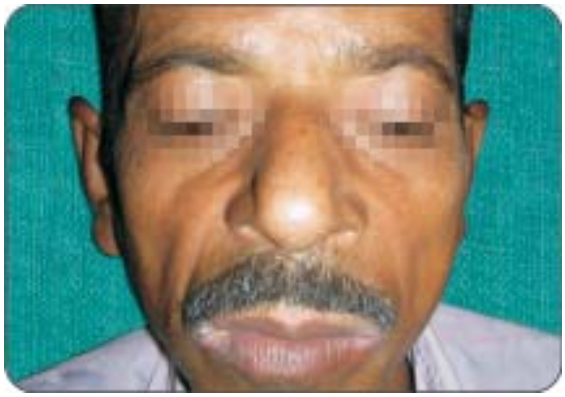

Fig. 3.2: Leukoplakia at commisure

may have some role in the development of leukoplakia.

Hormonal Imbalance

Imbalance or dysfunctions of both male and female sex hormones may induce some keratogenic changes in the oral epithelium and these changes may ultimately lead to the development of leukoplakia.

Chronic Irritation

Chronic irritation to the mucosa by ill-fitting dentures, sharp cuspal edges of teeth and hot or spicy foods, etc. may cause leukoplakia.

Actinic Radiation

Actinic or solar radiation may bring about some hyperkeratotic changes in the oral mucosa, especially the lip mucosa and this can be a predisposing factor for leukoplakia in rare cases.

Galvanism

Galvanic reactions may occur in the oral cavity when there is difference in the electrical potential between two dissimilar metallic restorations. These reactions often lead to the development of leukoplakia in the oral mucosa.

CLINICAL FEATURES OF LEUKOPLAKIA

Age: Usually, the lesion occurs in the fourth, fifth, sixth and seventh decade of life. Only about 5 percent lesions occur below the age of 30 years.

Sex: Leukoplakia occurs more often in males than females. However, this trend is changing very fast due to the gradual increase in the tobacco related habits among females, with subsequent increase in the incidence of leukoplakia among them.

Site: Buccal mucosa and commissural areas are the most frequently affected sites (Fig. 3.2), followed by alveolar ridge, tongue, lips, hard and soft palate, floor of the mouth and gingiva, etc. Multiple areas of involvement may be seen in few cases.

CLINICAL PRESENTATION

- Oral leukoplakias often present solitary or multiple **"white patches"**. They can be nonpalpable, faintly translucent, white areas over the mucosa.
- Many lesions can be **thick, fissured, indurated or papillomatous** in nature.
- The size of the lesion may vary from a small, welllocalized patch measuring about few millimeter in diameter to a diffuse large lesion, covering a wide mucosal surface.
- The surface of the lesion may be **smooth or finely wrinkled or even rough** on palpation, and the lesion cannot be removed by scrapping.
- The lesions are usually **white or grayish or yellowish-white** in color and in some cases, due to the heavy use of tobacco, they may take a brownish- yellow color.
- Some lesions may exhibit a **pumice-like surface**, which occurs due to the presence of multiple discrete keratotic striae on the surface of these lesions.

- Leukoplakia of the floor of the mouth sometimes has an ebbing-tide pattern of appearance.
- The thickness of the patch may vary from only faint to considerably thick.
- In most of the cases, leukoplakias lesions are asymptomatic, however, in some cases they may cause pain, a feeling of thickness and burning sensations, etc.

Clinical classification of leukoplakia

- Homogenous leukoplakia
- Ulcerative leukoplakia and
- Nodular or speckled leukoplakia.

The homogenous leukoplakia clinically presents extensive white patch having uniformly smooth, flat or corrugated surface with an irregular margin. These lesions usually maintain a relatively consistent pattern throughout the clinical course (Figs 3.3 and 3.4).

- These lesions are mostly associated with the oral use of snuff.
- They can be either non elevated or slightly elevated and the margin is not well-demarcated from the surrounding normal epithelium.

The ulcerative leukoplakia clinically exhibit either predominantly white or mixed red and white lesions, in which there is a central ulceration (Figs 3.5 to 3.7).

- The ulcerated center of the lesion appears red and it may have a yellowish fibrin coating.
- White patches are seen at the periphery of these lesions.

The nodular or speckled leukoplakia clinically present mixed red and white lesions; the mucosa is in which multiple small, slightly raised, rounded, keratotic nodules or granules are seen scattered through out the erythematous base (Fig. 3.8).

- This variety of leukoplakia often carries the maximum risk of malignant transformation.

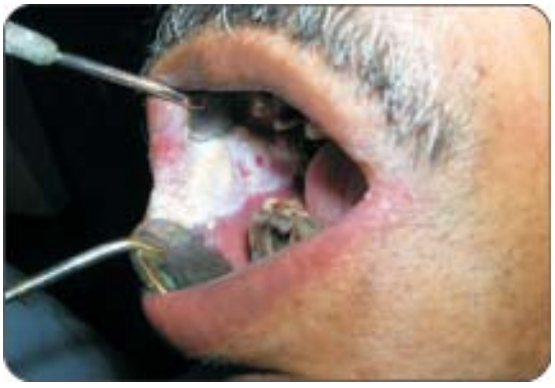

Fig. 3.3: Homogenous leukoplakia

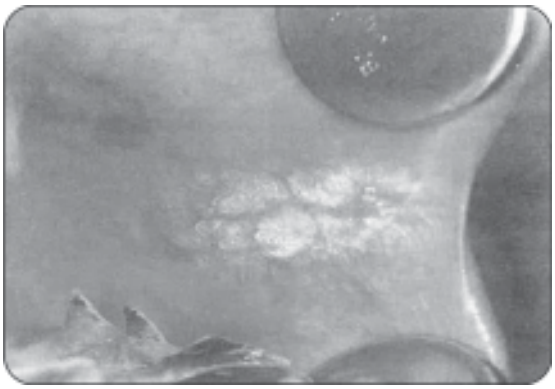

Fig. 3.4: Homogenous leukoplakia of the cheek

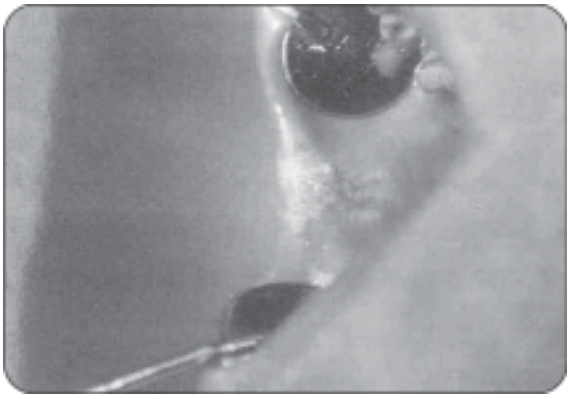

Fig. 3.5: Ulcerative leukoplakia of the angle of the mouth

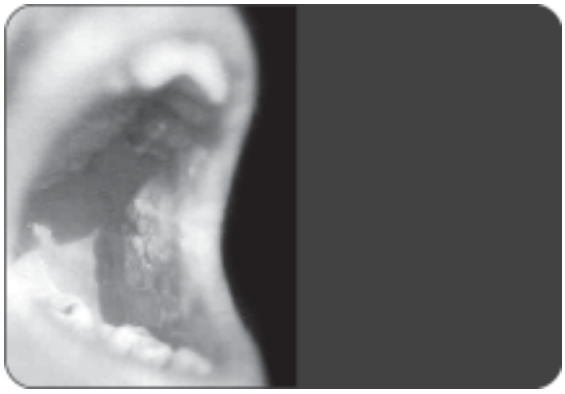

Fig. 3.6: Ulcerative leukoplakia of the cheek

HISTOPATHOLOGY

Under microscope leukoplakia generally presents **hyperorthokeratinization or hyperpara-**

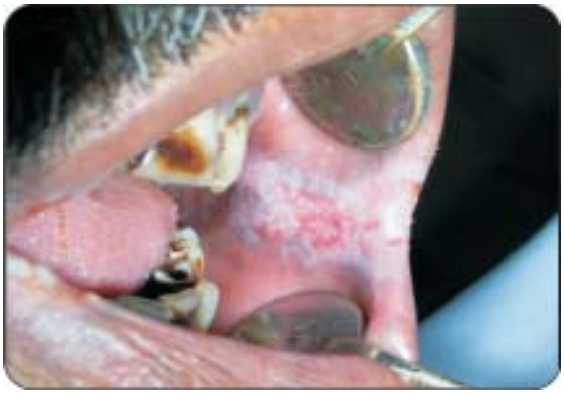

Fig. 3.7: Ulcerative leukoplakia

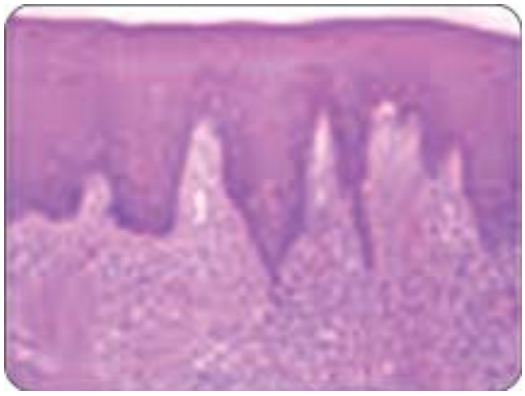

Fig. 3.9A: Normal stratified squamous epithelium

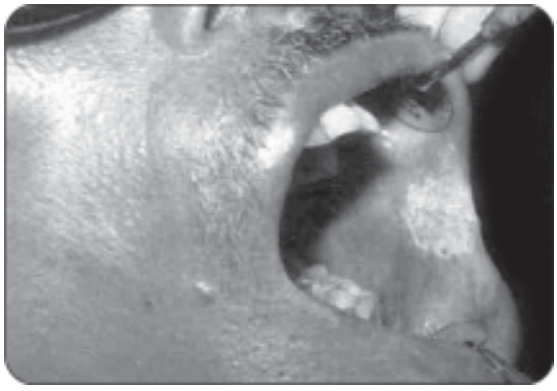

Fig. 3.8: Nodular leukoplakia of the cheek

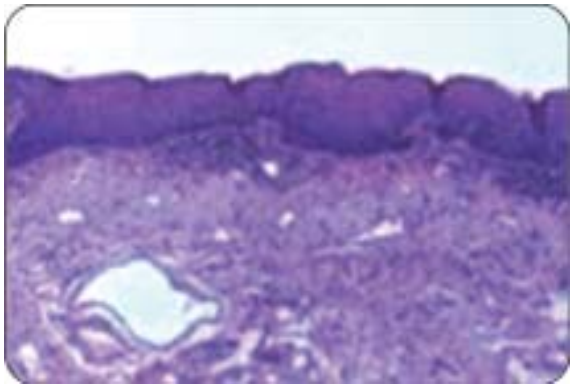

Fig. 3.9B: Photomicrograph of mild epithelial dysplasia

keratinization or both, with or without the presence of epithelial dysplasia.

Normal epithelium (Fig. 3.9A) shows a variety of histologic changes in terms of the following factors- (a) keratinization pattern (b) changes in the cellular layers (c) thickness of the epithelium and (d) alterations in the underlying connective tissue stroma.

CHANGES IN THE KERATINIZATION PATTERN

Hyperkeratinization of the epithelium refers to formation of keratinized layers in the epithelium which are normally nonkeratinized or abnormal increase in the thickness of the existing keratin layer in the epithelium, which are normally keratinized.

Hyperorthokeratinization

Orthokeratin is a homogenous layer of keratin present on the superficial part of the epithelium, which does not contain any nuclear remnants. In case of leukoplakia, an abnormal increase in the thickness of orthokeratin layer is seen in the areas of epithelium which are usually keratinized. Besides this, some degree of orthokeratinization may also be seen in the areas of epithelium, which are usually nonkeratinized.

Hyperparakeratinization

When there is an increase in the thickness of parakeratin layer (keratin that contains some nuclear remnants) on the epithelium, it is called hyperparakeratinization. An important histologic criteria of leukoplakia is the presence of hyperparakeratinization of the normally keratinized epithelium, or some amount of parakeratin deposition in the areas of epithelium which are usually non-keratinized. Epithelial dysplasia is more frequently associated with hyperparakeratinized lesions.

In few lesions of leukoplakia, both hyperorthokeratinization and hyperparakeratinization may be seen.

Thickness of the Epithelium

In leukoplakia, the thickness of the epithelium is often altered and it occurs in the form of epithelial atrophy or epithelial hyperplasia or acanthosis, etc.

Acanthosis: An abnormal increase in the thickness of stratum spinosum of the epithelium is called acanthosis. In case of leukoplakia, acanthosis is commonly observed in multiple areas of the epithelium, which often causes elongation, thickening and blunting of the retepegs.

CHANGES IN THE CELLULAR LAYER

When the precancerous changes in a lesion develop only at the cellular level, it is known as '**cellular atypia**'. At this situation, the overall alterations in the tissue in the direction of precancerous changes are not fully expressed.

When the precancerous changes in a lesion worsen further and the changes (both physical and morphological) begin to express themselves in the overall tissue levels, it is called '**epithelial dysplasia' (Fig. 3.9B)**.

The degrees of epithelial dysplasia in a lesion may change with time.

Dysplasia (dys–abnormal, plasia–formation)

Epithelial dysplasia is the hallmark in the histological changes seen in the epithelium, in case of leukoplakia and its presence is an important indicator of the precancerous nature of the disease.

The features of epithelial dysplasia include the following:

- Nuclear hyperchromatism (large and deeply stained nuclei)
- Cellular pleomorphism (altered size and shape of cells)
- Irregular epithelial stratifications (normal orientation of cell layers disturbed)

Key points of features of epithelial dysplasis

- Nuclear hyperchromatism
- Cellular pleomorphism
- Irregular epithelial stratifications
  Increased nuclear–cytoplasmic ratio
- Poikilocarynosis or division of nucleus without division of cytoplasm
- Loss of polarity of basal cells.
- Increased number of mitotic figures
- Presence of mitotic activity even in the superficial half of the epithelium
- Individual cell keratinization
- Dyskeratosis
- Enlarged nucleoli
- Diminished intercellular adherence
- Drop-shaped rete-pegs with basal cell hyperplasia
- More than one layer of cells having "basaloid" appearance.

- Increased nuclear–cytoplasmic ratio (size of nucleus increases and volume of cytoplasm decreases; in normal epithelial cells the ratio is 1:4 and in dysplastic cells the ratio changes to 1:1)
- Poikilocarynosis or division of nucleus without division of cytoplasm
- Loss of polarity of basal cells.
- Increased number of mitotic figures (few abnormal mitosis may also be present)
- Presence of mitotic activity even in the superficial half of the epithelium (normally, it is seen in the basal layer)
- Individual cell keratinization
- Dyskeratosis (abnormal expression of keratin production in the superficial as well as in the deep layers of epithelium)
- Enlarged nucleoli
- Diminished intercellular adherence
- Drop-shaped rete-pegs with basal cell hyperplasia
- More than one layer of cells having "basaloid" appearance.

Types of Dysplasia

Depending upon the degree and the extent to which the dysplastic changes have developed in a lesion of leukoplakia; epithelial dysplasias may be divided into three categories namely the:

- **Mild epithelial dysplasia (Fig. 3.9B),**
- **Moderate epithelial dysplasia (Fig. 3.10) and**
- **Severe epithelial dysplasia (Fig. 3.11)**

The degree of dysplasia is of immense value in predicting the malignant potential of a precancerous lesion.

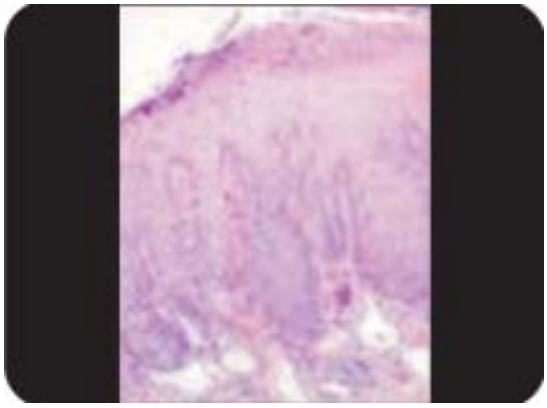

Fig. 3.10: Photomicrograph of moderate epithelial dysplasia

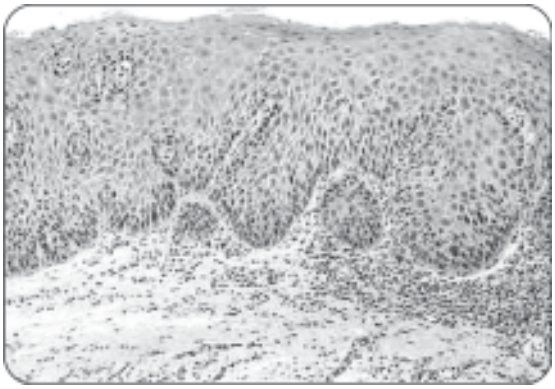

Fig. 3.11: Photomicrograph of severe epithelial dysplasia

The **severe dysplasia** in a lesion means it has more chances of undergoing malignant transformation; similarly **mild dysplasia** in a lesion means it carries the least chance of undergoing malignant transformation and likewise the **moderately dysplastic** lesion falls between the two extreme categories in terms of its risk for malignant transformation.

However, the dysplastic changes in a lesion are reversible and if the predisposing factors are removed, the dysplastic cells can turn back towards normal.

Factors determining the degree of epithelial dysplasia in leukoplakia

- Age and sex of the individual having precancerous lesion in the mouth
- Frequency and duration of oral habits
- Types of oral habits (tobacco, alcohol, snuff)
- Types of tobacco used and mode of consumption (smoking, chewing or others)
- Any synergism (combination) of multiple habits or not,
- Location of the lesion in the oral cavity (lips, tongue, floor of the mouth)
- Presence or absence of secondary infections (candidiasis, syphilis , HPV or HSV)
- Systemic health of the individual (hormonal factors/nutritional status).

Candidal Hyphae

Histologic sections of leukoplakia often reveal the presence of candidal hyphae in the epithelium. The candida associated leukoplakias may have an increased tendency for malignant transformation.

Reduction in thickness of basement membrane

In leukoplakia, there is a gradual reduction in the thickness of basement membrane of the epithelium, with the increase in the severity of the epithelial dysplasia.

CHANGES IN THE UNDERLYING CONNECTIVE TISSUE

Chronic Inflammatory Cell Infiltration

In leukoplakia, there are often variable degrees of destruction of the collagen fibers and moreover chronic inflammatory cell infiltration is also present in the underlying connective tissue stroma.

SPECIAL INVESTIGATIONS IN LEUKOPLAKIA

In leukoplakia, the presence of epithelial dysplasia and the malignant transformation potential of the lesion can not always be assessed properly with the help of simple histopathology alone. In such cases, special investigative techniques should be employed which are as follows:

- Histochemistry
- Enzyme histochemistry

- Immunohistochemistry
- Exfoliative cytology
- Cell proliferation study
- Stereological techniques
- DNA histograms
- *In vitro* testing of living tissue.

DIFFERENTIAL DIAGNOSIS OF LEUKOPLAKIA

- Lichen planus
- Candidiasis
- Frictional keratosis
- Verrucous carcinoma
- White sponge nevus
- Chemical burns
- Discoid lupus erythematosus
- Leukoedema
- Syphilitic patches
- White sponge nevus.

Key points of leukoplakia

- Leukoplakia is a common precancerous lesion of the oral cavity.
- It appears as a "white patch" or "plaque" in the oral mucosa, which cannot be scraped off or stripped off easily and more over, which cannot be characterized clinically or pathologically as any other disease.
- Clinically, it presents well defined solitary or multiple "white patches". They can be non-palpable, faintly translucent, white areas over the mucosa.
- The surface of the lesion may be smooth or finely wrinkled or even rough.
- The lesions are usually white or grayish or yellowish-white in color.
- Clinically, leukoplakias are divided into three types—homogenous leukoplakia, ulcerative leukoplakia and nodular or speckled leukoplakia.
- Under microscope, leukoplakia generally presents hyperorthokeratinization or hyperparakeratinization or both, with or without the presence of epithelial dysplasia.
- The epithelial dysplasia may be of mild, moderate and severe types.
- The overall malignant transformation rate of leukoplakia is about 3 to 6 percent.
- Treatment includes surgical excision of the lesion or cryosurgery along with stoppage of all oral habits.

MALIGNANT TRANSFORMATION IN LEUKOPLAKIA

According to WHO, the overall malignant transformation rate of leukoplakia is about 3 to 6 percent. The malignant potentiality of a leukoplakia lesion also depends upon several factors like the age and sex of the patient, type and duration of habits, frequency of habit, site of the lesion, clinical type of leukoplakia present and whether treatment provided or not etc.

Usually, the nodular leukoplakias show the highest rate of malignant transformation among all the clinical types. Malignant transformation in leukoplakia will lead to squamous cell carcinoma.

Generally, the homogeneous leukoplakias and leukoplakias of the palate have the least chances of malignant transformation.

Risk of malignant transformation increases with older age of the patients and in lesions persisting or remaining untreated for longer durations.

Leukoplakias of floor of the mouth and ventral surface of the tongue carry the highest risk for malignant transformation.

Women carry higher risks of malignant transformation, if they have leukoplakia as compared to men.

TREATMENT OF LEUKOPLAKIA

Stoppage of all oral habits, surgical excision of the lesion or cryosurgery and administration of heavy dose of vitamin A, etc.

ORAL HAIRY LEUKOPLAKIA

DEFINITION

Oral Hairy leukoplakia is a **HIV–associated mucosal disorder** and is considered as a reliable marker for the presence of HIV virus in the body and is also a precursor of full blown AIDS.

Homosexual men with HIV (human immnunodeficiency virus) infection may develop these white patchy lesions in the oral cavity. Moreover, these lesions can also be seen in other HIV / AIDS risk individuals like patients with hemophilia and other common transfusion recipients, etc.

CLINICAL FEATURES

- Clinically, oral hairy leukoplakia occurs most frequently on the **lateral borders** and **ventral**

surface of the tongue. However, it can also occur on the floor of the mouth, buccal or labial mucosa and palate, etc.

- The lesion often appears as a **slightly raised, white plaque with vertically corrugated, irregular surface.**
- The oral hairy leukoplakias characteristically exhibit an irregular surface with numerous linear vertical folds or projections on it and these projections are sometimes so marked as to resemble **"hairs"** (hence, the name hairy leukoplakia has been coined).
- The lesions vary in size from few millimeters to 3 centimeter in maximum dimension and they can not be rubbed off or scraped off from the surface.
- Some lesions are small and have a finely corrugated surface.
- Hairy leukoplakias are asymptomatic lesions, whenever they occur on the buccal mucosa.
- The lesions are nearly always colonized by *Candida albicans,* but the etiology of the disease itself is viral.
- Hairy Leukoplakia probably occurs due to opportunistic infection in immunosuppressed individuals; being caused by Epstein Barr virus.
- In HIV infected patients, presence of hairy leukoplakia indicates progression of the disease from asymptomatic seropositive states into the full blown AIDS.
- There is no evidence of malignant transformation in this form of leukoplakia.

HISTOPATHOLOGY

- In oral hairy leukoplakia, the **parakeratin layer is thick** and is often colonized by **candidial organisms.**
- A very characteristic finding in oral hairy leukoplakia is the presence of a sub corneal (below the keratin layer) upper spinus layer zone, made up of cytopathically altered keratinocytes. These are **large, pale staining epithelial cells,** which are often called '**balloon cells**'.
- These cells exhibit clear cytoplasm, vesicular nuclei with margination of the chromatin (peripheral condensation of chromatin along the nuclear membrane).
- No dysplastic changes are seen in oral hairy leukoplakia and neither there is evidence of any malignant transformation.
- The submucosa does not exhibit much inflammatory cell infiltration.

Key points of oral hairy leukoplakia

- Oral Hairy leukoplakia is a HIV–associated mucosal disorder, which clinically presents a slightly raised, white plaque with vertically corrugated, irregular surface.
- The lesion mostly develops on the lateral border and ventral surface of the tongue.
- Hairy leukoplakia often characteristically has numerous linear vertical folds or projections on the surface, which are sometimes so marked as to resemble "hairs".
- Presence of hairy leukoplakia indicates progression of the disease from asymptomatic seropositive states into the full blown AIDS.
- Histologically, the lesion shows a markedly thickened superficial parakeratin layer and below the surface layer large, pale staining epithelial cells are seen, which are often called **'balloon cells'**.
- No dysplastic changes are seen in oral hairy leukoplakia.

DIFFERENTIAL DIAGNOSIS

- Chronic candidiasis
- Lichen planus
- White sponge nevus
- Geographic tongue
- Verrucous leukoplakia
- Chronic tongue biting habits.

SPECIAL INVESTIGATION

Hairy leukoplakia is diagnostically confirmed by using DNA *in situ* hybridization with an Epstein Barr virus molecular probe on processed tissue section. It reveals positive staining of the upper spinus layer of cells.

TREATMENT

No treatment is specifically required since hairy leukoplakia is an asymptomatic lesion. However, it subsides after acyclovir therapy is given to the patient.

LEUKOEDEMA

DEFINITION

Leukoedema or preleukoplakia is an alteration of the oral epithelium characterized by intra-

cellular accumulation of fluid (edema) within the spinus cell layer.

ETIOLOGY

The etiology of leukoedema is not known. According to many investigators, the condition is a variation of normal epithelium rather than a disease.

CLINICAL FEATURES

- Leukoedema more commonly occurs among black population; age of occurrence is about 45 years.
- The oral mucosa exhibits an asymptomatic, **diffuse, translucent, grayish–white area** with a **filmy appearance**.
- It is commonly seen on the buccal mucosa (often bilaterally) near the occlusal plane. However, some lesions can occur on the lateral border of the tongue and inner surface of the lips.
- The affected mucosa may be wrinkled or corrugated in extreme cases.
- When the mucosa is stretched, the lesion often disappears or is greatly decreased.
- Few such lesions may turn into leukoplakia in future.

HISTOPATHOLOGY

- Histologically, leukoedema is characterized by thickening of the epithelium with mild degree of parakeratosis and acanthosis.
- Within the spinus cell layer, large amount of **intracytoplasmic fluid and glycogen** often accumulate, which results in enlarged spinus cells with pyknotic nuclei and clear cytoplasm.
- The rete-pegs are often broad and the underlying connective tissue is normal.
- The epithelium never exhibits any dysplastic changes.

TREATMENT

No treatment is necessary.

CARCINOMA *IN SITU*

DEFINITION

Carcinoma *in situ* is a **laterally spreading, intra-epithelial type of superficial carcinoma**, which mostly occurs over the skin and sometimes in the mucosa, including that of the oral cavity.

It is the most severe stage of epithelial dysplasia, which involves the entire thickness of the epithelium, however the **basement membrane remains intact** in this lesion.

These mucosal lesions resemble leukoplakia in all respects except that the dysplastic features are very pronounced and involve almost all layers of the epithelium. The most striking feature of carcinoma *in situ* is that dysplastic epithelial cells do not invade into the underlying connective tissue stroma.

CLINICAL FEATURES

Age: Elderly.

Sex: More common among males than females.

PRESENTATION

- Clinically, the lesions may appear either as **white plaques** or as **ulcerated, eroded** or **reddened** areas over the oral mucosa.
- The common sites of occurrence of these lesions are the **floor of the mouth, tongue or lips**, etc.
- The lession may sometimes clinically appearing either as leukoplakia or erythroplakia.
- In some other lesions, combined features of both leukoplakia and erythroplakia are found.

HISTOPATHOLOGY (FIG. 3.12)

- Histologically, hyperkeratosis may or may not be present on the surface of the lesion and if it is present, it will usually be the hyperparakeratosis.

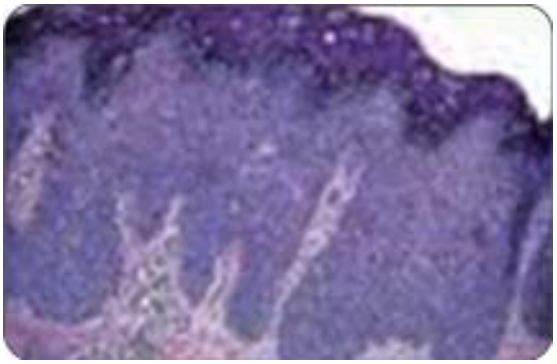

Fig. 3.12: Photomicrograph of carcinoma *in situ*

- The epithelium is generally **hyperplastic** or sometimes it can be atrophic.
- The features like individual cell keratinization and keratin pearl formation, etc. are exceedingly rare.
- In fact, if keratin pearls are found, invasive carcinoma should be suspected rather than carcinoma *in situ*.
- One of the most consistent features of carcinoma *in situ* is the **loss of orientation and loss of polarity of the dysplastic epithelial cells.**
- A **sharp line of division** between the normal and the dysplastic epithelium is always present, which extends from the surface up to the connective tissue.
- Basement membrane of epithelium always remains intact.
- Cytologically, carcinoma *in situ* is similar to squamous cell carcinoma except that architecturally the **epithelial basement membrane is intact** and no invasion of the dysplastic cells into the underlying connective tissue has occurred.
- Sometimes, multiple lesions of carcinoma *in situ* may develop in a single surface of epithelium, being separated from one another by the normal epithelium.

Key points of carcinoma *in situ*

- Carcinoma *in situ* is the most severe stage of epithelial dysplasia and is also called laterally spreading, intra-epithelial type of superficial carcinoma.
- The dysplastic process involves the entire thickness of the epithelium, However, the basement membrane remains intact.
- It commonly develops in the floor of the mouth, tongue or lips, etc.
- Histologically, the epithelium is generally hyperplastic or sometimes it can be atrophic
- The lesion often characteristically exhibits loss of orientation and loss of polarity of the dysplastic epithelial cells.
- Since the basement membrane is intact, there is no invasion of the neoplastic cells into the underlying connective tissue.

- Since, there is no invasion of the neoplastic cells into the underlying connective tissue, metastasis does not occur in carcinoma *in situ*.

TREATMENT

Treatment is done by surgery, radiotherapy or elctrocautery, etc. The untreated cases will eventually transform into invasive squamous cell carcinoma.

ERYTHROPLAKIA

Erythroplakia is a clinical term, which refers to "a **red patch or plaque** in the oral mucosa, which can not be characterized clinically or pathologically as any other condition and which has no apparent cause" (WHO-1978).

It was first reported by Queyrat in 1911 as a red, velvety lesion on the mucosa of the glans penis of elderly males. Oral erythroplakias represent the most severe type among all oral precancerous lesions and histologically, these lesions almost always exhibit dysplastic changes.

ETIOLOGY

The exact etiology is not known. However, excessive use of tobacco (cigarette or beede smoking) and heavy drinking of alcohol are believed to be responsible for the disease.

CLINICAL FEATURES

Prevalence rate: About 0.09 percent in U.S.A and 0.02 percent in India.

Age: Fifth, sixth and seventh decade of life.

Sex: Males and females are almost equally affected.

Site: Floor of the mouth and retromolar areas are most frequently involved. The other intraoral sites are buccal mucosa, gingiva, tongue (ventral and lateral surfaces) and soft palate, etc.

The gingiva and alveolar ridge lesions are more frequently seen among females.

PRESENTATION

Clinically, erythroplakia appears as a small or extensive, red, velvety lesion with clearly defined margins. The redness is not always a prominent feature of this disease since the color may not be uniformly present in all parts of the lesion. The oral erythroplakias are always clinically and histologically similar to those seen in the genitalia.

CLINICAL TYPES

Erythroplakia clinically presents **three distinctive patterns**, which are as follows:

Homogenous Erythroplakia

This type of lesion appears as bright red, velvety, soft areas on the oral mucosa, with an irregular but well defined margin.

Erythroplakia Interspersed with Patches of Leukoplakia

In this type of erythroplakia, there is presence of multiple, irregular erythematous areas in the oral epithelium and along with that few white leukoplakic patches are also present. The erythematous areas are not as red as those seen in the homogenous type.

Speckled Erythroplakia

These lesions are similar to the speckled leukoplakias of the oral cavity and are characterized by the presence of soft, irregular, raised, erythematous areas in the epithelium with a granular surface. There are some tiny, focal white plaques distributed all over the red surface.

HISTOPATHOLOGY

- Erythroplakia should be viewed with high degree of alert, since most of the lesions (80 to 90 percent) exhibit features of invasive epidermoid carcinoma or carcinoma *in situ* or at least severe epithelial dysplasia.
- The areas which clinically appear red histologically exhibit atrophy of the epithelium with reduction in the keratin production. Moreover, there is also an increase in the vascularity of the submucosal connective tissue.
- The underlying connective tissue shows intense chronic inflammatory cell infiltration.

DIFFERENTIAL DIAGNOSIS

- Erosive lichen planus
- Early squamous cell carcinoma
- Atrophic candidiasis
- Kaposi's sarcoma

Key points of erythroplakia

- Erythroplakias represent the most severe type among all oral precancerous lesions, with extreme risk of malignant transformation.
- Clinically, it appears as a small or extensive, red, velvety lesion with clearly defined margins.
- The disease has three distinct clinical types-homogenous erythroplakia, erythroplakia interspersed with patches of leukoplakia and speckled erythroplakia.
- Histologically, erythroplakia often exhibits features of invasive epidermoid carcinoma or carcinoma *in situ* or at least severe epithelial dysplasia.
- Deep and wide surgical excision of the lesion is the treatment of choice.

- Stomatitis associated with nutritional deficiency or denture irritation
- Contact allergy
- Palatal erythema due to heavy smoking.

TREATMENT

Deep and wide surgical excision of the lesion, regular follow-up examinations are mandatory.

STOMATITIS NICOTINA

DEFINITION

Stomatitis nicotina (**smoker's keratosis**) is a tobacco-related keratosis of the oral mucosa and is commonly seen in the palate of the excessive pipe or cigar smokers. The severity of the condition is directly related to the intensity and duration of smoking.

CLINICAL FEATURES

- The condition affects both **hard and the soft palates**, however, if the patients hard palate is covered with a denture then only the soft palate is affected (Fig. 3.13).
- The disease represents two separate abnormalities simultaneously; one is the **hyperkeratosis** of the epithelium and the other is the **inflammatory swelling of the palatal mucous glands.**

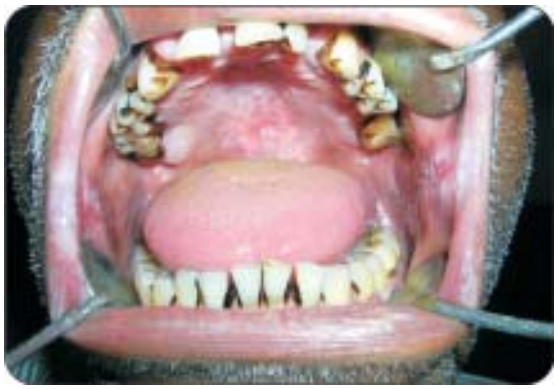

Fig. 3.13: Stomatitis nicotina palati

- Initially, the palatal mucosa becomes red and later on, it becomes white due to increased thickening and hyperkeratosis of the epithelium.
- On the surface of the lesion, few **red, dot-like areas** are seen, which are **surrounded by elevated, white keratotic rings**. These red dots represent the inflammed duct openings of the palatal minor salivary glands.
- The white background of the palatal mucosa may have a rough surface and it may be even fissured or wrinkled.
- In severe cases, the palatal mucosa may become completely ulcerated.
- Similar lesions can sometimes be seen over the buccal mucosa, particularly on that side of the mouth where the pipe or cigar is held.
- The lesion subsides to a great extent once the pipe smoking habit is discontinued.

HISTOPATHOLOGY

- The histopathology of stomatitis nicotina shows hyperorthokeratosis and acanthosis of the surface epithelium.
- The palatal mucous glands are **inflammed and swollen**.
- The ductal epithelium of the palatal minor salivary glands often exhibits **squamous metaplasia**.
- Sometimes, the minor salivary glands themselves exhibit partial or complete atrophic changes.
- Moderate degree of inflammatory cell infiltration is often seen in the connective tissue adjacent to the palatal minor salivary glands.
- Dysplastic changes may sometimes be seen either in the palatal surface epithelium or in the ductal epithelium of the minor salivary glands.

TREATMENT

Complete stoppage of all oral habits and observation. The malignant transformation of this lesion is rare, unless the patient is a reverse smoker. Palate is the least common site for the development of oral cancer. However, pipe smokers can develop cancer not directly in the palate but in the lingual retromolar areas.

ORAL SUBMUCOUS FIBROSIS (OSF)

DEFINITION

Oral submucous fibrosis (Figs 3.14 and 3.15) is the most predominant precancerous condition arising in the oral cavity, oropharynx, nasopharynx and esophagus, etc. The disease is

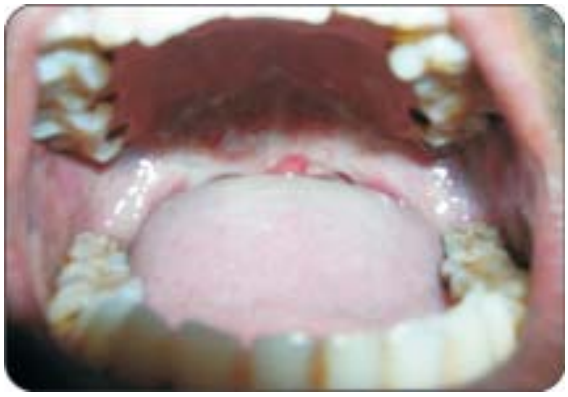

Fig. 3.14: Submucous fibrosis-I

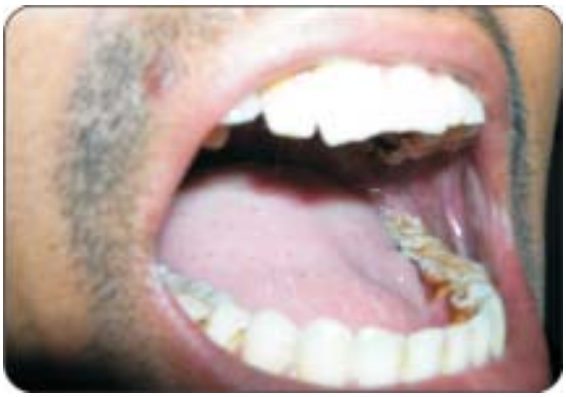

Fig. 3.15: Submucous fibrosis-II

characterized by juxta-epithelial inflammatory reaction in the oral mucosa, followed by a fibro-elastic transformation of the lamina propria leading to mucosal atrophy, rigidity and trismus.

The condition was first reported by Schwartz (1952) in the name of "Atrophia idiopathica (tropica) mucosae oris". The present name oral submucous fibrosis was coined by Dr Joshi from Bombay in the year 1953.

EPIDEMIOLOGY

The disease is more common among the people of South-East Asian countries, especially the Indians, Bangladeshis, Nepalese, Burmese, Vietnamese and South Africans, etc. The extreme climatic conditions in these regions and adherence of the people to more spicy foods, is believed to the main reason behind the higher incidence of the disease. Oral submucous fibrosis may undergo malignant transformation and develop squamous cell carcinoma in the mouth.

ETIOLOGY

- ***Excessive consumptions of red chilies:*** Indians and other Asiatic people consume large amount of chilies regularly because they like foods duly seasoned with hot peppers. Chilies contain an active ingredient called 'capsaicin' that produces allergic reactions in the oral mucosa.
- ***Excessive "areca nut" chewing:*** Excessive consumption of areca nut either alone or in combination with betel leaf, lime and tobacco, etc. increases the possibility of submucous fibrosis. According to many investigators, areca- nut contains a chemical substance called 'arecoline', which causes stimulation of the fibroblast cells to produce more and more collagen and this eventually results in the development of OSF.
- ***Nutritional deficiency:*** Deficiency of vitamin A, B complex and C, etc. as well as the deficiency of iron and zinc in the diet.
- ***Immunological factors:*** According to some investigators, oral submucous fibrosis exhibits increased number of eosinophils both in the circulation as well as in the tissue.

  Moreover, there is also presence of gamma-globulinemia and increased mast cell response, etc. All these factors indicate an immunologic background of the disease.
- ***Genetic factors:*** Some people are genetically more susceptible to this disease.
- ***Protracted tobacco use:*** Excessive use of chewable tobacco.
- ***Deficiency of micronutrients:*** Patients with deficiency of selenium, zinc, chromium and other trace elements may fail to prevent the free radical injury in the body and can therefore develop oral submucous fibrosis.

PATHOGENESIS

- It has been suggested by many investigators that the chronic exposure to areca nut, chili peppers along with prolonged deficiency of iron, zinc and vitamins, etc in the diet cause an alteration in the oral mucosa, which increases the risk of hypersensitivity to many other potential irritants.
- The hypersensitivity reaction to the oral epithelium often results in an juxta-epithelial inflammation and a fibrotic change in the lamina propria.
- Moreover, increased fibrosis in the sub-epithelial connective tissue cause atrophy of the oral mucosa, which in turn may be more and more vulnerable to irritants (For example, tobacco, alcohol, betel nut and other agents) and may eventually undergo malignant transformation.

CLINICAL FEATURES

Age: 20 to 40 years of age.

Sex: Female are affected more often than males

Site: In submucous fibrosis, fibrotic changes are frequently seen in the buccal mucosa, retromolar area, uvula, soft palate, palatal fauces, tongue, lips, pharynx and esophagus, etc.

It is believed, that the disease initiates from the posterior part of the oral cavity and then it gradually spreads to the anterior locations.

PRESENTATION (FIGS 3.16 TO 3.18)

- The onset of the disease is either insidious or it may develop gradually over a period of 2 to 5 years.
- Initially, the patient complains of burning sensations in the mouth, particularly during taking hot and spicy foods.

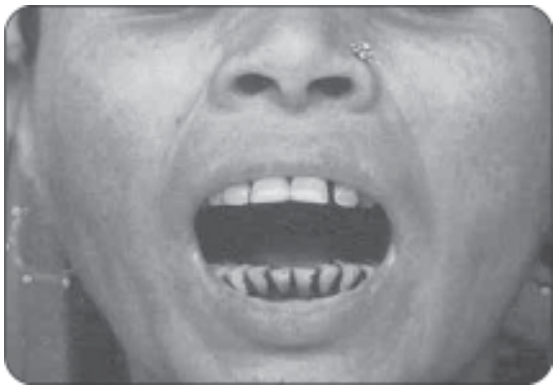

Fig. 3.16: Oral submucous fibrosis causing difficulty in mouth opening

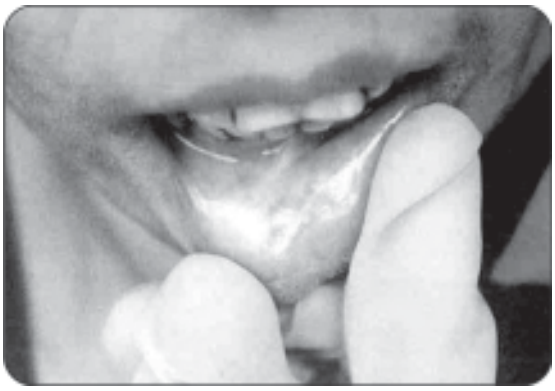

Fig. 3.17: Blanched appearance of mucosa with ulceration in submucous fibrosis

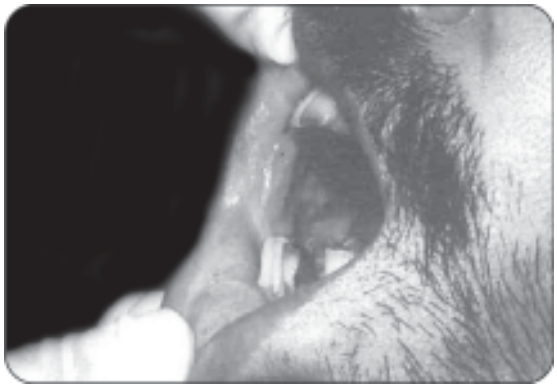

Fig. 3.18: Oral submucous fibrosis turning into squamous cell carcinoma

- This is often accompanied or followed by the formation of multiple vesicles over the palate or ulcers or inflammatory reactions in other parts of the oral mucosa.
- There can be either excessive salivation or decreased salivation (xerostomia) along with recurrent stomatitis. Patients also develop defective gustatory sensation.
- In the initial phases of the disease, palpation of the mucosa elicits a "**wet-leathery**" feeling.
- Petechial spots may also be seen in the early stages of the disease over the mucosal surfaces of tongue, lips and cheek, etc
- Oral mucous membrane is very painful upon palpation at this stage.
- One of the most important characteristic features of oral submucous fibrosis is the gradual stiffening of the oral mucosa with progressive reduction in the mouth opening **(trismus)** (Fig. 3.16).
- The stiffness of the oral mucosa and the subsequent trismus develops gradually within a few years after the development of the initial symptoms.
- In the advanced stage of OSF, the oral mucosa losses its resiliency to a great extent and it becomes blanched and stiff. Severe trismus develops at this stage.
- Because of stiffness of the lips and the tongue patients are unable to blow whistles or even blow out a candle.
- The oral mucosa is symmetrically affected on both sides of the mouth and it shows extreme pallor.
- The oral submucous fibrosis often causes a blanched opaque (**white marble-like**) appearance of the mucosa, on which, there may be occasional presence of leukoplakic or erythroplakic patches (Fig. 3.17).
- Palpation of the mucosa often reveals many vertical white fibrous bands on the inner aspect of the cheek.
- Patients of OSF often develops difficulty in deglutition, referred pain in the ear or deafness and nasal intonation of voice.
- Depapillation of the tongue with recurrent or sometimes persistent glossitis occurs. Later on the tongue becomes stiff and shows restricted movements.
- In mild cases, there may be white areas on the soft palate, but in severe cases, it shows restricted movements. Patients also have a 'bud-like' shrunken uvula.

- Thinning and stiffening of the lips causing microchelia and presence of circumoral fibrous bands.
- Areas of hypo or hyperpigmentations are seen in the oral mucosa.
- Loss of stippling occurs in the gingiva, and it becomes depigmented and fibrotic.
- Floor of the mouth becomes blanched and it gives a leathery feeling during palpation.
- Palate presents several fibrous bands, which are radiating from the pterygomandibular raphe to the anterior faucial pillars.
- The faucial pillars may be thick and short and the tonsils are often placed between them.
- When the disease progresses to the pharynx and esophagus, it causes extreme difficulty in deglutition.

HISTOPATHOLOGY

Microscopically, submucous fibrosis reveals the following features:

- The overlying hyperkeratinized, **atrophic**, epithelium often shows **flattening and shortening of the rete-pegs.**
- There can be variable degrees of cellular atypia or epithelial dysplasia.
- In oral submucous fibrosis, dysplastic changes that are found in the epithelium include marked irregular epithelial stratifications, nuclear pleomorphism and severe intercellular edema, etc.
- This type of dysplastic features are not seen in leukoplakia and instead there will be features like nuclear hyperchromatism, increased mitosis and basilar hyperplasia, etc.
- In the early stage of submucous fibrosis, the connective tissue stroma exhibits finely fibrillar collagen, inter cellular edema and increased fibroblastic activity.
- The stromal blood vessels in this stage are dilated and congested and there can be areas of hemorrhage.
- The underlying connective tissue stroma in the advanced stage of the disease shows "**homogenization**" and "**hyalinization**" of the collagen fibers (this is one of the most important features of the disease).
- Besides this, decreased number of fibroblast cells and narrowing or obliteration of the blood vessels due to '**perivascular fibrosis'** are also present.
- There can be presence of signet cells in some cases.
- **Degeneration of the muscle fibers** and chronic inflammatory cell (lymphocyte and plasma cell, etc.) infiltration in the connective tissue are commonly seen.
- The malignant transformation rate of OSF is about 4.5 to 7.6 percent.

Key points of oral submucous fibrosis

- Oral submucous fibrosis (OSF) is the most predominant precancerous condition arising in the oral cavity, oropharynx, nasopharynx and esophagus.
- The disease frequently occurs among the people of Indian subcontinent and is often related to factors like excessive consumption of red chilies, excessive areca nut chewing and nutritional deficiency, etc.
- These agents cause juxta-epithelial inflammation in the oral mucosa with increased fibrosis of the underlying connective tissue.
- Clinically, stiffness of the oral mucosa with gradual reduction in the opening of the mouth (trismus) is the hallmark features of the disease.
- The other important features of the disease include blanched opaque appearance of mucosa with thick fibrotic bands, burning sensations, decreased or increased salivations, dysphagia, referred pain in the ear and nasal intonation of voice, etc.
- Histologically, the disease presents atrophy of the epithelium with flattening and shortening of the rete-pegs; "homogenization" and "hyalinization" of the collagen fibers and degeneration of the muscle fibers, etc· The disease carries a high risk of malignant transformation.
- Treatment includes intralesional injections of collagenease, corticosteroids and fibrinolysins, etc.

ULTRASTRUCTURAL CHANGES

Following ultrastructural changes are found in submucous fibrosis:

- Fragmentations of the collagen fibers.
- Increased amount of fine immature collagen fibrils and interfibrillar matrix.

- Defective polymerization and maturation of collagen.
- Degeneration of mitochondria and nuclei of the muscle cells.
- Altered staining reaction of the collagen.
- PAS positive materials in the connective tissue.

LABORATORY INVESTIGATIONS

- Raised ESR
- Anemia
- Eosinophilia
- Hypergammaglobulinemia
- Increased serum alkaline phosphatase levels
- Alteration in the zinc and iron ratio in the tissue as well as in the blood
- Decreased serum vitamin A levels
- Scanning and transmission electron microscopy.

TREATMENT

Stoppage of all habits, grinding and rounding of sharp cuspal edge of teeth, routine extraction of all third molars are the preliminary steps in the treatment plan.

The definitive treatment of OSF includes intralesional injections of collagenase, corticosteroids and fibrinolysins, etc.

Systemic administration of steroids is also done in severe cases.

Biopsy is mandatory before treatment and if the dysplastic features are present in the epithelium, steroids should be avoided from the treatment schedules.

SIDEROPENIC DYSPHAGIA

DEFINITION

Sideropenic dyphagia or Paterson-Brown-Kelly syndrome (or Plummer-Vinson syndrome) occurs primarily due to chronic iron deficiency and this disease is often associated with a high risk of cancer of the oral cavity and the aerodigestive tract.

In developing countries, iron deficiency is common problem, which may occur either due to nutritional deficiency or due to hookworm infestations

Increased numbers of oral cancer cases are often found in the geographic areas, where iron deficiency is common.

CLINICAL FEATURES

- Sideropenic dysphagia is found more often among the middle aged females.
- Patients often suffer from weakness and generalized fatigue.
- Difficulty in swallowing is a common problem, which occurs as a result of formation of esophageal webs.
- Angular cheilosis, mucosal pallor with atrophy and a depapillated, smooth, glossy, tongue is frequently present.
- Buccal mucosa is pale in appearance and it also exhibits atrophic changes.

INVESTIGATIONS

- Examination of blood reveals the presence of severe iron deficiency anemia.
- Histological examination of oral and aerodigestive tract mucosa often exhibits mucosal atrophy and increased mitotic activity.

SIDEROPENIC DYSPHAGIA AND ORAL CANCER

- Sideropenic dysphagia is often associated with an increased risk of cancer.
- Malignant transformation of sideropenic dysphagia leads to the development of squamous cell carcinoma, which often occurs in relation to the tongue, buccal mucosa and the aerodigestive tract, etc.
- Although, the exact pathogenesis of the disease is unclear, it is believed that chronic iron deficiency causes atrophic changes in the mucosa and also causes suppression of the reprative potential of the mucosal tissue. This results in an increased susceptibility of the tissue towards malignancy when it is subjected to common irritants.

LICHEN PLANUS

DEFINITION

Lichen planus is a rather common chronic mucocutaneous disease, which probably arises due to an abnormal immunological reaction and

the disease have some tendency to undergo malignant transformation.

ETIOPATHOGENESIS

- The exact etiologic factors causing lichen planus are unknown, however psychological stress often aggravates the condition.
- It is believed that an abnormal recognition and expression of basal keratinocytes of the epithelium as foreign antigens by the Langerhans cells, induces an autoimmune reaction in the body, which results in the initiation of this disease.
- Initially, Langerhans cells recognize an antigen, which is similar to the antigens on the epithelial keratinocytes of the susceptible patient with certain classes of major histocompatibility antigens (MHA).
- Thereafter, during the processing of antigens and subsequent stimulation of the T-lymphocytes by the langerhans cells, some lymphocytes which are cytotoxic to the epithelial keratinocytes are produced.
- These cytotoxic T-lymphocytes accumulate in the subbasilar connective tissue region of the epithelium and interact with the basal keratinocytes and eventually cause 'liquefaction degeneration' of these cells.

CLINICAL FEATURES

Incidence: Lichen planus is a common skin disease and it occurs in about 1% of the population. The cutaneous lesions alone occur in about 35% cases, the mucosal lesions alone occur in about 25% cases, however, 40% patients exhibit both mucosal and cutaneous lesions together.

In India, the average incidence rate of lichen planus is about 2.1 per 1000 men and 2.5 per 1000 women.

Age: Lichen planus occurs among the middle aged or elderly people. Rarely, it can affect children.

Sex: Both sexes are affected but there is often a slight predilection for females.

Site: Lichen planus can involve several areas of the body and important among those areas or sites are as follow:

- *Cutaneous lesions*: Lichen planus of the skin usually involves (a) fexor surface of the wrist and forearms, (b) inner aspect of the knee and thigh, (c) upper part of the trunk, (d) scalp, nail beds and genitalia, etc.
- *Oral lesions:* Oral lesion of lichen planus commonly occurs on the mucosal surfaces of the buccal mucosa, vestibule, tongue, lips and gingiva, etc. palate and floor of the mouth are the least affected sites (Fig. 3.25).

In many cases, oral lesions develop bilaterally.

PRESENTATION

Cutaneous Lesions of Lichen Planus

- The cutaneous lesions of lichen planus clinically appear as clusters or diffuse areas of raised, purplish or reddish papules, which are covered by a white glistening scale (or a white keratotic **"cap").**
- These lesions often occur in a **bilaterally symmetrical** pattern.
- Lichen planus lesions increase in size, if it is subjected to some irritation.
- As the skin lesions produce itching sensation, patients often produce linear excoriations, which result in the development of linear pattern of additional lesions along the scratch marks.
- ***Koebner phenomenon:*** It refers to the development of skin lesions of lichen planus, which are extending along the areas of injury or irritation.
- Cutaneous lesions of lichen planus sometimes exhibit periods of regression and recurrence.

Oral Lesions of Lichen Planus (Figs 3.19 to 3.22)

- The classic form of oral lichen planus clinically exhibits numerous interlacing white keratotic lines, which often produce a typical **'lace-like' or 'annular' pattern**, against an erythematous base.
- A tiny white elevated dot like structure is frequently present at the point of intersection of the white lines, which is known as **"striae of Wickham".**
- Oral lesions are generally asymptomatic, although few lesions can cause pain and burning sensation while taking hot or spicy foods.

Fig. 3.19: Lichen planus involving the cheek-I

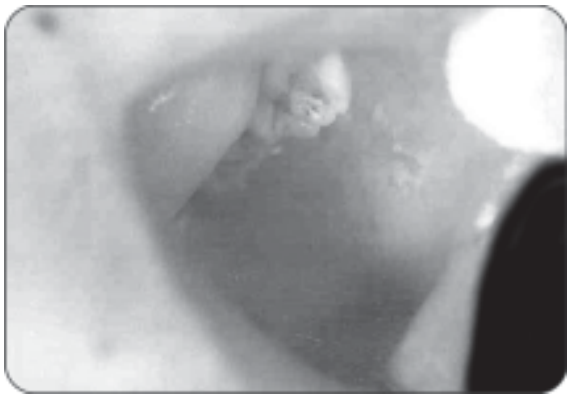

Fig. 3.20: Lichen planus of the cheek in another patient-II

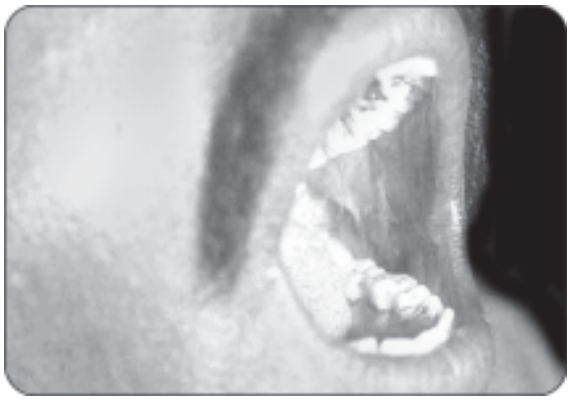

Fig. 3.21: Ulcerative lichen planus of the cheek

- These lesions also normally occur in a bilaterally symmetrical pattern.
- In some cases, patients with lichen planus may also simultaneously have other mucosal lesions like submucous fibrosis and leukoplakia, etc. in the oral cavity.

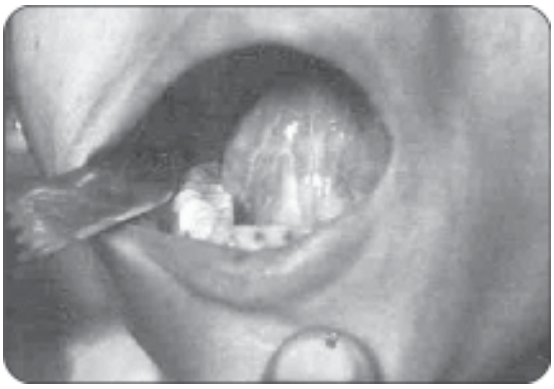

Fig. 3.22: Ulcerative lichen planus of the undersurface of tongue

CLINICAL TYPES OF LICHEN PLANUS

Clinically, lichen planus often presents several distinct clinical forms or types, which often correlate closely to the severity of the disease process.

Reticular Type

Reticular type of lichen planus of the mucous membrane produces a unique and distinctive clinical appearance.

- It usually consists of numerous raised, thin, snowy- white lines, which produce a lacework or a reticular appearance and they radiate from a central erythematous area.
- The lines are usually wavy, parallel and non–elevated.
- Reticular lichen planus commonly occurs on the buccal mucosa and buccal vestibule. Sometimes, they can occur on the mucosal surfaces of the tongue and gingiva.
- These lesions are usually asymptomatic and they often occur bilaterally.
- In some cases, reticular lichen planus may occur in association with the erosive form of the disease.

Erosive Type (Fig. 3.23)

- The erosive form of lichen planus exhibits shallow irregular areas of epithelial destructions.
- Clinically, the lesion presents a mixture of erythematous, ulcerated and white areas, which are often covered with a yellowish-white pseudomembranous coating.

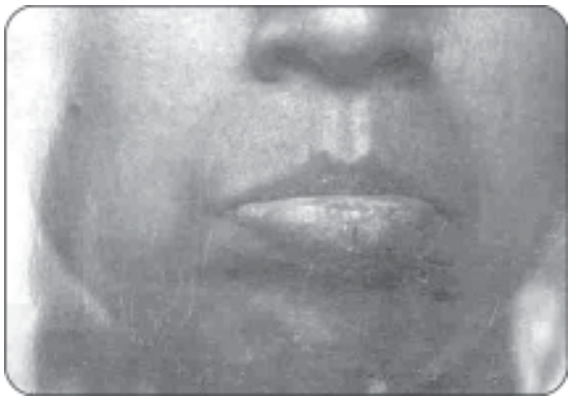

Fig. 3.23: Erosive lichen planus of the lower lip

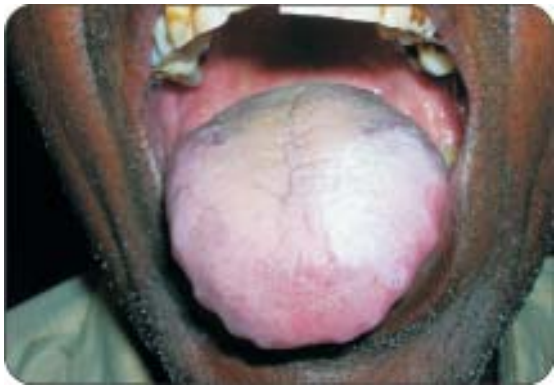

Fig. 3.24: Plaque type of lichen planus

- There can also be atrophic erythematous areas with central ulceration (Fig. 3.22).
- A faint white zone resembling radiating striae is frequently seen at the junction where the erosive area meets with the normal epithelium.
- Most of the lesions develop on the buccal mucosa and the vestibule.
- When the epithelial atrophy and ulcerations are confined only to the gingival area, the condition is referred to as 'desquamative gingivitis'.
- Patients with erosive lichen planus often complain of severe pain and burning sensation in the mouth, at the time of taking hot or spicy foods or during taking alcoholic beverages.
- In some cases, patients restrict themselves to only the bland liquid diet.
- Palpation of the affected mucosa often elicits pain and bleeding.
- The areas of mucosa where the lesion has already healed up exhibit melanotic hyperpigmentations.
- The margin of the lesion may be slightly depressed due to fibrosis and healing at the periphery.

Plaque Type (Fig. 3.24)

- The plaque type of lichen planus clinically presents a raise or flattened, white area on the mucous membrane.
- Dorsal surface of the tongue is mostly affected, where it produces irregular, white, smooth or raised plaques.
- These forms of lichen planus lesions often clinically resemble leukoplakias.

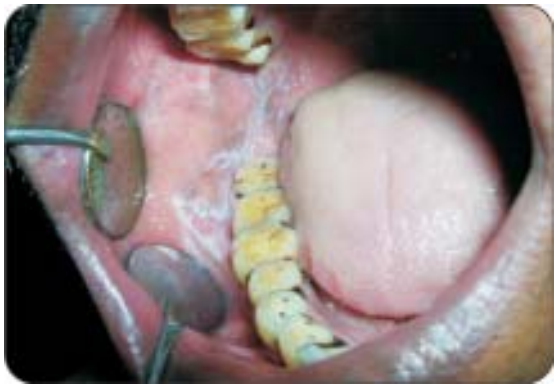

Fig. 3.25: Oral lichen planus

Atrophic Type (Fig. 3.25)

- Atrophic lichen planus often clinically presents smooth, poorly defined, erythematous areas on the oral mucosa, with or without the presence of peripheral radiating striae.
- The condition commonly affects the gingiva or the buccal mucosa.
- Patients often complain of pain and burning sensation in the mouth especially during tooth brushing and taking hot or spicy foods.
- The aggravated sensations to hot and spicy foods are due to lack of protective function of the epithelium as a result of thinning.

Bullous Type

- It is a rare form of lichen planus and is characterized by the formation of large vesicle or bullae (size ranges between 4 mm to 2 cm in diameter) on the oral mucosa.
- The lesions usually develop within an erythematous base and they rupture almost

immediately after their formation, thereafter leaving painful ulcers on the mucosal surface.
- Bullous lichen planus usually have peripheral radiating striae and these lesions are often seen over the posterior part of the buccal mucosa.

DIFFERENTIAL DIAGNOSIS

- Leukoplakia
- Candidiasis
- Mucous membrane pemphigoid.
- Discoid lupus erythematosus
- Syphilis
- Graft *versus* host reaction
- Erythema multiforme.

Key points of lichen planus

- Lichen planus is a common skin disease, which often affects the mucous membrane and the disease arises probably due to some immunlogical abnormality.
- Oral lichen planus clinically exhibits numerous interlacing white keratotic lines, which often produce a typical 'lace-like' pattern, against an erythematous base.
- A tiny white elevated dot like structure is frequently present at the point of intersection of the white lines, which is known as "striae of Wickham".
- Oral lesions are generally asymptomatic, although few lesions can cause pain and burning sensations while taking hot or spicy foods.
- Clinically, lichen planus has several types, which include reticular, erosive, bullous, ulcerative, plaque and atrophic, etc.
- Histologically, the disease presents hyperortho or hyperparakeratinization of the epithelium with thickening of the granular cell layer and acanthosis.
- A characteristic finding of the disease is the necrosis and liquefaction degeneration of the basal cell layer of the epithelium, which brings the spinus cell layer of epithelium directly in contact with the connective tissue.
- Thick 'band-like' infiltration of chronic inflammatory cells (predominantly lymphocytes) occurs in the juxta-epithelial region.
- Local and systemic steroid therapy is the main treatment.

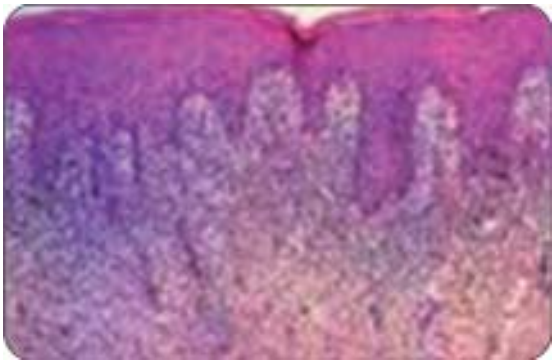

Fig. 3.26: Photomicrograph of lichen planus

HISTOPATHOLOGY

Microscopically lichen planus often reveals the following features (Fig. 3.26):
- The overlying surface epithelium exhibits hyperorthokeratinization or hyperparakeratinization or both.
- Thickening of the granular cell layer.
- Acanthosis or thickening of the spinus cell layer.
- Intercellular edema in the spinus cell layer.
- Shortened and pointed rete-pegs of the epithelium, which often produces a so called **"saw-tooth"** appearance. This appearance is not often seen in histologic sections of oral lesions of lichen planus rather it is more commonly seen in the skin lesions.
- One of the most important histologic features of lichen planus is the presence of **"necrosis and liquefaction (hydropic) degeneration"** of the basal cell layer of the epithelium.
- Due to the liquefaction degeneration of the basal cell layer, the epithelium becomes thin and the spinus cell layer often comes in direct contact with the underlying connective tissue.
- In erosive type of lichen planus, the epithelium is often extremely thin and it shows areas of complete loss of rete-pegs formation. Moreover, chronic inflammatory cells may often extend into the middle or upper layer of the epithelium.
- In lichen planus, few round or ovoid, amorphous, eosinophilic bodies are sometimes present within the epithelium, which are known as **"civatte bodies".**

- These civatte bodies probably represent apoptotic (dead) keratinocytes or other necrotic epithelial components, which are transported to the connective tissue for phagocytosis.
- A **thick 'band-like' infiltration** of chronic inflammatory cells (predominantly lymphocytes) in the juxta-epithelial region is often seen.
- In lichen planus, the affected epithelium exhibits dysplastic changes in about 4 percent cases, out of which about 0.3 to 10 percent cases may undergo malignant transformation.

SPECIAL INVESTIGATIONS

- Direct immunofluorescent test demonstrates deposition of fibrinogen along the basement membrane of the epithelium with vertical extensions into the immediate underlying connective tissue.
- In immunofluorescent tests, all forms of lichen planus lesions are usually negative for IgG, IgA and IgM antibodies but positive for fibrinogen.
- Immunohistochemical study by using the antibody to S–100 protein, indicates an increase in the langerhans cells in the mid layers of the epithelium.

TREATMENT

Small lesions of lichen planus are treated well with topical steroids, e.g. fluocinonide.

In more resistant cases, systemic administration of methyl prednisolone is effective either alone or in combination with topical steroids. Intralesional injections of steroid have been used with some degree of success but are often not well tolerated by the patient.

Patient's psychological balance must be restored.

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CHAPTER 4

Diseases of the Salivary Glands

Oral cavity normally has a moist environment and it is because of the continuous secretion of saliva in the mouth by the salivary glands. Salivary glands comprise of three paired major glands namely the Parotids, the Submandibular and the Sublingual glands. Besides these major glands, there are numerous minor salivary glands (their number may be up to 300) present in almost every part of the oral cavity, except the gingiva and the anterior part of the hard palate. These minor glands are also found in the paranasal sinuses. The secretion of saliva is essential for the normal health and function of the mouth. Disorders of salivary gland function, which affects the composition and secretion of saliva, predisposes to many oral diseases. Salivary gland diseases are broadly divided into two categories–non-neoplastic disease and neoplastic disease.

Non-neoplastic salivary gland diseases comprise of a heterogeneous group of entities of diverse etiopathogenic background. Most of the organic diseases of the salivary gland have a specific or nonspecific developmental, inflammatory, immunological or metabolic background. The diagnosis of salivary gland diseases is often difficult and although clinical findings are of major help in many cases, it may not be sufficient to define a firm diagnosis in every single case. Therefore, several special investigative procedure may be needed such as biopsy, sialometry, sialography, sialochemistry, CT scan, scintigraphy and ultrasonography, etc. for comprehensive diagnosis of many unusual diseases. Moreover, careful examination of salivary gland tissue may be helpful in establishing the diagnosis of many systemic conditions, e.g. amyloidosis, sarcoidosis and Sjogren's syndrome, etc.

CLASSIFICATION OF SALIVARY GLAND DISEASES

NON-NEOPLASTIC DISORDERS

DEVELOPMENTAL ANOMALIES

- Aplasia (agenesis) of the salivary gland
- Hypoplasia
- Aberrant salivary gland
- Atresia
- Accessory ducts
- Diverticuli
- Lingual mandibular salivary gland depression.

REACTIVE LESIONS

- Mucus retention cyst
- Mucus extravasation cyst
- Sialolithiasis
- Postradiation sialadenitis
- Chronic sclerosing sialometaplasia.

INFECTIVE LESIONS

Bacterial Sialadenitis

- Acute
- Chronic
- Recurrent.

Viral Sialadenitis

- Mumps
- Cytomegalic inclusion disease.

IMMUNE-MEDIATED DISEASES

- Mikulicz's disease
- Sjogren's syndrome

MISCELLANEOUS DISEASES

- Heerfordt's syndrome
- Sialosis

- Ptyalism and aptyalism
- HIV associated salivary gland disease.

NEOPLASTIC DISORDERS

Classification: Thackray and Sobin, 1972.

EPITHELIAL TISSUE NEOPLASMS

Adenomas

- Pleomorphic adenoma (mixed tumor)
- Monomorphic adenoma
- Adenolymphoma (Warthin's tumor)
- Oxyphil adenoma.

Other Types

- Mucoepidermoid tumor
- Acinic cell tumor
- Carcinomas
- Adenoid cystic carcinoma
- Adenocarcinoma
- Epidermoid carcinoma
- Undifferentiated carcinoma
- Carcinoma in pleomorphic adenoma (malignant mixed tumor).

CONNECTIVE TISSUE NEOPLASMS

- Fibroma
- Fibrosarcoma
- Lipoma
- Neurilemmoma
- Hemangioma
- Melanoma
- Lymphoma

DEVELOPMENTAL ANOMALIES OF THE SALIVARY GLAND

APLASIA OR AGENESIS OF THE SALIVARY GLAND

DEFINITION

Congenital absence of the salivary glands (both major and minor glands) due to complete failure of their development or genesis is called salivary gland aplasia.

CLINICAL FEATURES

- It is an exceptionally rare anomaly in which either a single gland or multiple glands can be involved either unilaterally or bilaterally.
- In some patients, salivary gland aplasia may occur alone, however, in other patients this condition is associated with some congenital facial malformations.
- The anomaly may affect several members of the same family.
- Aplasia of the major salivary gland commonly produces xerostomia (dryness of mouth), due to lack of production of saliva in the oral cavity.
- Patients with xerostomia often have difficulty in taking food and they also have increased incidence of caries, which often results in early tooth loss.
- Clinically, the oral mucosa appears dry, smooth or pebbly and it shows areas of food accumulation.
- Cracking of the lips and fissuring at the angle of the mouth are commonly seen.
- Congenital aplasia of the salivary glands may be associated with hereditary ectodermal dysplasia, mandibulofacial dysostosis, congenital aplasia of the lacrimal glands and hemifacial microstomia etc.

TREATMENT

Patients with congenital salivary gland aplasia will require continuous dental supervision and administration of systemic or topical fluorides to prevent dental caries.

HYPOPLASIA OF THE SALIVARY GLANDS

Relative underdevelopment of the salivary gland is known as salivary gland hypoplasia. Hypoplasia of the salivary glands may occur either due to their congenital absence or due to atrophy of the gland secondary to lack of neuromuscular stimulations.

Salivary gland hypoplasia is often associated with Melkersson-Rosenthal syndrome, which consists of cheilitis granulomatosa, facial paralysis and fissured tongue.

According to some investigators, salivary gland hypoplasia may occur secondary to hereditary ectodermal dysplasia.

The clinical features of salivary gland hypoplasia are the same as seen in salivary gland aplasia but the features are comparatively less

severe in nature. It is important to note that hypertrophy of the salivary glands may occur sometimes as congenital anomaly and it is often associated with a fibrocystic disease called mucoviscidosis.

ECTOPIC SALIVARY GLANDS (ABERRANT)

DEFINITION

The occurrence of normal salivary gland tissue in anatomically unusual locations is known as salivary gland **ectopia** and such glands are known as ectopic salivary glands.

- Besides the major salivary gland tissues, which are having their specific sites of occurrence, there are several other minor salivary glands located throughout the oral cavity including the palate, lips, cheek, floor of the mouth, retro molar area and tongue, etc.
- Therefore, it is important to know that **ectopic salivary glands are those** salivary gland tissues, which are **found beyond these normal anatomical locations.**
- Sometimes, the salivary gland tissue may be present within the body of the mandible and in such cases, the intraosseous gland maintains a communication with the extra osseous normal salivary gland with the help of a stalk, which has perforated through the lingual cortical plate of bone.
- Majority of the Stafne's bone cysts and the intraosseous salivary gland tissue within the body of the mandible may occur as part of the phenomenon called lingual mandibular salivary gland depressions.
- Ectopic salivary gland tissues may be found in the gingiva and where it produces a tumor-like mass, which is known as gingival salivary gland choristoma.
- Sometimes, the ectopic salivary gland tissue may occur within the masseter muscle. Moreover, ectopic salivary glands can also be found in the upper portion of the neck in the region of branchial cleft.
- The ectopic salivary glands despite having their various locations intraorally and extraorally, always exhibit histologically normal salivary gland lobules and ducts.
- Pathological conditions like sialolithiasis, neoplasms and cysts, etc. which commonly affects the normal salivary gland can also involve the ectopic salivary gland tissues.
- Intraosseous ectopic salivary glands may sometimes produce diagnostic confusion during radiographic examinations.
- These glands may sometimes occur in association with other facial anomalies.

Common locations of ectopic salivary glands

- Mandibular body
- Gingiva
- Masseter muscle
- Upper portion of neck near the branchial cleft.

ATRESIA

Atresia of the salivary gland excretory ducts refers to the **congenital absence** or narrowing of excretory duct system.

Atresia is an extremely rare condition, which may produce severe xerostomia. It can also results in the formation of retention cyst of the salivary gland. According to some investigators, there can be another developmental defect in the excretory salivary duct system, which is characterized by absence of the duct orifices. This also can produce salivary retention cyst and xerostomia.

ACCESSORY DUCTS

Accessory salivary ducts are relatively common developmental malformations, which can occur in relation to any gland, though it is seen more often in association with the parotids. The accessory parotid ducts are usually found either above or below the normal Stensen's duct. Accessory ducts of the salivary glands most often remain undetected since their presence does not produce any clinical effect in the mouth.

DIVERTICULI

Diverticuli refer to the small pouches or outpocketings of the ductal system of major salivary glands and is predominantly found in relation to parotids. Diverticuli may produce recurrent swellings and acute sialadenitis due

to retention of saliva in those areas where the pouches are present along the course of the duct. Diverticuli can be diagnosed by sialogram.

LINGUAL MANDIBULAR SALIVARY GLANDS DEPRESSION

It is **developmental concavity in the lingual cortex of mandible** usually in the third molar area, which forms around an accessory salivary gland. The condition is also referred by several other names such as Stafne's bone cyst, static bone cyst or latent bone cyst, etc.

CLINICAL FEATURES

- Clinically, lingual mandibular salivary gland depression is a completely asymptomatic condition.
- It is almost exclusively seen among males.
- Usually seen in the mandibular third molar areas. Occasionally, the condition can also involve the lingual aspect of anterior mandible.

RADIOGRAPHIC FEATURES

- Radiographically, this relatively uncommon entity presents a distinct, localized, deep concavity or depression located on the lingual aspect of mandible.
- In most cases, it is found in the mandibular third molar region in between the mandibular canal and the lower border of mandible.

DIFFERENTIAL DIAGNOSIS

Hemorrhagic bone cyst, lies above the mandibular canal while the lingual mandibular salivary gland depression lies below the canal.

SIALOGRAPHY

Sialography reveals that the concavities in the mandible are usually occupied by accessory lateral lobe of the submandibular salivary gland.

FURTHER INVESTIGATIONS

- Surgical exploration and subsequent biopsy of the contents of the lingual concavity generally reveals normal submandibular salivary gland tissue.
- Sometimes CT scan and MRI (Magnetic Resonance Imaging) techniques can be employed to confirm the nature of tissue present within the concavity.

TREATMENT

No treatment is required.

REACTIVE LESIONS OF THE SALIVARY GLAND

SALIVARY GLAND CYSTS

Mucous retention cyst and mucous extravasation cysts are discussed in the chapter of 'Cysts of the oral regions'.

SIALOLITHIASIS

DEFINITION

Sialolithiasis is a pathological condition, characterized by the presence of one or more calcified stones (sialoliths) (Fig. 4.1) within the salivary gland itself or within its duct.

PATHOGENESIS

- The exact mechanism of formation of sialolith is not known. It is generally believed that initially a small and soft nidus forms within the salivary glands or its ducts, due to some unknown reason.
- The nidus is made up of mucin, protein, bacteria and desquamated epithelial cells.
- Once a small nidus forms, it allows concentric lamellar crystallizations to occur due to the precipitation of calcium salts.
- The sialolith increases in size with time as layer after layer of salts become deposited, just like growth rings in a tree.
- Small sialoliths (microliths) can be expelled in the mouth along with the salivary secretions but those, which are not expelled usually, continue to enlarge until a duct or its branch is completely obstructed.
- It is important to note that the formation of sialolith is **more common in relation to the submandibular gland and its ducts**. (About 70 to 90 percent cases) and the reason for this could be the following:

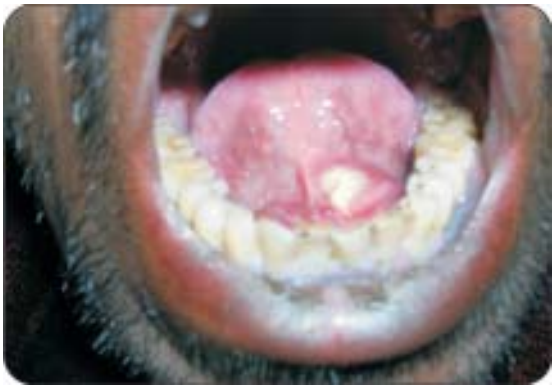

Fig. 4.1: Sialolith-I

- The submandibular gland ducts (Wharton's ducts) usually have **multiple sharp curvatures**, which often trap mucin plugs or cellular debris and eventually help in the formation of sialolith.
- Submandibular gland secretes **saliva, which is usually more viscous in nature** due to high mucin content as compared to the saliva secreted by other glands. The higher viscosity of the saliva helps in adhering more foreign particles and thereby easily forms a cellular nidus.
- The **calcium levels are also high** in submandibular saliva.
- The **dependent position** of the submandibular gland often **increases the chance of stasis** in the salivary flow.

Why sialoliths form more in relation to submandibular glands

- Multiple sharp bends or curvatures in the Wharton's duct
- More viscous nature of saliva of this gland
- Higher calcium levels in saliva of this gland
- Dependent position of the gland often increases the chance of stasis of saliva.

CLINICAL FEATURES

Age: Sialolithiasis usually occurs among the middle-aged adults, however some cases are reported in children.

Sex: There appears to be a slight predilection for males.

Sites: Majority (70 %) of the sialoliths form within the excretory ducts of the submandibular gland and sometimes they may occur within the substance of the submandibular gland itself.
The parotid gland is the next most commonly involved gland (about 23% cases), where as the sublingual and the minor salivary glands are affected in about 4% of cases.

CLINICAL PRESENTATION

- In many cases, sialoliths do not produce any symptoms and are detected only on routine radiographic examination.
- The chief complaints are intermittent pain, discomfort and recurrent submandibular swellings especially during meals (as the taste and smell of the food increase the salivary secretion).
- The pain occurs due to occlusion of the salivary gland duct by the sialolith, resulting in retention of saliva in the blocked portion of the duct.
- The pain can be felt like a pulling, drawing or a stinging sensation in mild cases due to partial obstruction of the duct by the sialolith.
- However, swelling increases and the pain can be very severe and stabbing type when there is complete obstruction of the duct.
- Clinically symptoms are more obviously felt when the patient takes any sour food or when direct stimulation of salivary secretion is done with a lemon drop candy.
- The affected glands become enlarged and firm but are still movable.
- The stone or the sialolith in the submandibular gland duct can often be palpated by bimanual palpation with finger of both hands.
- During examination, the flow and the clearness of the saliva at the duct orifice should also be checked. Small sialoliths may sometimes be seen at the duct orifices.
- A persistent swelling of the duct due to chronic obstruction by the sialolith eventually leads to chronic sclerosing sialadenitis.
- Sialoliths usually form unilaterally, however bilateral cases are sometimes reported.
- Multiple stones may develop within ductal branches throughout the gland and long standing lesions may result in complete calcification of the entire gland.

- Involvement of the submandibular gland often produces unilateral glandular enlargement medial to the inferior border of the mandible. The swelling is often firm and tender on palpation.
- Secondary infection cause pain, swelling and formation of sinus tracts or fistulas. Ulcerations in the area may also develop in chronic cases.
- In chronically obstructed glands, necrosis of the gland acini and lobular fibrosis may occur, which results in complete loss of secretion from the gland.
- When the secretory capacity is destroyed, pyogenic infections often develop in the gland, producing recurrent swelling, acute continuous pain, fever and malaise, etc.
- Parotid stone often causes firm swelling over the ramus of the mandible. The swelling also increases during meals.
- Minor salivary gland stone formation occurs commonly in the upper lip and buccal mucosa. Clinically, these lesions produce palpable, hard, movable nodule within the submucosa.
- Sialoliths do not cause xerostomia since, they involve only one or two glands.

DIAGNOSIS OF SIALOLITHIASIS

Radiography (Figs 4.2 and 4.3)

- Submandibular sialolithiasis are easily detected by mandibular standard occlusal radiographs (Fig. 4.2) which typically disclose the presence of calcification in the floor of the mouth.
- When a sialolith is located within the submandibular gland a lateral jaw film may be helpful in detecting its exact location.
- A panoramic radiograph usually detects parotid stones.
- If only branches of the submandibular gland duct are affected, a posterior occlusal film, submentovertex and sometimes a lateral jaw film may be required.
- Sometimes, radiographs fail to disclose the presence of the sialolith and it may be either due to superimposition of the stones with the mandibular bone during radiograph or it may occur if the sialolith is not fully calcified.

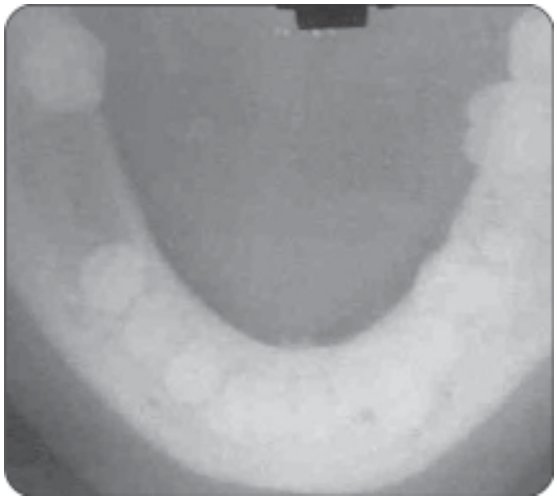

Fig. 4.2: Sialolith of the Rt. submandibular gland duct (occlusal view)

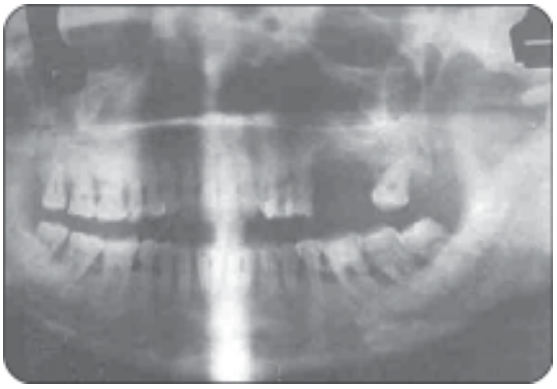

Fig. 4.3: Orthopantomogram showing sialolith in the Rt. submandibular gland duct

Sialography

Sialography, refers to the method by which detection of salivary stones within the gland or its duct is done by giving a retrograde injection of a radiopaque dye within the duct system and obtaining a radiograph thereafter in order to see the size and distribution of the sialolith.

Ultrasonography and CT scan

These can help in detecting accurate position and size of sialolith.

MACROSCOPIC APPEARANCE OF SIALOLITH

- On gross examination, sialoliths appear as round or oval, rough or smooth solid masses, which vary considerably in their size.

- These stones are heavily calcified and are often multinodular, although some stones are found in small aggregates.
- The color of the stone is usually yellowish or yellowish-white.

COMPOSITION OF SIALOLITH

Following are the general constituents of a sialolith:

Calcium phosphate	75%
Calcium carbonates	12%
Soluble salt	5%
Organic matter	5%
Water	3%

HISTOPATHOLOGY

- Microscopically, the salivary stone is acellular and amorphous and when decalcified, it presents concentric laminations of amorphous basophilic matrix.
- The outer margin may exhibit aggregates of microbial colonies.
- The ductal lining which surrounds the stone shows oncocytic, squamous and/or mucous metaplasia of varying degree.
- As a result of the metaplastic change, the ductal lining of the gland is often changed into a stratified squamous type of epithelium, which contains numerous mucous goblet cells.
- The rest of the gland tissue shows varying degrees of acinar degeneration and intense mononuclear cell infiltration.
- The gland acini are eventually replaced by fibrous connective tissue.
- In some lesions, secondary retrograde infiltrations may occur and such lesions exhibit infiltration by neutrophils and purulent material in the ductal lumens.

DIFFERENTIAL DIAGNOSIS

- Endemic parotitis
- Salivary gland neoplasm
- Mesenchymal neoplasm
- Hypervitaminosis-A
- Calcification of lymph node in chronic long-standing tuberculosis.

ULTRASTRUCTURAL FINDINGS

Ultrastructural studies reveal that the microcalculi (the structural units of salivary stones) are actually formed in the acinar cells of the gland. Normally, these microcalculi are eliminated through the orifice of the duct but whenever there is secretory inactivity or disturbance, the calculi accumulate and lead to the formation of large stones.

Key points of sialolithiasis

- Sialolithiasis is a pathological condition characterized by formation of calcified stones (sialoliths) within the salivary gland or within its duct.
- It occurs more commonly in relation to the submandibular gland and its ducts.
- The sialolith causes occlusion of the salivary gland duct resulting in retention of saliva which results in intermittent pain, discomfort and recurrent swelling of the affected gland.
- Pain and discomfort occurs especially during meals (as the taste and smell of the food increase the salivary secretion).
- Moreover, the symptoms become more severe when the patient takes any sour food or when direct stimulation of salivary secretion is done with a lemon drop candy.
- The sialolith can be palpated by bimanual palpation with finger of both hands.
- Untreated cases may cause secondary infections in the affected gland which produce pain, ulcerations, swelling and formation of sinus tracts or fistulas, etc.
- The sialolith can be easily detected by mandibular standard occlusal radiographs or by sialography.
- Structurally, the sialolith is acellular and amorphous and it contains about 75 percent calcium phosphate.
- Surgical removal of the stone is the treatment of choice.

Fig. 4.4: Sialolith-II

TREATMENT

- Small stones in the distal parts of the duct can be removed through the orifice by digital manipulation only.
- Whenever, digital maneuvers fail, surgical removal of the stone is indicated. However, during surgery care should be taken not to push the stones into the salivary gland tissue.
- Lithotripsy sometimes can be used as a non-invasive technique for disintegrating large sialoliths (Fig. 4.4).
- Whenever the conditions like intraglandular stones, multiple stones in a single gland or diffuse glandular calcification, etc. occur in association with pain, indurations and chronic lack of function, removal of the stone along with the gland (sialoadenectomy) should be recommended.
- Minor salivary gland stones are treated by simple surgical excision of the stone along with the surrounding minor salivary gland tissue.

POSTRADIATION SIALADENITIS

Radiation induced sialadenitis is a **common complication of radiotherapy** in the head and neck region.

- The severity of damage of the salivary gland tissue is usually directly proportional to the doses of radiation.
- When the dose of radiation is not very high, it may cause reversible damage to the salivary gland tissue and therefore some degree of salivary function may return after several months.

  However, in cases of very high dose of radiation, irreversible damage generally occurs in the salivary gland tissue and in such cases the gland acini are replaced by fibrous tissue with complete loss of function of the gland.
- Serous acini of the salivary gland are more susceptible to radiation damage than the mucus acini.
- Most of the salivary glands are affected which are coming within the field of radiation during radiotherapy.
- In the early phase of therapy, destruction of acinar cells begins and it is often accompanied by increase in the serum amylase.
- After full course of therapy, all exposed glands are damaged with subsequent fibrosis and this leads to xerostomia. The condition may result in cervical caries, oral mucositis and candidiasis, etc.
- Loss of secretory granules, cloudy swelling with edema and neutrophilic infiltration occur, which is followed by mononuclear cell infiltrations.

CHRONIC SCLEROSING SIALADENITIS

DEFINITION

Chronic sclerosing sialadenitis can be defined as chronic inflammation of the salivary gland tissue resulting in degeneration and subsequent replacement of acini by fibrous tissue.

ETIOLOGY

- Autoimmune disease
- Systemic and metabolic disorders
- Direct trauma
- Infection
- Occlusion of the duct by calculi
- Compression of the gland or duct by neoplasms
- Salivary glands cysts
- Radiation therapy
- Medication and drugs.

CLINICAL FEATURES

- The affected salivary gland may be either the major glands or the minor glands.
- There may be presence of sialolith in the gland or there can be mucous extravasations within the gland tissue.
- The affected gland is often enlarged either due to accumulation of saliva in the duct or due to inflammatory change.
- The enlarged gland is firm, but it is freely movable.
- The firmness increases with time due to more and more fibrosis.

HISTOPATHOLOGY

- There will be progressive destruction of the salivary gland acinar cells, as a result of both apoptosis and necrosis.
- There is chronic inflammatory cell infiltration in the gland comprising of lymphocytes and plasma cells.
- Once the acini are lost, the gland parenchyma undergoes progressive sclerosis or fibrosis.
- In chronic sclerosing sialadenitis, the ductal elements often remain unaffected while the acini are completely degenerated.
- Sometimes, there can be retrograde bacterial infection within the remaining duct tissue.

TREATMENT

- Etiologic factors should be removed.
- If the gland parenchyma is completely destroyed, sialoadenectomy should be done.
- Oral hygiene to be maintained.
- Artificial saliva should be prescribed to give some relief from the dryness of mouth.
- When there is partial destruction of the gland resulting in reduced salivary flow, pilocarpine should be used to stimulate salivary flow.
- Electrostimulatory devices can be effective in these cases, which can also stimulate the salivary flow.

NECROTIZING SIALOMETAPLASIA

DEFINITION

Necrotizing sialometaplasia is a spontaneous disease of unknown etiology, characterized by necrosis of minor salivary glands of the palate along with the surface epithelium and the underlying connective tissue.

PREDISPOSING FACTORS

- Odontogenic infections
- Traumatic injury
- Ill-fitting dentures
- Tumor in the adjacent areas
- Chronic throat infections.

PATHOGENESIS

Many investigators believe that necrotizing sialometaplasia occurs due to infarction of the tissue, although the underlying cause of the infarction is unknown. Moreover, it is not due to the systemic microvascular occlusion or any thromboembolic disease. Some people have reported about initiation of the disease following a local palatal anesthetic injection.

CLINICAL FEATURES

Age: The disease often occurs in adults and the mean age is about 47 years, although this disease affects women at a much younger age.

Sex: It occurs in males more often than the females.

Site: Mostly the palate is affected at the region of the junction between hard and soft palate.

In some rare cases, the disease can occur in other gland bearing oral mucosal sites. Parotid gland is occasionally affected.

CLINICAL PRESENTATION

- Necrotizing sialometaplasia initially presents one or two non ulcerated swellings on the palate with pain and paresthesia, etc
- Later on, one or two **deep-seated, punched-out ulcerations** characteristically develop over the hard or the soft palate.
- Majority of these lesions occur unilaterally, sometimes these are located bilaterally or even in other cases they may be seen at the midline also.
- The deeply excavating ulcers do not have any raised or rolled borders.
- The ulcer measures about 2 to 3 cm in diameter and at the base, there is presence of few grey,

granular lobules representing the necrosed minor salivary glands.
- Although, many patients are completely asymptomatic, some people complain of numbness or a burning type of pain in the area.
- Many lesions are clinically mistaken for malignant salivary gland neoplasms or epidermoid carcinomas.
- The lesions heal spontaneously usually within 1 to 3 months.

HISTOPATHOLOGY

The histologic features of necrotizing sialometaplasia are characteristic and highly specific:
- The base of the ulcer shows absence of epithelium, which is replaced by necrotic debris and eosinophilic fibrinous materials.
- The minor salivary gland tissues, which are present below the necrotic debris, exhibit features of **coagulation necrosis**.
- The salivary **acinar cells show absence of nuclei**, these cells are distended and often appear pale and basophilic.
- The cytoplasmic borders of the necrotic acinar cells remain intact and despite the cell damage, the lobular architecture of the salivary gland is often maintained.
- In the zone of necrosis, accumulated mucin is often seen and also there is presence of numerous scattered neutrophils and foamy histiocytes.
- The salivary epithelium adjacent to the necrotic zone shows **squamous metaplasia** with loss of normal acinar morphology.
- These metaplastic foci often appear as round or oval epithelial islands.
- The microscopic appearance of necrotizing sialometaplasia is to some extent similar to that of the mucoepidermoid carcinoma.

DIFFERENTIAL DIAGNOSIS

- Mucoepidermoid carcinoma
- Squamous cell carcinoma
- Adenocarcinoma
- Tuberculous ulcer
- Syphilitic ulcer
- Traumatic ulcer
- Chemical burns.

TREATMENT

Once the diagnosis is confirmed, no treatment is required and the lesion heals spontaneously in about 1 to 3 months time.

INFECTIVE LESIONS (SIALADENITIS)

BACTERIAL SIALADENITIS (FIG. 4.5)

ACUTE BACTERIAL SIALADENITIS

Acute bacterial sialadenitis is an uncommon disease, which frequently affects the parotid gland. Therefore, the disease can be synonymous to "acute parotitis or acute suppurative parotitis". In some cases, the condition can affect the submandibular salivary gland also.

CAUSATIVE ORGANISMS

- Acute parotitis is mostly caused by *Streptococcus pyogenes* and *Staphylococcus aureus*.
- Less commonly *Hemophilus* and *Bacterioid* groups may be involved.

ROUTE OF SPREAD OF INFECTION

In case of acute parotitis, the infection is usually of ascending type and the bacteria reach the gland via the Stensen's duct.

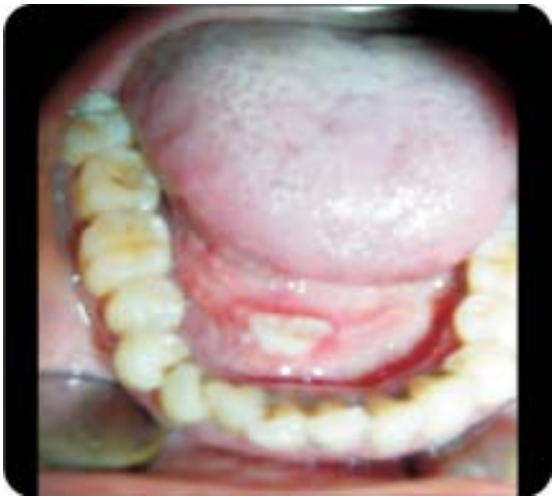

Fig. 4.5: Sialadenitis

PREDISPOSING FACTORS

- Previous major surgery (especially abdominal surgery)
- Debilitated and dehydrated patients
- Diabetes
- Malignancy
- Prematurely born infants
- Sjogren's syndrome
- Sialolithiasis
- Immunocompromised patients
- Use of drugs having xerostomic effects.

CLINICAL FEATURES

- Sudden onset of painful swelling in the pre-auricular region.
- The parotid gland may be involved either unilaterally or bilaterally.
- The constitutional symptoms like fever, malaise and redness of the skin overlying the parotid are often present.
- Many patients complain of trismus and difficulty in swallowing.
- Intraorally, the parotid papilla may be inflammed and often pus or exudates may be expressed from the duct opening.
- In some cases, acute parotitis may occur as a result of acute exacerbation of the pre-existing chronic sialadenitis.

INVESTIGATION

Bacterial culture from saliva or from parotid secretions.

TREATMENT

Drainage and antibiotic therapy, management of pre-existing systemic diseases is essential.

CHRONIC BACTERIAL SIALADENITIS

DEFINITION

Chronic bacterial sialadenitis is a nonspecific inflammatory disease of the salivary gland secondary to duct obstruction or low grade sustained ascending infection.

CLINICAL FEATURES

- The condition occurs in adults as well as in children and it more frequently affects the parotid gland, usually unilaterally.
- Recurrent tendered swelling of the affected gland is a common feature.
- The duct orifice may be inflammed and in case of acute exacerbation, there can be purulent discharge from it.
- The condition is often associated with decreased salivary flow.

INVESTIGATION

- Sialography
- Radiography
- Bacterial culture from saliva or secretion of the gland
- Biopsy.

HISTOPATHOLOGY (FIGS 4.6 AND 4.7)

- Acinar atrophy of the salivary gland with subsequent fibrosis

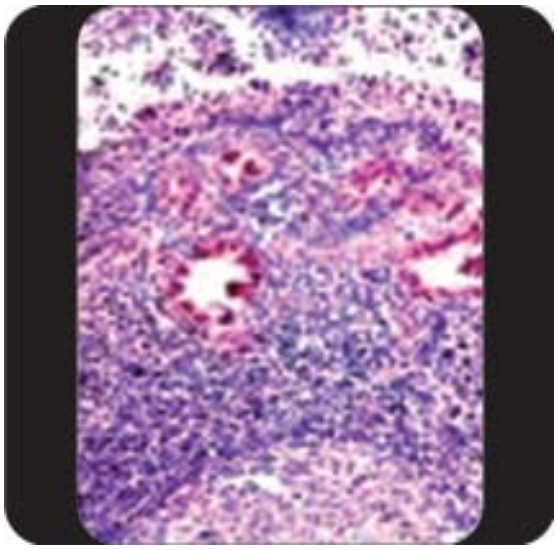

Fig. 4.6: Photomicrograph of acute bacterial sialadenitis

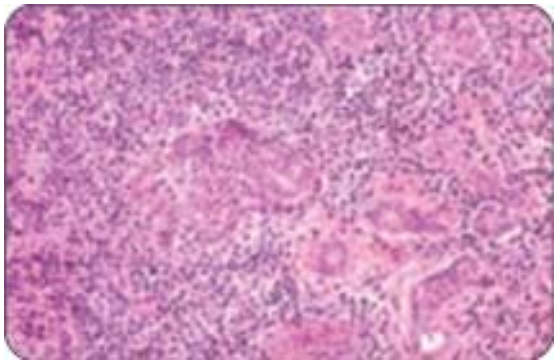

Fig. 4.7: Photomicrograph of chronic sialadenitis

- Dilatations of the ductal system
- Hyperplasia of the ductal epithelium
- Periductal fibrosis
- Chronic inflammatory cell infiltration.

RECURRENT PAROTITIS

Recurrent parotitis is a rare condition, which affects both children and adults.

PREDISPOSING FACTORS

- Salivary gland calculi.
- Stricture of the ducts.
- Abnormally low secretion of saliva due to any cause.
- Congenital absence of the duct system.
- Immunosuppression

CLINICAL FEATURES

- The condition may occur either unilaterally or bilaterally
- Recurrent painful swelling of the affected gland.
- Discharge of pus from the duct orifice.
- Several conditions may resolve spontaneously.

VIRAL SIALADENITIS

MUMPS (ENDEMIC PAROTITIS)

DEFINITION

Mumps is an acute contagious infection of the salivary gland caused by the paramyxovirus.

- It mostly occurs in children between the age of 5 to 18 years and it often spreads in the form of minor epidemic.
- Parotid gland is mostly affected. However, the disease can also involve the submandibular gland on few occasions.
- The virus is transmitted by direct contact with the infected saliva or by airborne droplets. The incubation period is about 2 to 3 weeks.
- Parotid is affected often bilaterally and there is rapid swelling of the gland with acute pain during salivation.
- Recurrent exudation from the duct orifice is often seen.
- Sometimes, other internal organs may also be affected by this virus, which include, testes, central nervous system (CNS), ovaries and pancreas, etc.

Details of the disease is discussed in the chapter "Bacterial, Viral and Fungal Diseases".

CYTOMEGALIC INCLUSION DISEASE

Cytomegalic inclusion disease of salivary gland is a common infective disease caused by cytomegalovirus.

Most of these infectious diseases are asymptomatic and histologically the affected salivary gland tissue exhibits the presence of large, doubly contoured, **"owl-eye"** shaped inclusion bodies within the nucleus or cytoplasm of the ductal epithelial cells of the parotid gland.

- Disseminated form of the infection may also affect other vital organs, e.g. kidney, liver, spleen, lungs and brain, etc.

(For detailed description of the disease kindly see the chapter Bacterial, Viral and Fungal Diseases).

IMMUNE-MEDIATED DISEASE

MIKULICZ'S DISEASE

DEFINITION

Mikulicz's disease is a **progressive autoimmune disease of the salivary gland** characterized by replacement of gland acini by dense infiltrates of T lymphocytes along with squamous metaplasia of the ductal epithelium.

It is a localized benign lymphoepithelial lesion, which frequently involves the parotid and lacrimal glands. According to many investigators, the disease is closely related to Sjogren's syndrome.

ETIOLOGY

The exact etiology of the disease is not known, some people believe that genetic abnormality or defective cell-mediated immunity probably causes the disease.

CLINICAL FEATURES

Age: Middle aged or elderly adults.

Sex: Male predilection.

Site: Parotid, submandibular and lacrimal glands.

PRESENTATION

- There is often **unilateral or bilateral diffuse swelling** of the involved glands.
- The swelling is soft, movable and painless. It frequently measures about few centimeters in diameter.
- The disease can be associated with **xerostomia**, which is sometimes very severe.
- The onset of the disease is often marked with fever, upper respiratory tract infection and any other oral or orofacial infections, etc.
- Sometimes, mikulicz's disease can be a manifestation of Sjogren's syndrome or AIDS.
- However, mikulicz's disease should not be confused with mikulicz's syndrome, which refers to parotid and lacrimal gland enlargements accompanied by the enlargement of lymph nodes. The mikulicz's syndrome may represent some generalized specific diseases, e.g. lymphomas or tuberculosis, etc.

HISTOPATHOLOGY

- Histologically, mikulicz's disease is characterized by **replacement of the salivary gland acini by benign infiltration of lymphocytes and squamous metaplasia** of the ductal epithelium.
- There is presence of several myoepithelial islands or epimyoepithelial islands that represent persisting salivary gland ducts in which the epithelial lining has undergone extensive proliferation.
- The proliferating epithelial cells may obliterate the lumen of these ducts.
- There may be presence of some eosinophilic hyaline material in the epithelial islands especially in advanced lesions.

DIFFERENTIAL DIAGNOSIS

- Sjogren's syndrome
- Chronic sialadenitis
- Adenolymphoma
- Uveoparotitis.
- Malignant lymphoma
- Disseminated tuberculosis.
- Metastatic carcinoma of the salivary gland.

Key points of Mikulicz's disease

- Mikulicz's disease or localized benign lympho-epithelial lesion is a progressive autoimmune disease of the salivary gland.
- The disease starts with fever, upper respiratory tract infection and any other oral or orofacial infections, etc.
- Clinically, the disease presents unilateral or bilateral, diffuse, soft, painless swelling of the involved glands with xerostomia.
- It is histologically characterized by replacement of gland acini by dense infiltrates of T lymphocytes along with squamous metaplasia of the ductal epithelium.
- Treatment is done by steroids.

TREATMENT

Moderate doses of steroid (20 to 30 mg prednisolone daily) may help to control the disease.

SJOGREN'S SYNDROME

DEFINITION

Sjogren's syndrome is a multi-system immune-mediated chronic inflammatory disease, characterized by lymphocytic infiltration and acinar destruction of salivary and lacrimal glands, with a marked predilection for women.

PATHOGENESIS

Although, exact etiopathogenesis of Sjogren's syndrome is not known, it is strongly believed that the disease is an **autoimmune disorder**. Rheumatoid factors, which are associated with many autoimmune disorders, are frequently present in Sjogren's syndrome. Presence of serum antinuclear antibodies (ANA), e.g. anti-Sjogren's syndrome-A (anti-SS-A) and anti-Sjogren's syndrome-B (anti-SS-B) also further increase the probability of this disease.

CLINICAL FEATURES

Incidence rate: Sjogren's syndrome occurs in 0.5 to 1% of the population.

Age: Middle aged adults.

Sex: Strong predilection for females (M:F ratio is about 20:80)

Sjogren's syndrome is generally classified into two groups:

PRIMARY SJOGREN'S SYNDROME

- When the disease affects only salivary and lacrimal glands without other co-existing systemic autoimmune diseases, it is called primary Sjogren's syndrome.
- Primary Sjogren's syndrome is also referred to as "**sicca syndrome**" in which dry mouth (xerostomia) and dry eyes (xerophthalmia or keratoconjunctivits sicca) are the principal features.

SECONDARY SJOGREN'S SYNDROME

- Secondary Sjogren's syndrome characteristically have xerostomia, xerophthalmia and an associated autoimmune connective tissue disease, usually the rheumatoid arthritis. The associated disease could also be any of the following:
  - Lupus erythematosus,
  - Systemic sclerosis,
  - Primary biliary cirrhosis,
  - Periarteritis nodosa,
  - Polymyositis,
  - Dermatomyositis or macroglobulinemia, etc.

CLINICAL PRESENTATION

- The most common symptoms of Sjogren's syndrome are xerostomia, xerophthalmia and arthralgia (pain in the joints).
- The primary Sjogren's syndromes produce more severe oral and ocular changes than the secondary Sjogren's syndromes.
- Severe tiredness and fatigue are the important features of the disease with depression in few cases and most of the patients may sleep for about 10 to15 hrs in a day.
- Xerostomia or dryness of mouth often causes soreness of mouth with difficulty in eating, swallowing and talking, etc
- About 88 percent cases exhibit decreased salivary flow of the submandibular and sublingual glands and parotid salivary flow decreases in about 55 percent cases.
- The saliva appears frothy and there can be disturbance of taste sensation and associated oral candidiasis. Some patients develop angular cheilitis as well.
- Oral mucosa appears red, dry, tendered, smooth and glazed. This is often called a "**parchment-like appearance**" of the mucosa.
- Patients often feel difficulty in wearing dentures. Persistent dryness also causes change in the oral flora with increased susceptibility to secondary infections in the oral mucosa.
- Xerostomia and recurrent candidiasis affects the tongue and the dorsum of the tongue reveals red and atrophic mucosa with varying degrees of fissuring and labulations on the surface ("**cobble-stone**" appearance).
- There is often secondary acute bacterial sialadenitis characterized by fever and purulent discharge from the duct orifeces. Moreover, development of rapidly progressive dental caries (typically in the cervical areas of teeth) is also common.
- Keratoconjunctivitis sicca is an extremely important manifestation of Sjogren's syndrome which often manifests as dryness of the eyes with conjunctivitis (occurs due to decreased secretion from the lacrimal glands).
- The 'sicca syndrome' produces a gritty, burning sensation in the eye. Patients may feel like there is a foreign body inside the eye, which is causing blurred vision and itching pain in the eye.
- In case of Sjogren's syndrome, parotid glands are persistently enlarged, often bilaterally and the swelling is usually painless.
- However, in case the parotid swelling is due to suppurative parotitis and not Sjogren's syndrome, then the affected gland will be hot on palpation, tendered and the overlying skin will be red and inflammed.
- Although parotid gland is predominantly affected, sometimes submandibular or minor glands can also be affected.
- Enlargement of lacrimal glands is rare.
- Sjogren's syndrome, is associated with an increased risk of development of extra-salivary malignant lymphoma.
- Patients may have dryness of the nasal, pharyngeal and laryngeal mucosa.

HISTOPATHOLOGY

Histologically, Sjogren's syndrome reveals the following features (Fig. 4.8):

- Initially, there is infiltration of lymphocytes in the intralobular ducts of the involved salivary gland, which gradually replaces the entire lobule.
- The infiltration is accompanied by atrophy of the salivary gland acini and proliferation of the ductal epithelial cells.
- There is an increased risk for the development
- The hyperplasia of the ductal epithelium eventually obliterates the ductal lumen and this leads to the formation of discrete islands of epithelial tissue, which are known as the myoepithelial islands.

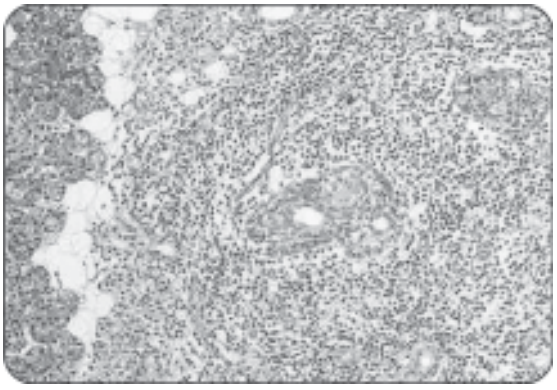

Fig. 4.8: Photomicrograph of sjogren's syndrome

- In the fully developed lesions, the entire glandular tissue is replaced by multiple myoepithelial islands, which are surrounded by proliferating lymphoid tissue.

INVESTIGATIONS IN SJOGREN'S SYNDROME

- ***Biopsy:*** Labial salivary gland biopsy is a helpful investigative method in establishing the diagnosis of Sjogren's syndrome.
- ***Sialography:*** In Sjogren's syndrome, sialography often produces a "snow-storm" or "cherry tree in blossom" like appearance.
- ***Scintigraphy:*** Salivary scintiscanning using [Tc-Pertechnetate] reveals reduced uptake of the isotope in Sjogren's syndrome.Although, the normal salivary gland tissue usually shows an increased uptake of the said isotope.
- ***Staining:*** The keratoconjunctivitis sicca is characterized by corneal keratotic lesions, which stain pink when "rose bengal" dye is used.
- ***Schirmer test:*** The reduced lacrimal flow rate in Sjogren's syndrome is measured by this test. A strip of filter paper is placed in between the eye and the eyelid to determine the degree of tearing, which should be measured in millimeter. When the flow is reduced to less than 5 mm in a 5 minutes sample period, the patient should be considered positive for Sjogren's syndrome.

Key points of Sjogren's syndrome

- Sjogren's syndrome is a multi-system immune-mediated chronic inflammatory disease of the salivary and lacrimal glands which predominantly affects women.
- The disease occurs in two forms- primary and secondary:
  - When the disease affects only salivary and lacrimal glands without other coexisting systemic autoimmune diseases, it is called primary Sjogren's syndrome.
  - Secondary Sjogren's syndrome affects salivary and lacrimal glands and it is also characteristically associated with autoimmune connective tissue disease, usually the rheumatoid arthritis.
- Although, exact etiopathogenesis of Sjogren's syndrome is not known, it is strongly believed that the disease is an **autoimmune** disorder.
- Primary Sjogren's syndrome is also referred to as "**sicca syndrome**" in which dry mouth (xerostomia) and dry eyes (xerophthalmia or keratoconjunctivitis sicca) are the principal features.
- Severe tiredness and fatigue are the important features of the disease with depression.
- Secondary Sjogren's syndrome has all the above features and in addition has Rheumatic arthritis and SLE, etc. the former disease causes severe joint pain.
- Histologically the disease is characterized by lymphocytic infiltration and acinar destruction of salivary and lacrimal glands

Specific Laboratory Tests

- Raised ESR
- Diminished total salivary flow rate
- Hypergamaglobulinemia-elevated β2 microglobulin
- Positive serologic test for rheumatoid factors.
- *Immunohistochemistry* detects the presence of antinuclear antibodies ANA (anti -SS-A and anti-SS-B) in the serum of large number of patients.

TREATMENT

- Use of artificial saliva
- Use of systemic steroids
- Antibiotic eye drops
- Anti fungal drugs
- Maintenance of oral hygiene, avoidance of sweets and fluoride applications to control caries.

MISCELLANEOUS DISORDERS OF SALIVARY GLAND

HEERFORDT'S SYNDROME

The Heerfordt's syndrome or uveoparotitis is a rare syndrome and is characterized by the following features:

- Swelling of the parotid gland
- Fever
- Paralysis of the facial nerve.

SIALOSIS

DEFINITION

Sialosis or sialadenosis is a condition characterized by **bilateral, recurrent, non-inflammatory, non-neoplastic swelling** of the salivary glands.

ETIOLOGY

Sialosis occurs probably due to the following reasons:

- Disturbance in the neurosecretory control
- Hormonal disturbance such as thyroid insufficiency
- Administration of certain sympathomimetic drugs
- Malnutrition
- Liver cirrhosis/chronic alcoholism
- Mucovicidosis
- Diabetes mellitus
- Bulimia
- Pregnancy
- Idiopathic.

CLINICAL FEATURES

- It frequently affects the parotid and occasionally the submandibular salivary gland.
- The swelling may cause little pain and discomfort. However, in some cases the condition may produce severe pain.

HISTOPATHOLOGY

- Hypertrophy of the serous acinar cells, which may be up to twice the normal size.
- The cytoplasm may be packed with secretory granules.
- Edema of the interstitial connective tissue.
- Lipomatosis may occur in the gland.

TREATMENT

No treatment is generally required. Elimination of the causative systematic factors is usually enough.

However, in case of severe pain in the affected gland, surgical excision of the gland may be necessary.

PTYALISM

DEFINITION

Ptyalism is an abnormal condition characterized by **increased secretion of saliva** in the mouth.

Etiology of ptyalism (hypersecretion of saliva)

- Metal poisoning
- Abnormal neurosecretory stimulation.
- ANUG
- General stomatitis
- Aphthous ulcer
- Psychological factor
- Following oral examination procedure
- Major surgery in the oral cavity
- Improper swallowing due to any cause
- Insertion of new prosthesis in the mouth
- Idiopathic

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APTYALISM (XEROSTOMIA)

Aptyalism is the pathological condition characterized by a decrease or complete cessation of secretion of saliva, causing dryness of mouth.

Lack of salivary secretion often leads to clinical phenomenon known as xerostomia.

In xerostomia, several oral diseases develop due to the following reasons:

- Decreased oral pH with increased accumulation of plaque.
- Increased trauma and irritation due to dryness of mucosa.
- Decreased remineralization of tooth enamel by saliva.
- Increased periodontal diseases.
- Increased susceptibility to opportunistic infections.

CLINICAL FEATURES

- Soreness, burning or pain sensations in the mouth.
- Due to dry, sticky oral mucosa, **tongue always sticks to the palate** and there is **difficulty in swallowing.**
- Constant sore throat, hoarseness of voice and speech difficulty.
- Erythematous changes in the oral mucosa with cracking, fissuring and occasional ulceration.
- **Difficulty in taking foods** (especially dry and crispy foods, e.g. cereals and crackers) as it causes irritation and burning sensation.
- Red spots over the mucosal surfaces of tongue, hard and soft palate.
- Taste disorder (**dysgeusia**) and burning tongue (**glossodynia**).
- Increased need to drink water especially at night.

Causes of xerostomia

Temporary causes:	• Playing or outdoor activity for long time on a hot day • Psychological disorders, e.g. anxiety and depression • Consumption of alcohol • Sialadenitis • Use of drugs, e.g. atropine, antihistaminics,bronchodialators, diuretics and antidepressants • Dehydration due to diarrhea, vomiting and hemorrhage • Lack of mastication • Mouth breathing
Permanent causes:	• Aplasia of salivary glands (hereditary ectodermal dysplasia) • Atresia of salivary glands . • Radiotherapy in the Head / Neck region (destruction of gland acini and reduced vascularity) • Sjogren's syndrome • Diabetes mellitus and diabetes insipidus • Vitamin deficiency (A and B complex) • Sarcoidosis, HIV-associated salivary gland disease, amyloidosis • Pernicious and iron deficiency anemia • Graft versus host reaction • Parkinson's disease • Defective secretomotor stimulations and ageing.

- Parotid swelling with sialadenitis.
- Little or no pool of saliva in the floor of the mouth.
- Whatever saliva is present, it looks **stringy, ropy or foamy.**
- **'Lipstick sign'** is positive for women (lipstick always sticks to the upper front teeth).
- Inflammation and fissuring of the lips (**cheilitis**).
- Atrophy of the tongue papilla with cracking, fissuring and occasional ulceration of the surface.
- **Increase** in the incidence of **dental caries** due to lack of protective action of saliva.
- Increased incidences of periodontal disease with gum bleeding.
- Difficulty in maintaining proper oral hygiene and persistent halitosis.
- **Early tooth loss** in adults.
- **Difficulty in wearing artificial prosthesis.**
- **Candidiasis** is the most common oral infection, which is persistently present.
- Dry nasal passage.

DIAGNOSIS OF XEROSTOMIA

- Patients history.
- Clinical features in the mouth.
- Sialometry-detects the salivary flow rate; salivary flow rate can be increased by giving the patient some citrus materials to chew. Generally the resting or unstimulated salivary flow rate is about—0.3 to 0.5 ml/minute, while the stimulated salivary flow rate is about 1 to 2 ml/minute, values below 0.1 ml/minute are considered xerostomia.
- Sialography—Imaging techniques to detect stones or other mass inside the gland.
- Salivary scintigraphy—Helps in assessing salivary gland function.
- Biopsy—Helps to detect cellular changes in the gland.

TREATMENT

- Removal of local or systemic causes
- Frequent sipping of sugarless fluids
- Chewing xylitol containing gums
- Regular use of artificial saliva (carboxymethyl cellulose containing saliva)
- Antifungal drugs
- Administration of pilocarpine and use of transmucosal neurostimulatory devices to stimulate the salivary secretion in patients, who still retain some degree of salivary function.
- Avoidance of antihistaminic and decongestant drugs.

NEOPLASM OF THE SALIVARY GLANDS

The salivary gland neoplasms are relatively uncommon entities and they comprise about 3% of all neoplastic disorders of the human body. These neoplasms may be derived from salivary epithelium (parenchymal) or the supportive connective tissues stroma (mesenchymal).

The epithelial tissue neoplasms are more prevalent among adults whereas the mesenchymal tissue neoplasms are more often encountered among children.

The overall incidence rate of salivary gland neoplasms among general population is about 1 to 3 percent per 100,000 people. However, the people of Inuit and parts of Scotland exhibit a slight to tenfold increase in the prevalence rate of these lesions.

About 70% of the neoplasms are derived from the major glands and the rests are developing from the minor glands. Among the major gland neoplasms 90% occur in the parotid gland and about 10% occur in the submandibular gland, however the sublingual gland lesions are exceptionally rare.

More than 50% of minor salivary gland neoplasms occur in the palate, about 20% lesions develop in the upper lip, lower lip lesions are rare. Malignant variety of salivary gland neoplasms occur far more frequently in relation to the minor glands.

On rare occasion, salivary gland neoplasms may occur as central jaw lesions (mainly in relation to mandible) and in such cases, the neoplasms can be derived from either the ectopic entrapped salivary glands or from mucous metaplasia in the lining of the odontogenic jaw cyst.

PLEOMORPHIC ADENOMA

DEFINITION

Pleomorphic adenoma or **benign mixed tumor** is the most common neoplasm of the salivary glands, which is histologically characterized by complex intermingling of epithelial components and the mesenchymal areas. The neoplastic cells exhibit differentiation of epithelial cells (luminal), myoepithelial cells (albuminal) as well as a very characteristic stromal tissue comprising of chondroid, myxoid, osseous and myxochondroid elements.

The complexity and diversity of appearance of this neoplasm account for the term "Pleomorphic", however the term does not imply cellular pleomorphism.

ORIGIN

According to the multicellular theory, these tumors originate from intercalated duct cells and myoepithelial cells of the salivary glands.

CLINICAL FEATURES

Age: Pleomorphic adenomas can occur at any age but they develop more frequently in the 5th and 6th decade of life (mean age is 40 years), 10% cases occur in children.

Sex: More common among females than males (60:40).

Site: It accounts for 60 to 65% of all neoplasms of the parotid, 50% of submandibular and 25% of sublingual gland. Approximately 45% of minor gland lesions are pleomorphic adenomas and intraorally palate (posterolateral aspect) is the most frequent site for their development (55% intraseally). Minor gland neoplasms may also occur in upper lip (25%) and cheek (10%), 10% lesions occur in other oropharyngeal sites.

CLINICAL PRESENTATION (FIGS 4.9 TO 4.14)

- Pleomorphic adenoma usually produces a **slow growing, painless, well-delineated, nodular exophytic growth** of the affected salivary gland.

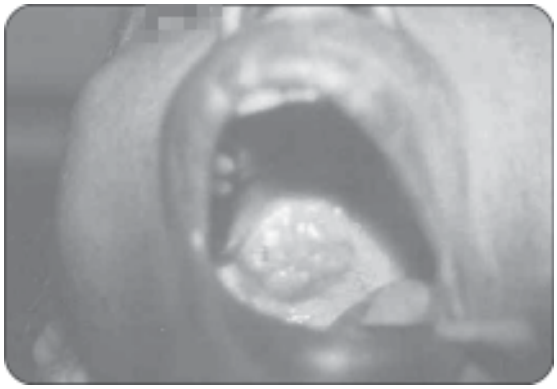

Fig. 4.9: Pleomorphic adenoma of the soft palate

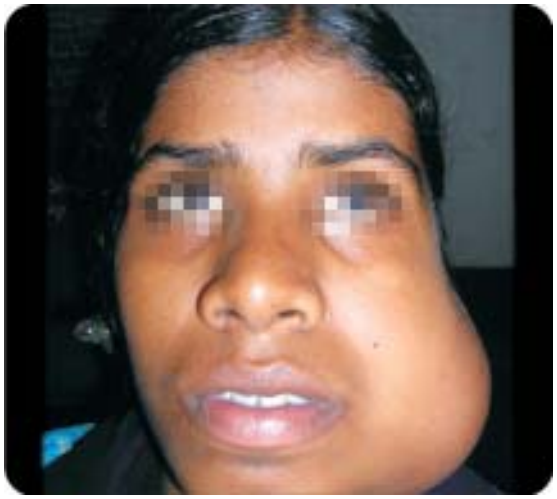

Fig. 4.10: Pleomorphic adenoma-I

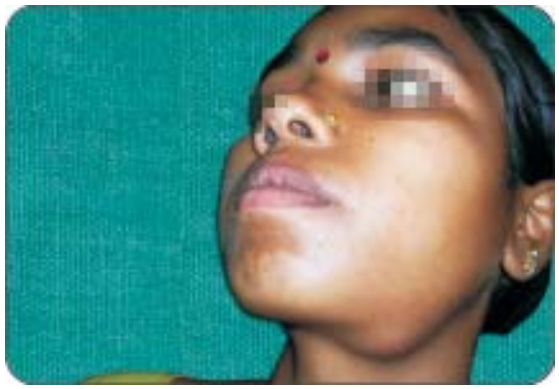

Fig. 4.11: Pleomorphic adenoma-II

- These lesions take several years to grow to a size of 1 inch in diameter.
- The neoplasm is usually **solitary** but sometimes there can be multiple lesions (multinodular) especially in case of recurrent lesions.

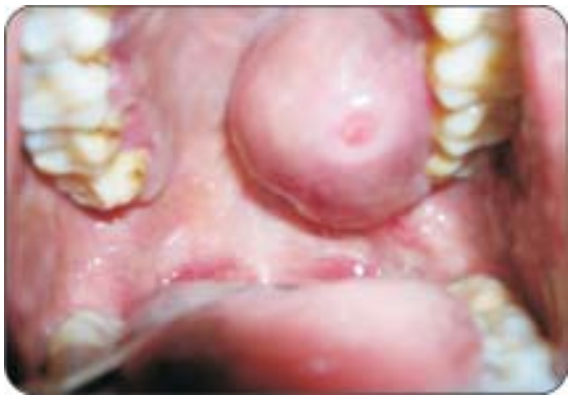

Fig. 4.12: Pleomorphic adenoma-III

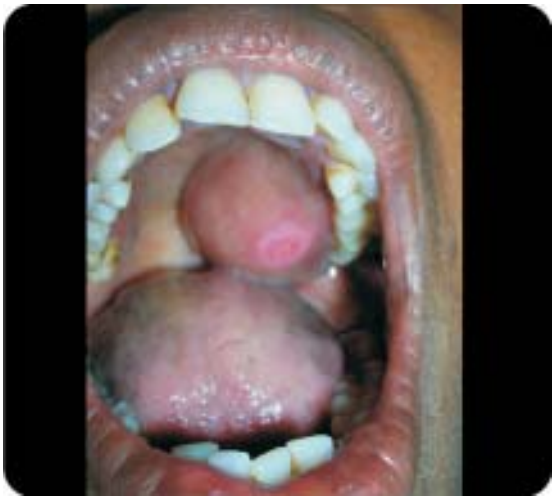

Fig. 4.13: Pleomorphic adenoma of palate

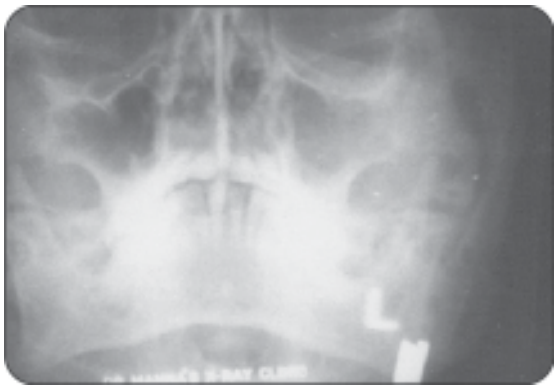

Fig. 4.14: Pleomorphic adenoma of the palate extending into the maxillary antrum

- The surface of the lesion is mostly non-ulcerated, smooth and lobulated, and generally there is no pain.
- Anesthesia or paresthesia of the facial nerve in benign pleomorphic adenomas is rare.
- The neoplasm is usually **soft or rubbery** in consistency and since it is **not fixed** to the overlying or the underlying tissues the tumor is always freely movable. However, the larger tumors are relatively less movable as compared to the smaller lesions.
- Some lesions can be present for many years and **assume massive size** and the overlying skin or mucosa is generally intact.
- The parotid gland lesions are usually superficial and often arise in the superficial lobe as a small mass overlying the angle of mandible or anterior to the external ear.
- Neoplasms arising from the deep lobe of parotid may not always be detected as a facial mass, since these may protrude in to the lateral wall of the oropharynx.
- Sometimes the lesion can be multinodular and they can assume an enormous size, especially the longstanding lesions.
- The minor gland neoplasms in the oral cavity frequently exhibit **smooth surfaced**, soft or slightly firm, **dome-shaped nodular swellings** on the hard or soft palate without any ulceration on the surface.
- The palatal neoplasms are usually firm in consistency and are less movable due to the tough nature of the palatal mucosa, these lesions sometimes exhibits surface ulceration especially when traumatized.
- Large intraoral lesions are often associated with disturbance in speech and mastication, etc
- In the buccal mucosa or the lip pleomorphic adenoma presents small, painless, well-defined, movable nodular lesion with intact overlying mucosa.
- Malignant transformation is uncommon in pleomorphic adenomas but may occur on rare occasions.

MACROSCOPIC FINDINGS

- Macroscopically, pleomorphic adenoma appears as a **well-circumscribed, lobulated, globular mass**, which is surrounded by a **capsule** of variable thickness or completeness.
- On palpation, these lesions feel like rubbery, resilient masses with bosselated surface.

- The cut surface shows a **variegated appearance** with presence of few hemorrhagic or **cystic areas**. The tumor sometimes causes compression of the surrounding capsule.
- Isolated nodules of the neoplasm may sometimes be seen within or even outside the capsule.

HISTOPATHOLOGY (FIGS 4.15 AND 4.16)

- The microscopic appearance of pleomorphic adenoma is highly variable because of the diverse (**pleomorphic**) nature of the epithelial and the mesenchymal tissue components of the neoplasm.
- The neoplasm often exhibits proliferation of glandular, basophilic epithelial cells in the form of diffuse **sheets or clusters**.

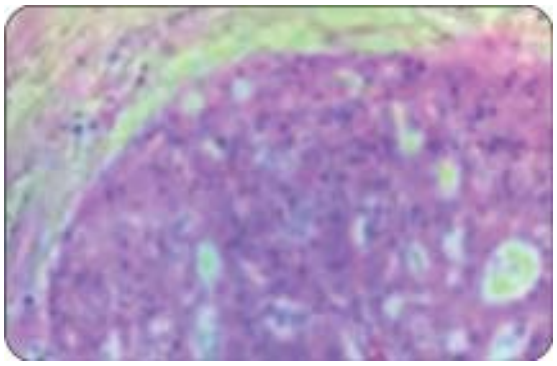

Fig. 4.15: Photomicrograph of pleomorphic adenoma-I

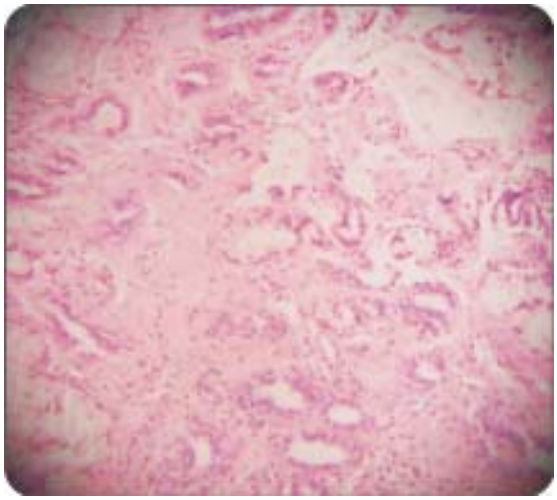

Fig. 4.16: Photomicrograph of pleomorphic adenoma-II

Key points of pleomorphic adenoma

- Pleomorphic adenoma or **benign mixed tumor** is the most common neoplasm of the salivary glands.
- It predominantly affects the parotid glands, however submandibular, sublingual and minor salivary glands are also frequently affected.
- Clinically, pleomorphic adenoma usually produces slow growing, painless, well-delineated, nodular exophytic growths.
- Lesions are mostly solitary and may be present in the mouth for years together without giving any symptoms.
- The surface of the lesion is generally nonulcerated, smooth and lobulated, moreover most of the lesions have a soft, rubbery consistency.
- The cut surface of the lesion exhibits a well-circumscribed, lobulated, globular mass, which has a variegated surface and is surrounded by a capsule.
- Microscopically the neoplasm exhibits proliferation of glandular, basophilic epithelial cells in the form of diffuse sheets or clusters.
- These neoplastic have a tendency to form duct-like structures, which are often filled with eosinophilic mucins.
- The connective tissue stroma of pleomorphic adenoma often characteristically exhibits metaplastic changes, which results in the formation of mucoid, myxoid, chondroid and osseous tissues within the tumor.
- Treatment is done by surgical excision, for parotid lesions care must be taken during surgery not to damage the facial nerve.

- The neoplastic epithelial cells are polygonal, spindle or stellate shaped and they have a tendency to form **duct-like** structures.
- These neoplastic cells of the glandular epithelium can also be arranged in clumps or interlacing strands.
- The duct-like structures are of varying size, shape, number and are widely distributed within the lesions.
- Histologically, each duct-like structure exhibits an **inner row of cuboidal or columnar cells** and an **outer row of spindle-shaped** myoepithelial cells.

- In the center of each duct-like structure, there is often presence of either clear or brightly eosinophilic, PAS-positive material (**epithelial mucin**).
- The myoepithelial cells of the tumor often appear cuboidal, flattened or spindle shaped, they gradually merge into the surrounding connective tissue stroma. Moreover, these cells sometimes constitute the bulk of the neoplastic tissues and in such cases the neoplasm may have a 'fibroma-like' appearance.
- Neoplastic myoepithelial cells sometimes proliferate to form a thick, ill-defined sheath around the salivary gland ducts or in other cases these cells become swollen or hydropic to, appear cartilage-like cells (chondroid change).
- In some lesions of pleomorphic adenoma the epithelial cells may be ovoid shaped, having concentric nuclei and abundant hyaline cytoplasm, these cells often produce a **plasmacytoid** appearance in the neoplasm.
- The ductal epithelial cells in pleomorphic adenoma often show **"squamous metaplasia"** and sometimes there may be even formation of keratin pearls by these metaplastic epithelial cells.
- The connective tissue stroma often characteristically exhibits metaplastic changes, which results in the formation of **mucoid, myxoid, chondroid and osseous tissues**. Such diverse variety of mesenchymal tissues is formed within the tumor due to the pluripotential nature of the myoepithelial cells.
- In some lesions, there may be presence of hyaline, elastic or myxochondroid elements in the stromal tissue.
- The connective tissue may be fibrous in nature and is consisting either of a delicate network or of dense bundles of collagen, which may undergo hyalinization to form a structureless, homogeneous material.
- In myxoid areas, strands or clumps of epithelial cells are seen widely separated and surrounded by mucoid material.
- Sometimes fibromyxoid appearance of the stroma is seen with abundant elastic tissues.
- The chondroid areas of the stroma exhibit isolated, rounded epithelial cells lying in lacunae within the mucoid material.
- The mucoid materials in myxochondroid areas are composed of glycosaminoglycans and consist mainly of chondroitin sulphates.
- The presence of capsule is also not a consistent finding in pleomorphic adenoma and sometimes extra capsular stellate cell nests are found.
- Histologically, benign lesions may sometimes cause metastasis and such lesions are known as "metastasizing benign pleomorphic adenomas".
- Malignant transformations can occur (less than 1% cases), usually in neoplasms, which have been present from many years.

DIFFERENTIAL DIAGNOSIS

- Adenolymphoma
- Oncocytoma
- Adenocarcinoma
- Fibroma
- Lipoma
- Chondroma
- Myxoma.

SPECIAL INVESTIGATION

FNAC: Aspiration cytology can be helpful in making the diagnosis of pleomorphic adenomas.

MRI: Magnetic resonance imaging is a reliable diagnostic method in determining the extent of the disease present in major glands.

Special stain: Special stains may be used for the detection and differentiation of specific tissue components, e.g. myxoid, osseous or chondroid tissues of the neoplasm.

Immunohistochemistry: Immunohistological analysis may provide important information regarding the biological and histological nature of tissues present in this neoplasm.

TREATMENT

Complete surgical removal of the small lesion is generally curative.

For parotid lesions, surgical excision (lobectomy or gland extirpation) is the frequent choice. Recurrence rate is less than 2 percent, facial nerve palsy and the auriculotemporal syndrome may be the common complications occurring following surgical intervention in the neoplasms of the parotid gland.

MONOMORPHIC ADENOMA

DEFINITION

Monomorphic adenomas are a group of rare benign salivary neoplasms, characterized by proliferation of a single epithelial cell type that has a distinctive architectural pattern.

Monomorphic adenomas do not exhibit the wide cellular diversities, which are normally encountered in pleomorphic adenomas.

Types of monomorphic adenomas

- Basal cell adenoma
- Canalicular adenoma
- Sebaceous adenoma
- Glycogen rich adenoma
- Clear cell adenoma.

Among the different types of monomorphic adenomas, basal cell adenoma is the most common type, moreover only the basal cell adenomas and the canalicular adenomas exhibit distinct clionicopathologic characters.

CLINICAL FEATURES OF DIFFERENT MONOMORPHIC ADENOMAS

The monomorphic adenomas are generally slow growing, encapsulated lesions, similar to pleomorphic adenomas, however they have a much lower tendency for recurrence after treatment.

Basal Cell Adenoma

- This monomorphic adenoma commonly occurs in the 6th decade of life and it is more frequently seen among females.
- The lesion involves parotid in about 75% cases, where it develops mostly from the superficial lobe.
- 20% of the lesions are seen in the oral cavity and intraoral lesions commonly arise from the upper lip and buccal mucosa (Figs 4.17 and 4.18).
- Clinically, basal cell adenomas present slow enlarging, firm, encapsulated, movable lesions and they usually measure less than 3 cm in maximum diameter.
- On palpation, these lesions are firmer than pleomorphic adenomas and have a smooth surface.

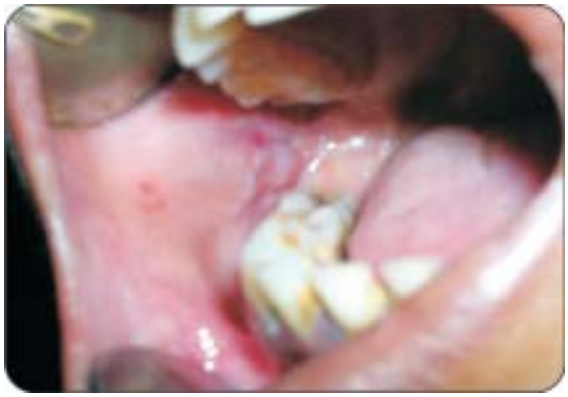

Fig. 4.17: Monomorphic adenoma of cheek

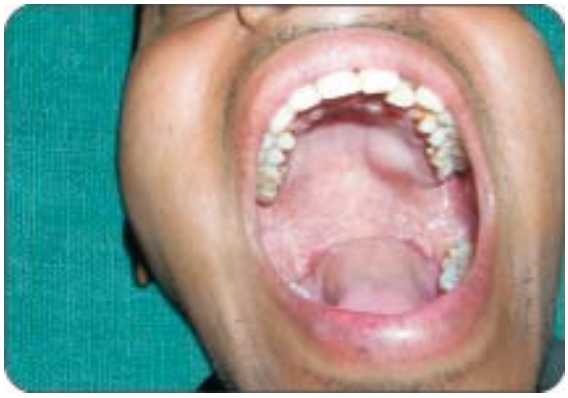

Fig. 4.18: Monomorphic adenoma of palate

Canalicular Adenoma

- Canalicular adenomas usually occur in the 7th decade of life and are rarely seen among children.
- Like other adenomas, these are also more prevalent among females.
- Minor salivary glands of the upper lip are the most frequent sites of development of this neoplasm (75% cases), followed by buccal mucosa (25% cases), however involvement of the major gland is rare.
- Canalicular adenomas clinically appear as small, painless, movable encapsulated lesions being covered by a smooth intact epithelium.
- The color of the overlying mucosa is generally normal, however in some cases the covering epithelium may have a slight bluish tinge.
- Capsule may or may not be present and there can be multifocal growth on some occasions.

HISTOPATHOLOGY

Basal Cell Adenoma

- Basal cell adenomas histologically present clusters of proliferating neoplastic glandular epithelial cells in the form of oval shaped nests.
- The outermost layer of cells, which surround each cell nest are cuboidal type, while the inner core of cells are uniform in size and resemble basal cells of the stratified squamous epithelium.
- The lesion is usually surrounded by a well-defined fibrous capsule.
- The individual, small, well-defined cell nests often resemble basal cell carcinoma of skin.
- In some lesions, there may be proliferation of basaloid cells in diffuse sheets within which keratin pearl formation may be seen.

On the basis of their microscopic appearance basal cell adenomas are divided into four subtypes—solid type, trabecular type, tubular type and membranous type.

Solid type: In solid type of basal cell adenoma, the neoplastic cells proliferate in solid sheets.

Trabecular type: This pattern of basal cell adenoma exhibits elongated, anastomizing cords of basal cells, which are surrounded by mature connective tissue stroma.

Tubular type

- In this pattern, nests of basal cells often surround a duct-like structure.
- The ducts are filled with homogeneous eosinophilic material and are lined by cuboidal epithelial cells.

Membranous type

- This type of basal cell adenomas exhibit islands of neoplastic basaloid cells surrounded by a hyalinized basal lamina.

Canalicular Adenoma

Canalicular adenomas are histologically characterized by numerous anatomizing networks of cuboidal and columnar cells, which give the impression of multiple, interconnecting canals and hence the term canalicular has been given.

- The nuclei of the cuboidal or columnar cells are elongated or oval and are monomorphic.
- The ductal luminas are often prominent with nuclei polarized towards the basement membrane.
- The connective tissue stroma is myxomatous and is composed of an eosinophilic, hypocellular mucoid matrix.
- The poliferating neoplastic cells are surrounded by a well-delineated capsule.

TREATMENT

Monomorphic adenomas are mostly non-aggressive lesions and are treated by surgical excision along with little bit of surrounding normal tissue. Recurrence is extremely uncommon.

MYOEPITHELIOMA

These are rare salivary gland neoplasms and they account for only 1.5 percent of all salivary gland tumors.

CLINICAL FEATURES

Age: Mostly occurs in the 5th and 6th decade of life.

Sex: More common in females.

Site: Mostly occurs in relation to Parotids (40 percent) followed by Palatal minor glands (21 percent).

CLINICAL PRESENTATION

Slow growing, painless mass, the parotid lesions never cause facial nerve palsies and the palatal lesions never ulcerate.

MACROSCOPIC FINDINGS

Myoepitheliomas macroscopically appear as well-circumscribed, frequently encapsulated growths, with features similar to pleomorphic adenomas except the absence of grossly myxoid or chondroid areas. The lesions have solid, tan-yellow, glistening surface, the palatal lesions may not always have capsules but the parotid lesions are almost always encapsulated.

HISTOPATHOLOGY

Microscopically, myoepitheliomas exhibit three distinct patterns:

A. ***Spindle cell pattern:*** It is the most common histologic type and consists of proliferating spindle shaped neoplastic cells having eosinophilic cytoplasms. The neoplastic cells are often arranged in diffuse sheets or in interlacing fascicles. Myoepitheliomas are hypercellular lesions although there is limited mucoid or myxoid stroma present in them. Due to the presence of spindle shaped myoepithelial cells, it is always difficult to distinguish myoepithelioma from lesions like fibrous histiocytoma, neurilemmoma or leiomyoma, etc

B. ***Plasmacytoid pattern:*** Microscopically this pattern reveals group of round cells with eccentric nuclei and eosinophilic cytoplasm. The neoplastic cells proliferate either as closely packed sheets of round cells or in group of cells separated by a loose myxoid stroma.

C. ***Combination pattern:*** This type exhibits the combined features of both plasmacytiod and solid patterns.

Malignant counterpart of this tumor is known as myoepithelial carcinoma or malignant myoepithelioma, it is a high grade malignancy and often occurs in the preexisting pleomorphic adenomas.

ONCOCYTOMA (OXYPHILIC ADENOMA)

DEFINITION

Oncocytomas are rare benign salivary gland neoplasms occurring primarily in the parotid and are composed of clusters of large eosinophilic granular cells (**oncocytes**).

It was first reported by Duplay in 1875 and according to the multicellular theory of salivary gland neoplasms, oncocytomas originate from the striated duct cells.

CLINICAL FEATURES

- Oncocytoma accounts for about 1% of all the salivary gland neoplasms.
- They usually occur among older individuals, in their 8th decade of life.
- There is definite female predilection.
- Superficial lobe of the parotid is the most favored location. Minor salivary glands are rarely affected.
- Clinically the tumor often produces slow enlarging, painless, uninodular or sometimes multinodular, movable swelling anterior to the ear or over the ramus of the mandible.

HISTOPATHOLOGY

- Histologically, oncocytoma exhibits proliferation of numerous **polygonal or cuboidal oncocytes**, showing **prominent eosinophilic and granular cytoplasm with compact nuclei**.
- These neoplastic cells are often arranged in organoid or acinar pattern.
- Some oncocytomas exhibit organoid cell clusters, which form solid cords or "**doughnut-shaped"** cellular configurations.
- The cluster of neoplastic cells stain intensely eosinophilic and are surrounded by a fine vascular stroma.
- The individual neoplastic cell of the cluster exhibits a copious amount of granular cytoplasm with centrally placed small, pyknotic nuclei.
- Sometimes a clear cell variant of oncocytoma occurs in which the oncocytes exhibit clear vacuolated cytoplasms with absence of the characteristic granules.
- A malignant variety of this neoplasm is also reported and is called 'malignant oncocytoma'.

DIFFERENTIAL DIAGNOSIS

- Adenolymphoma
- Pleomorphic adenoma
- Enlarged parotid lymph node.

TREATMENT

Surgical excision by lobectomy.

ADENOLYMPHOMA (WARTHIN'S TUMOR)

Adenolymphoma is a benign salivary gland neoplasm with limited growth potential (Figs 4.19 and 4.20). It is primarily occurring in the **parotid**

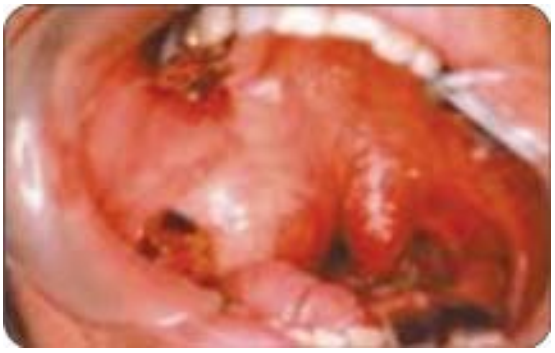

Fig. 4.19: Warthin's tumor

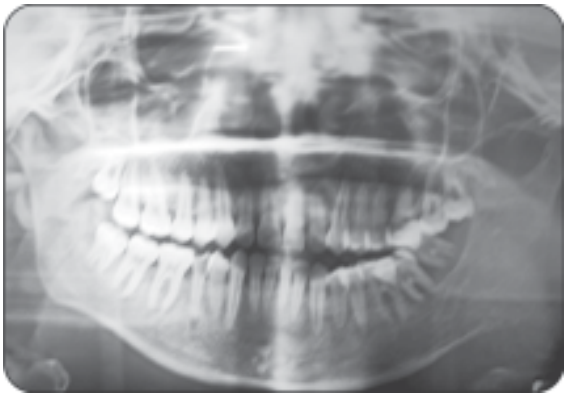

Fig. 4.20: Radiograph of Warthin's tumor

and is composed of cystic spaces with intraluminar projections lined by double layer of cells. The tumor also contains abundant **lymphoid tissue** in the stroma.

Adenolymphoma was first reported by Albrecht and Arzt in the year 1910.

PATHOGENESIS

The pathogenesis of adenolymphoma is debatable mainly because of the presence of lymphoid tissue components in its stroma. Some investigators propose that the tumor develops as a result of neoplastic proliferation of ectopic salivary gland tissues, which are situated within the intraparotid or paraparotid lymph nodes.

Other investigators believe that neoplastic proliferation of the salivary gland epithelial cells initiates a secondary reactive response in the lymphoid tissue of the stroma.

However, many people consider adenolymphoma as a hamartomatous growth rather than a true neoplastic lesion.

CLINICAL FEATURES

Age: The neoplasm is commonly seen among elderly people between the ages of 50 to 70 years.

Sex: It is more prevalent among males (M:F— 5:1).

Site: Adenolymphoma occurs almost exclusively in relation to the parotid gland (mostly tail of the parotid). It comprises of about 20% of all parotid gland neoplasms. The lesion rarely occurs in other major or minor glands.

PRESENTATION

- Adenolymphoma clinically presents a slow enlarging, well-circumscribed, soft, painless swelling in the parotid gland.
- It is usually well-encapsulated, movable and consistently found over the angle of the mandible in the superficial lobe of parotid.
- The maximum size of the lesion could be up to 2 to 4 cm in diameter.
- In almost 10% cases, the lesion occurs bilaterally and moreover, sometimes multiple lesions can develop from a single gland.
- In some cases adenolymphomas may develop in association with pleomorphic adenomas in the parotid.
- Adenolymphomas produce a compressible and doughy feeling upon palpation and they are usually not fixed to the adjacent tissues.

MACROSCOPIC APPEARANCE

- Cut section of a "fresh" specimen of adenolymphoma exhibits exudation of watery or sometimes **chocolate-colored** fluid from the tissue.
- Macroscopically the neoplasm also exhibits **multiple confluent cystic spaces** and variable amount of **lymphoid tissue** with follicles.
- A dense fibrous capsule surrounds the neoplasm.

HISTOPATHOLOGY

Microscopically, adenolymphoma presents the following features:

- There is presence of multiple cystic spaces, which are lined by pseudostratified tall columnar epithelial cells having distinct eosinophilic cytoplasm (columnar oncocytes).
- The epithelial cells are arranged in a double layered pattern with the nuclei oriented in the basilar area of the bottom row and in the superior aspect of the upper row.
- The epithelial cells cover papillary folds, which extend into the cystic spaces.
- The papillary folds are supported by large amounts of lymphoid tissue with scattered germinal centers.
- The cystic lumens are often filled with a homogeneous eosionophilic material.
- In some lesions, mucous goblet cells are interspersed within the neoplastic pseudostratified epithelial cells.
- The infected or infarcted lesions may exhibit extreme tissue necrosis and presence of many epitheloid cells and some times multinucleated giant cells.
- Sebaceous lymphadenoma is a histologic variant of adenolymphoma, which contains nests of squamous epithelial islands showing cyst formation and sebaceous acinar differentiation.

DIFFERENTIAL DIAGNOSIS

- Pleomorphic adenoma
- Oncocytoma
- Enlarged parotid lymph node.
- Mucoepidermoid tumor
- Lipoma
- Mucous retention cyst
- Malignant lymphoma.

SPECIAL INVESTIGATION

Sialography: In adenolymphoma sialography reveals features of benign neoplasm.

Scintigram: The neoplasm appears as a hot-spot or hot nodule on a scintigrams.

TREATMENT

Simple surgical enucleation.

MALIGNANT SALIVARY GLAND NEOPLASMS

MALIGNANT PLEOMORPHIC ADENOMA (MIXED TUMOR)

Malignant pleomorphic adenoma (mixed tumor) is a relatively uncommon malignant tumor of salivary gland and it accounts for 3% of all salivary glands tumors.

Malignant mixed tumors are broadly divided into two groups:

A. Carcinoma ex-pleomorphic adenoma
B. De-novo type.

A. ***Carcinoma ex-pleomorphic adenoma:*** This lesion is developing as a result of malignant transformation in a pre-existing benign pleomorphic adenoma (occurs in about 2 to 7 percent cases).

B. ***De-novo type:*** A tumor in the salivary gland, which is malignant from the very beginning.

The later type often shows malignant change in both the epithelium and the connective tissue components of the salivary gland, and therefore it is called "**carcinosarcoma**". These lesions carry a much poorer prognosis than the other.

CLINICAL FEATURES (FIGS 4.21 AND 4.22)

- Malignant mixed tumor usually occurs at the age of around 60 years and it most frequently involves the parotid. Besides that submandi-

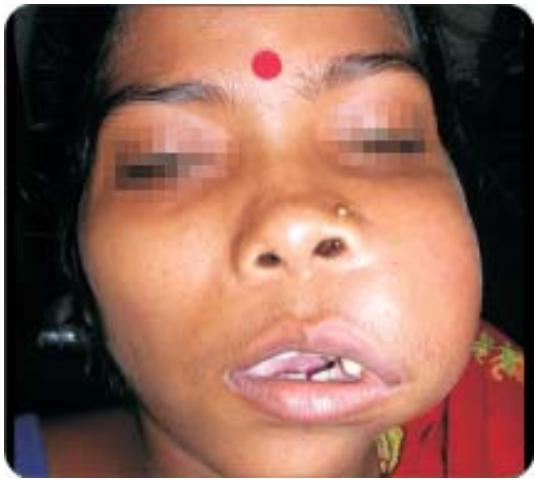

Fig. 4.21: Malignant mixed tumor-I

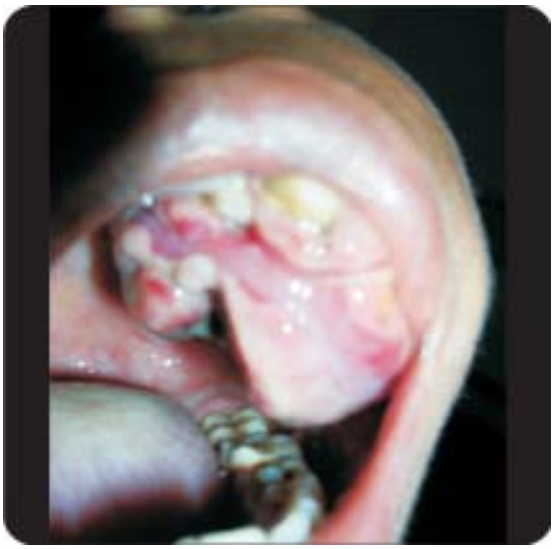

Fig. 4.22: Malignant mixed tumor-II

bular, sublingual and minor gland of the palate, lips paranasal sinuses and nasopharynx may be affected.

- The tumor occurs more frequently among males.
- Majority of the patients have a benign mixed tumor for about 15 to 20 years and that few of them may undergo malignant transformation.

Symptoms indicating malignant transformation in a pre-existing pleomorphic adenoma

- Very rapid growth in the recent time, within 3 to 6 months
- Severe pain
- Anesthesia or paresthesia of the facial nerve
- Fixation of the tumor to the overlying skin or underlying muscle or bone
- Non-healing ulcer of the overlying skin and mucous membrane
- Hemorrhage
- Regional lymphadenopathy
- Secondary candidal infection on the superficial ulcerated surface.

- In case of *de novo* lesions, small innocuous looking tumor may eventually show severe malignant change.

HISTOPATHOLOGY

- Microscopically, bulk of the tumor appears benign, but there are small areas of **cytologically altered malignant glandular epithelial cells** found within the lesion.
- These malignant cells often cause invasion into the surrounding normal tissue.
- Malignant transformation in a benign tumor results in the development of adenocarcinoma, undifferentiated carcinoma or epidermoid carcinoma.
- During histopathological evaluation in a suspected malignant mixed tumor the following histological changes should be checked cautiously.
  - Destructive infiltrative growth pattern.
  - Marked cytologic atypia with abnormal mitotic activity.
  - Cellular pleomorphism and nucler hyperchromatism.
  - Areas of micronecrosis.
  - Hemorrhage.
  - Excessive hyalinization.
  - Dystrophic calcification.
  - Vascular permeation or perineural invasion.
- Malignant mixed tumor, the entity should only be recognized if there is histological evidence of benign pleomorphic adenoma tissues in the lesions.
- In some cases, the tumor is completely filled with more than one malignant cells, which may be epidermoid type, adenocarcinoma type or spindle cell type, and there is little evidence of any pre-existing benign lesion.
- If the malignant cells remain within the confinement of pre-existing adenoma its prognosis is good. If the malignant cells infiltrate into the surrounding normal tissue its prognosis is poor.

TREATMENT

Extensive surgery followed by radiotherapy and chemotherapy. Prognosis is mostly poor.

- 5-year survival rate is—55% approx.
- 10-year survival rate is—30% approx.

ADENOID CYSTIC CARCINOMA (CYLINDROMA)

Adenoid cystic carcinoma is a malignant neoplasm arising from the glandular epithelium of either major or minor salivary glands. It has

profound **tendency to invade into the perineural lymphatic spaces**.

The important biologic characteristics of this neoplasm are—prolonged natural history, long clinical course, slow growth rate, multiple recurrences and late metastasis, etc.

The cyllindromas were first reported by Bilroth in 1856, Spies first used the term adenoid cystic carcinoma in 1930.

CLINICAL FEATURES

Incidence: Adenoid cystic carcinoma accounts for about 6% of all parotid tumors and 30% of minor salivary gland tumors.

Age: The tumor frequently occurs at the age of 50 to 70 years.

Sex: Slightly more prevalent among females.

Site: Adenoid cystic carcinomas affect both major as well as the minor glands, however these tumors affect minor glands more often than the major glands.

The common sites for development of this lesion in minor glands are the palate (Fig. 4.24) and tongue.

In the major gland category, **it is the most common malignant tumor of submandibular salivary gland,** although it also frequently affects parotid.

Besides this the lesions also develop from the lacrimal glands, breasts, prostate, uterine cervix, esophagus and glands of the paranasal sinuses, etc.

PRESENTATION (FIGS 4.23 TO 4.25)

- The lesion often produces a relatively slow enlarging growth, with frequent surface ulcerations.

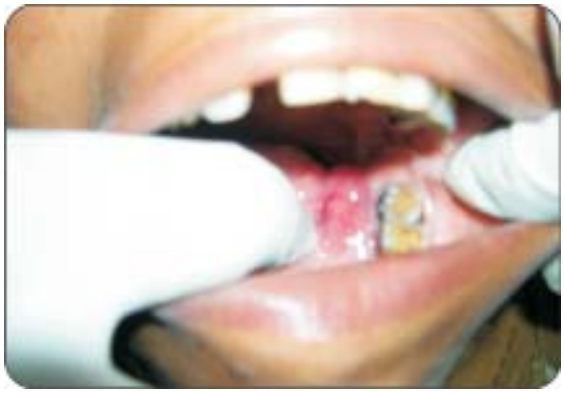

Fig. 4.23: Adenoid cystic carcinoma

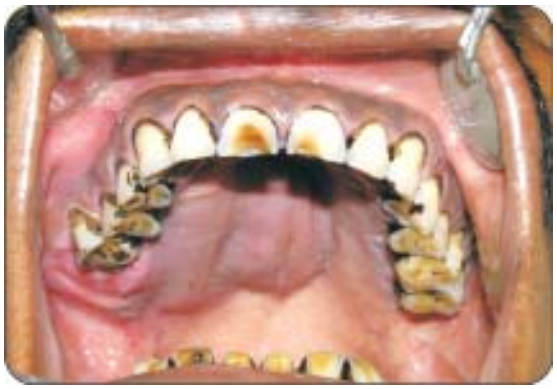

Fig. 4.24: Adenoid cystic carcinoma-II

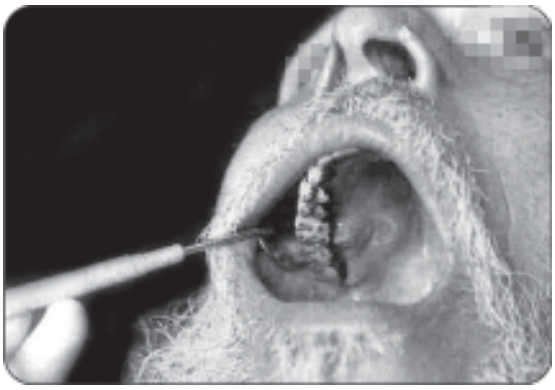

Fig. 4.25: Adenoid cystic carcinoma of the palate

- Parotid tumors produce asymptomatic subcutaneous mass anterior to or below the external ear.
- Since this tumor **has a propensity to surround nerve trunk**, parotid lesions often surround and invade the **facial nerve sheath**. Besides facial nerve, Adenoid cystic carcinomas frequently invade the **lingual** and the **hypoglossal nerves**.
- **Pain** is very common feature in this tumor and severe neurological signs like **anesthesia, paresthesia or palsy** frequently develop.
- Often there is **fixation and induration** of the tumor to the underlying structures along with local invasion.
- Submandibular gland tumors become quite large before patients notice it.
- Palatal lesions are often accompanied by toothache, loosening of teeth and delayed healing of the socket in case the tooth is extracted.
- Tumor developing in association with minor glands of palate produces a nodular growth,

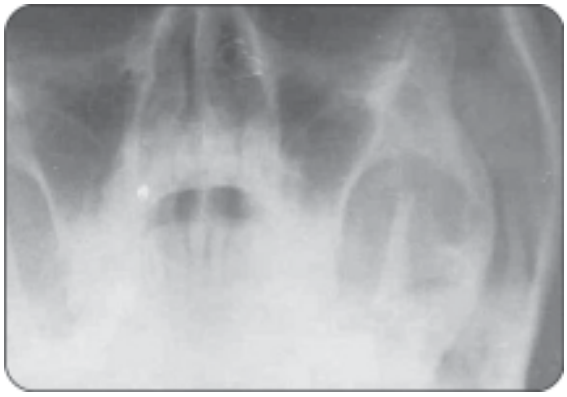

Fig. 4.26: Adenoid cystic carcinoma causing expansion and clubbing of the maxillary antrum (Rt.)

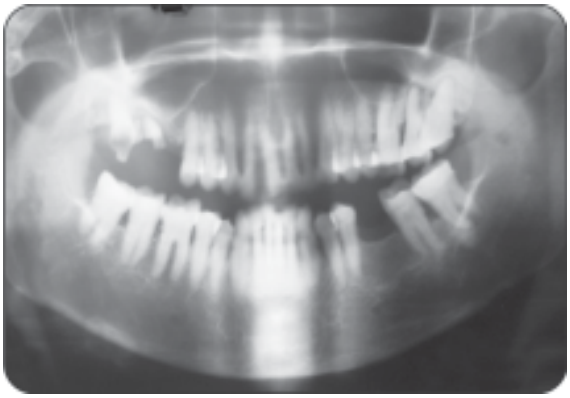

Fig. 4.27: Radiograph of adenoid cystic carcinoma

resembling an eccentric node with an ulcerated surface.

- Palatal paresthesia may be present due to involvement of greater palatine nerve.
- Extensive bone involvement may occur in few cases, but as the tumor spreads via the marrow spaces its actual dimension can be much bigger than what the radiography shows (Figs 4.26 and 4.27).

HISTOPATHOLOGY (FIGS 4.28 TO 4.30)

- Adenoid cystic carcinoma histologically characterized by the presence of numerous small, darkly staining, polygonal or cuboidal cells of uniform size.
- These cells often resemble basal cells of the oral epithelium and they have hyperchromatic nuclei and minimum mitotic activity.
- **Double layer** of tumor cells are often arranged in a **duct-like or 'cylinder-like'** pattern that

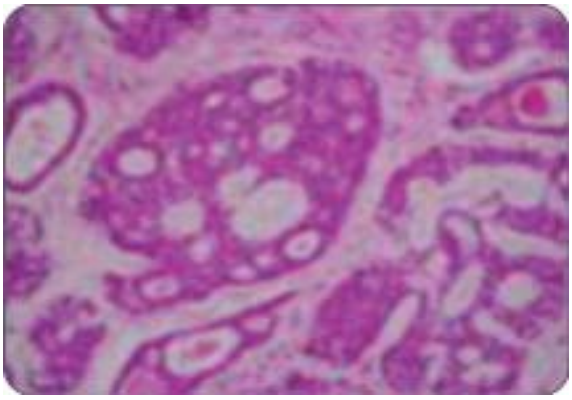

Fig. 4.28: Photomicrograph of adenoid cystic carcinoma-I

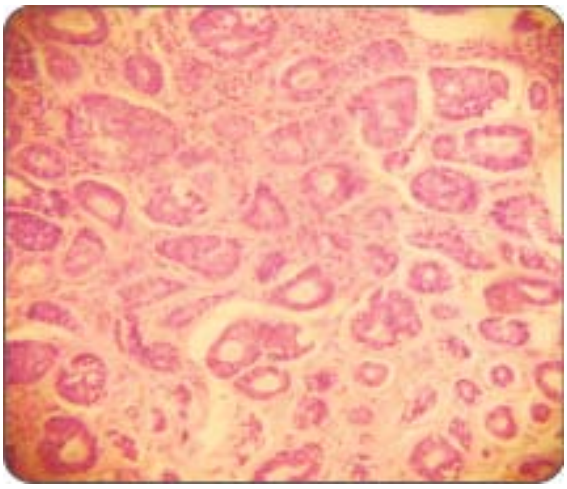

Fig. 4.29: Phtomicrograph of adenoid cystic carcinoma-II

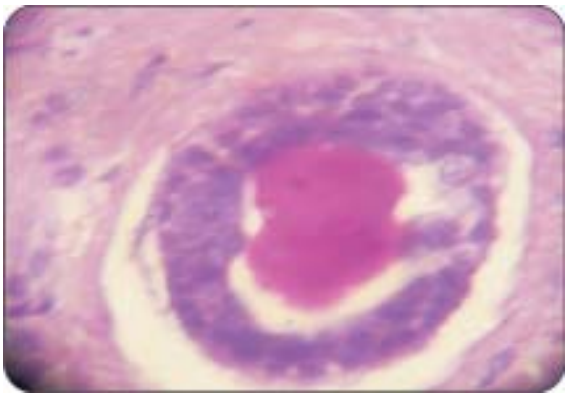

Fig. 4.30: Photomicrograph of adenoid cystic carcinoma-III

contains an eosinophilic coagulum at the center and this often gives rise to a classic **"Swiss cheese"** appearance of the adenoid cystic carcinoma.

- Microcystic spaces often divide the gland lobules; the tumor cells which are lining the microcysts are not well-polarized as seen in case of true ductal cells.
- The stromal connective tissue of the tumor is hyalinized, which surrounds the tumor cells by forming the structural pattern of many **cylinders** (from this the name "cylindroma" has evolved).

Histologically, adenoid cystic carcinomas have three subtypes:

A. Cribriform pattern
B. Solid pattern
C. Tubular pattern.

A. Cribriform pattern: It is the most classical histologic pattern of adenoid cystic carcinoma. Here the neoplasic epithelial components consist of small, uniform, polygonal cells with basophilic cytoplasms. This pattern is characterized by proliferating mass of epithelial cells being penetrated by numerous cylindrical spaces and thereby producing a 'cribriform' appearance.

B. Solid pattern: In this pattern, the tumor cells proliferate to form solid masses with areas of central necrosis.

C. Tubular pattern: In this pattern, the tumor cells exhibit less stratification and they proliferate as **small tubular units** with a single central lumen.

- Besides these usual patterns, some lesions consist of solid nests of basal cells and resemble basal cell carcinoma or basal cell adenoma.
- Some tumors even show scanty amount of tumor cells being dispersed in an abundant hyalinized stroma. These cells often exhibit hyperchromatism and pleomorphism and an increased mitotic activity.
- One of the most striking features of adenoid cystic carcinoma is the spread of the tumor cells via the perineural or intraneural spaces. This phenomenon is known as **"neurotrophism"** and it occurs in about 80 percent cases of this tumor.
- In such cases concentric laminations of tumor cells wrap around the perineurium of nerve fibers and invade the perineural lymphatic vessels, this accounts for the higher rate of recurrence of these tumors.
- Besides the perineural invasions, the tumor cells often make intravascular or perivascular invasions in the surrounding tissue, thus distal metastasis occurs via the hematologic spread of the tumor cells to the bone and lung, etc.
- Palatal cilindromas may extend to the pterygomandibular space via the greater palatine nerve.

DIFFERENTIAL DIAGNOSIS

- Pleomorphic adenoma
- Monomorphic adenoma
- Mucoepidermoid carcinoma
- Adenocarcinoma
- Acinic cell tumor
- Basal cell carcinoma.

Key points of adenoid cystic carcinoma

- Adenoid cystic carcinoma is a malignant neoplasm of the major or minor salivary glands, which characteristically shows a tendency to invade into the perineural lymphatic spaces.
- The tumor affects both minor and major salivaly glands, however it is the most common malignant tumor of submandibular salivary gland.
- Clinically adenoid cystic carcinoma presents slow enlarging, painful swelling with frequent surface ulcerations.
- Anesthesia and paresthesia of the facial, lingual and hypoglossal nerves, etc. frequently occur, as the tumor has a tendency to invade into the nerve sheath.
- Fixation of the tumor to the overlying skin and underlying bone and connective tissue is commonly seen.
- Microscopically, the tumor exhibits proliferation of double layered, darkly staining, cuboidal shaped, glandular epithelial cells in 'duct-like' structures.
- These ductal structures are filled with eosinophilic coagulum and thereby produce a typical 'swiss-cheese' appearance.
- The stromal connective tissue of the tumor is hyalinized, which surrounds the tumor cells by forming the structural pattern of many cylinders.
- In adenoid cystic carcinoma the tumor cells spread via the perineural or intraneural spaces.

TREATMENT

By wide surgical excision. Post surgical radiotherapy is effective since the tumor cells are radiosensitive. Short-term prognosis is good but long-term prognosis is grave.

MUCOEPIDERMOID TUMOR

Mucoepidermoid tumor is an unusual type of malignant salivary gland neoplasm with varying degree of aggressiveness. According to the multicellular theory, the mucoepidermoid tumors arise from the excretory duct cells of the salivary gland (Fig. 4.31).

CLINICAL FEATURES

Age: The tumor usually occurs at the age of 30 to 50 years (sometimes in children also).

Sex: There is a slight female predilection.

Site: The tumor frequently involves the parotid and the minor salivary glands of the palate, lips, buccal mucosa, tongue and retromolar areas, etc.

PRESENTATION

- The tumor mostly produces a slow growing, painless swelling that often has a **cystic** feeling.
- It often clinically resembles the pleomorphic adenoma.
- In many cases, rapid growth of the tumor with pain, hemorrhage, ulceration and paresthesia, etc. may occur.
- Mucoepidermoid tumor may also develop as a **central jaw lesion** especially in mandible and such intraosseous lesions may develop either from the ectopic intrabony salivary glands or from the metaplastic lining epithelium of the odontogenic cysts.
- These jaw tumors (occur in about 4% cases) cause bony expansions in the lower third molar areas. Radiographically, these lesions produce unilocular or multilocular radiolucent areas in the jawbone.
- The parotid tumor presents a relatively well-defined, focal, movable, nodular swelling. The size of the tumor varies between 1 to 4 centimeters in diameter.
- Facial nerve paralysis sometimes occurs in relation to parotid lesions.
- Low-grade tumors are often fluctuant in nature while the high-grade tumors are firm and are fixed to the adjacent tissues.
- Low-grade tumors clinically appear as non-ulcerated, fluctuant growths with a slight bluish color, these tumors contain several cystic structures and are often confused with mucoceles.

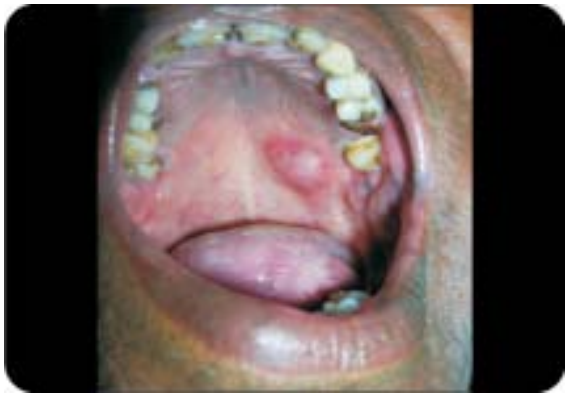

Fig. 4.31: Mucoepidermoid tumor

HISTOPATHOLOGY (FIGS 4.32 AND 4.33)

Histologically this unencapsulated tumor consists of three distinct types of cells: (A) Large pale mucous secreting cells, (B) Epidermoid cells, and (C) Intermediate type of cells (these cells can

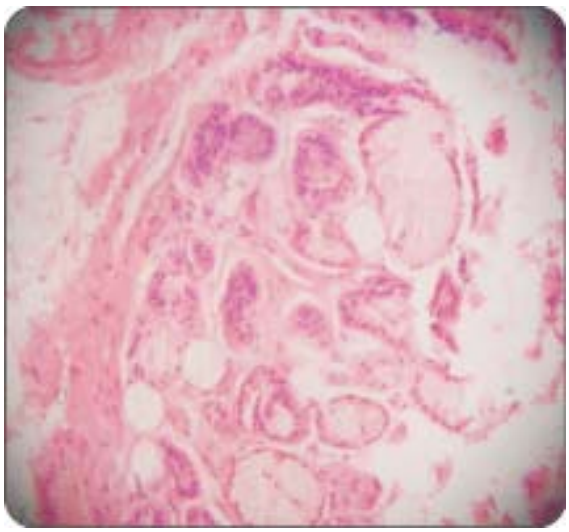

Fig. 4.32: Photomicrograph of mucoepidermoid tumor-I

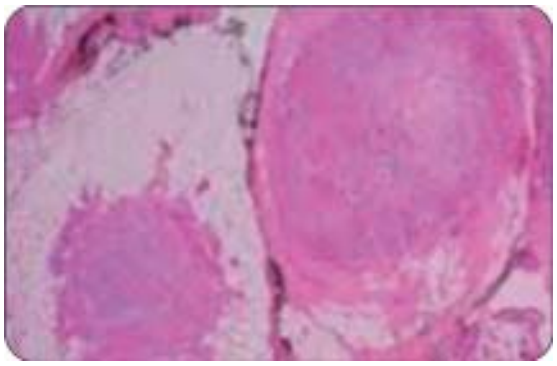

Fig. 4.33: Photomicrograph of mucoepidermoid tumor-II

Key points of mucoepidermoid tumor

- Mucoepidermoid tumor is an unusual type of malignant salivary gland neoplasm, which occurs between the ages 30 to 50 years and sometimes in children.
- It predominantly affects parotid and minor salivary glands, it also frequently affects the jawbone.
- Clinically, the tumor presents slow growing, painless swelling that often has a **cystic** feeling. Some lesions cause fast enlarging swelling, with pain, ulceration, paresthesia and hemorrhage, etc.
- Intraosseous tumors cause expansion of jawbone and their radiographs exhibit multilocular radiolucency.
- Histologically, mucoepidermoid tumor consists of three distinct types of cells: (A) large pale mucous secreting cells, (B) epidermoid cells, and (C) intermediate type of cells.
- The well-differentiated or low-grade tumors consist mainly of mucous secreting cells and epidermoid cells, these lesions often have a cystic appearance.
- The poorly differentiated or high-grade tumor consists mainly of solid proliferations of epidermoid and intermediate cells.

differentiate into either of the two cells mentioned earlier).

According to the distribution of these cell types, the mucoepidermoid tumor is divided into two grades.

WELL-DIFFERENTIATED OR LOW-GRADE TUMOR

- This tumor consists mainly of mucous secreting cells and epidermoid cells with no evidence of cellular pleomorphism.
- Cells of either type may predominate in a mucoepidermoid tumor, if the mucous cells predominate, the tumor tends to become cystic type and if the epidermoid cells predominate then the tumor becomes solid type. The solid tumors are often more aggressive in nature than the cystic type.
- The mucous cells frequently line many **"cyst-like"** spaces within the tumor in single or double layers.
- The epidermoid cells either line the cysts or they form **solid sheets or strands** and thereby give the impression of an **epidermoid carcinoma**, although the keratinization is minimum.
- Discharge of mucous in the cyst causes distension and even rupture of the cyst and this often results in hemorrhage, inflammation, fibrosis and foreign body type giant cell reaction in the stroma.
- The tumor islands and the cystic areas are demarcated by a mature fibrous stroma.
- The intermediate cells lack true squamous differentiation and are smaller than the other two types.
- These polygonal cells have dark nuclei and pale eosinophilic cytoplasm.

POORLY DIFFERENTIATED OR HIGH-GRADE TUMOR

- These lesions consist mainly of **solid** proliferations of epidermoid and intermediate cells, these cells often exhibit cellular pleomorphism, nuclear hyperchromatism and infiltrative growth into the surrounding tissue and the lymph nodes.
- The low-grade lesions often appear to advance on a broad **"pushing front"** and these lesions are very aggressive in nature.
- Cystic spaces are not prominent and sometimes it is difficult to distinguish these tumors from the squamous cell carcinomas.
- The cells are often poorly differentiated and they often exhibit highly infiltrative growth.

Distant metastasis into the lung, bone and brain may occur.
- Local infiltration of the tumor cells commonly occur into the adjacent normal salivary gland tissue or connective tissue or muscles, etc.
- A clear cell variant of the mucoepidermoid tumor exists, which often shows sheets of clear vacuolated cells that do not stain for mucin and these cells gradually merge with the squamous epithelial cells.

DIFFERENTIAL DIAGNOSIS

- Pleomorphic adenoma
- Adenocarcinoma
- Squamous cell carcinoma
- Metastatic carcinoma.

TREATMENT

By surgical excision and radiotherapy.

The overall 5 years survival rate is 70% (for high grade it is 80%). In low-grade tumors local recurrence is seen in about 10% cases.

ACINIC CELL TUMOR

Acinic cell tumors are uncommon neoplasms of the salivary gland and they are often composed of cells that resemble the **serous cells** of the salivary gland. According to the multicellular theory these tumors originate from the cells of the salivary gland acini.

CLINICAL FEATURES

- The tumor chiefly occurs among middle-age or elderly persons, with a slight predilection for females.
- Parotid is most frequently affected (it is the second most common malignant tumor of parotid after mucoepidermoid tumor) and it is rarely seen in intraoral sites.
- The lesion presents a well-defined, slow growing, painless, firm, well-demarcated, movable swelling that often resembles pleomorphic adenoma.
- The size of the lesion is usually about 3 cm in diameter, the overlying skin or epithelium is intact and few lesions can be fluctuant in nature due to the presence of intralesional cystic spaces.
- Rarely intraoral lesions of acinic cell tumor may occur on the lip or cheek region and they present well-defined, firm, painless, submucosal nodular growths.
- On few occasions, the growth may be rapid, with associated pain, ulceration, induration and paresthesia, etc.

HISTOPATHOLOGY

- Histologically the tumor consists of either serous or mucous acinar cells of the salivary gland.
- The malignant cells are large, round or polyhedral in shape and have granular basophilic cytoplasm and dark eccentrically placed nuclei.
- These cells are often arranged in **acinus-like clusters** and they often resemble the serous acinar cells of the salivary gland.
- The cell cytoplasms may be vacuolated or sometimes entirely clear.
- These tumor cells may also be arranged in sheets or solid or cystic or even papillary cystic patterns within a lymphoid stroma.
- Acinic cell tumor is nonencapsulated and it often shows either a "pushing-margin" type or a definite infiltrative pattern of growth.

DIFFERENTIAL DIAGNOSIS

- Pleomorphic adenoma
- Stromal tumor
- Enlarged lymph nodes.

TREATMENT

By wide local excision or superficial parotidectomy. 5-years survival rate is seen about 75% cases.

ADENOCARCINOMA

Adenocarcinomas occur more commonly in relation to intraoral minor salivary glands and are less common in the parotid, however some lesions may develop from the pre-existing pleomorphic adenomas (Figs 4.34 and 4.35).

CLINICAL PRESENTATION

- The majority of the patients are in their sixth decade of life and females are more likely to suffer.

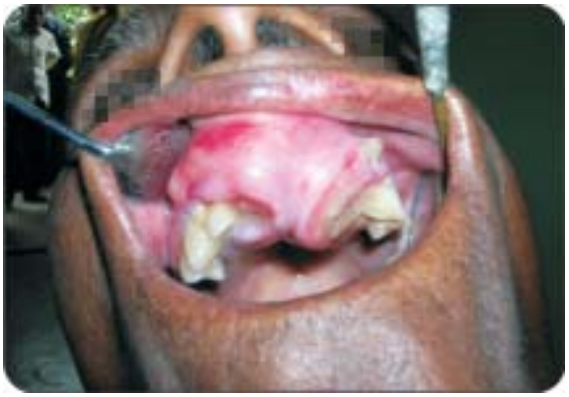

Fig. 4.34: Adenocarcinoma

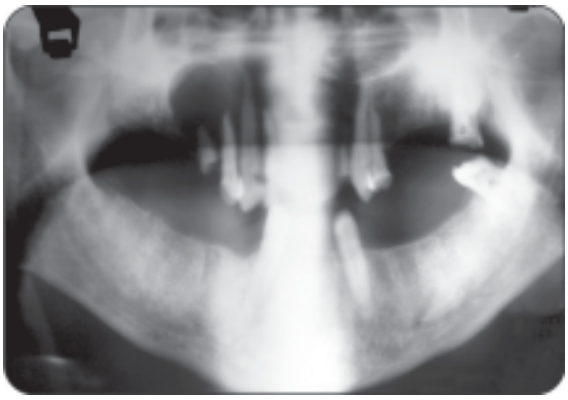

Fig. 4.35: Radiograph of adenocarcinoma

- Initially the tumor presents a slow growing, firm, painless mass with no surface ulceration.
- Later on the tumor develops a fast enlarging, painful swelling with ulceration and paresthesia, etc.
- The palatal lesions are often fixed to the adjacent tissues and they usually measure about 3 cm in diameter.

HISTOPATHOLOGY (FIGS 4.36 AND 4.37)

- Microscopy reveals numerous proliferating malignant ductal epithelial cells with areas of hemorrhage and necrosis.
- At the periphery of the lesion the tumor cells are arranged in parallel arrays of elongated tubular formations and thereby produce an "onion-skin" appearance.
- Some tumors produce many cyst-like spaces, containing large quantity of mucus and in few casesm, papillary in-growths into the cystic spaces are also seen.

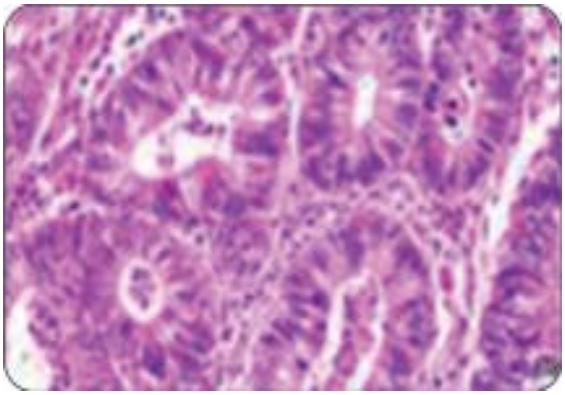

Fig. 4.36: Photomicrograph of adenocarcinoma-I

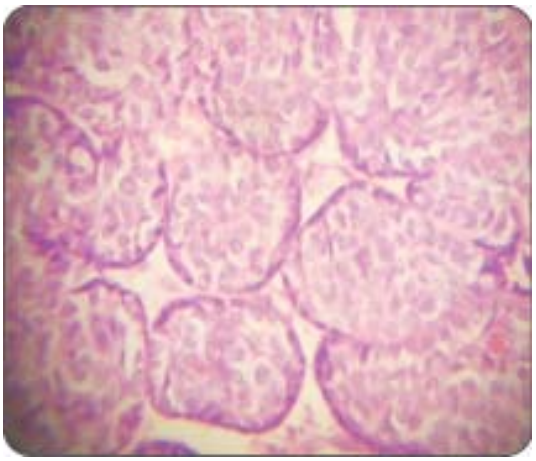

Fig. 4.37: Photomicrograph of adenocarcinoma-II

- The tumor cells often invade into the surrounding normal tissues.

TREATMENT

Wide surgical excision. Prognosis is usually poor.

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CHAPTER 5

Odontogenic Neoplasms

DEFINITION

Odontogenic neoplasms are **a complex group of lesions derived from the dental formative tissues or their remnants (tissues associated with the development of tooth and its supporting structures).** The constituent tissues in each of these neoplasms can resemble the various tissues found during normal odontogenesis, from inception of the tooth germ to tooth eruption.

The tooth formation or odontogenesis begins in the 6th week intrauterine life and it originates from the oral epithelium covering the maxillary and mandibular alveolar processes. During the initial period "bud-like" swellings appear from the basal layer of the oral epithelium at specific locations, where individual teeth are to be fromed in future.

The development of tooth occurs in the following stages:

Stage of formation of dental lamina: The epithelial bud elongates in the form of a solid 'tube-like' structure that projects into the underlying connective tissue and this process is known as "elongation".

The elongated epithelial structure is called the 'dental lamina', from which the future tooth develops.

Cap stage: Once the appropriate depth is achieved, the basal layer at the tip of the dental lamina thickens and forms a concavity.

Early bell stage: The cap shaped structure enlarges as odontogenesis proceeds and within few days the bottom layer of the epithelium (inner enamel epithelium) separates from the top layer (outer enamel epithelium). The intervening zone is composed of loosely arranged 'star-shaped' epithelial cells called stellate reticulum cells. During this stage elongation of the periphery of the epithelial structure occurs, which gives shape of the crown of the individual teeth.

Late bell stage (formation of dental papilla): During this stage the cells of the inner enamel epithelium becomes elongated and palisaded, the nuclei of these cells are often elongated away for the basement membrane and these cells are called 'pre-secretory ameloblasts'.

These pre-secretory ameloblasts induce the undifferentiated cells of the adjacent dental papilla to differentiate into pre-secretory odontoblasts. The later group of cells aligns in a palisaded manner adjacent to the basement membrane opposite the pre-secretory ameloblasts. Once the ameloblasts become mature the odontoblasts are stimulated to secrete dentin matrix, which in turn initiates the deposition of enamel matrix on the opposite side of the basement membrane.

FORMATION OF DENTAL PAPILLA

During the early bell stage the mesoderm immediately adjacent to the inner enamel epithelium proliferates and forms a zone of embryonic and myxomatous connective tissue called 'dental papilla'. It may be further induced to form dentin or pulp tissues.

DENTAL FOLLICLE

During early bell stage an outer zone of dense and fibrous connective tissue forms, which encapsulates the developing of tooth bud and is known as the 'dental follicle'. The dental follicle encloses the developing tooth until it erupts into the oral cavity.

After eruption of the tooth the coronal portion of the dental follicle becomes part of the connective tissue of the free gingival margin.

Likewise the radicular part of the follicle eventually becomes the periodontal ligament, which separates the cementum from the alveolar bone.

FORMATION OF ROOT

After formation of the tooth crown the outer enamel epithelium elongates and forms a thin, transient membrane called the "epithelial root sheath of Hertwig" which determines the shape and length of the roots of the individual teeth. During root formation, initially the dentin is formed. This newly formed dentin stimulates the adjacent dental follicle to differentiate into cementoblasts. The cementoblast cells form a calcified layer over the root dentin, which is known cementum. Cementum serves to anchor the periodontal ligament and collagen of the dental follicle to the tooth root.

Once the process of odontogenesis is completed, the dental lamina leaves behind some cell remnants in the connective tissue, which are called the "**cell rests of sarre**". Similarly, the remnants of the epithelial root sheath of Hertwig also remain within the periodontal ligament and are known as "**cell rests of Malassez**". These cellular remnants play important role in the development of various odontogenic tumors.

CLASSIFICATION OF ODONTOGENIC TUMORS (MODIFIED WHO CLASSIFICATION)

A. BENIGN

I. Odontogenic epithelium without odontogenic ectomesenchyme
- Ameloblastoma
- Squamous odontogenic tumor
- Calcifying epithelial odontogenic tumor (Pindborg tumor)
- Adenomatoid odontogenic tumor

II. Odontogenic epithelium with odontogenic ectomesenchyme with or without hard tissue formation
- Ameloblastic fibroma
- Ameloblastic fibrodentinoma
- Ameloblastic fibroodontoma
- Odontoameloblastoma
- Calcifying odontogenic cyst
- Complex odontoma
- Compound odontoma

III. Odontogenic ectomesenchyme without included odontogenic epithelium

Compound odontoma
- Odontogenic fibroma
- Myxoma
- Cementoblastoma (Benign cementoblastoma, True cementoma).

B. MALIGNANT

I. Odontogenic carcinomas
- Malignant ameloblastoma
- Primary intraosseous carcinoma
- Clear cell odontogenic carcinoma.

II. Odontogenic sarcomas
- Ameloblastic fibrosarcoma
- Ameloblastic fibro-odontosarcoma
- Ameloblastic fibrodentinosarcoma.

NEOPLASMS OF DEBATABLE ORIGIN

- Melanotic neuroectodermal tumor of infancy
- Congenital gingival granular cell tumor (congenital epulis).

AMELOBLASTOMA

DEFINITION

Ameloblastoma is a benign locally aggressive neoplasm arising from the odontogenic epithelium and it is the most common odontogenic neoplasm of the oral cavity.

Ameloblastoma the word has evolved from the early English words—'Amel' meaning enamel, and 'blastos'— meaning germ.

It was first recognized by Cusack in 1827 and it was named 'adamentinoma' in 1885 by Luis-Charles Malassez. It was finally renamed as 'ameloblastoma' in 1934 by Ivey and Churchill.

ETIOLOGY

Exactly not known however, the following factors may predispose the formation of ameloblastoma:
- Trauma
- Infection
- Previous inflammation
- Extraction of tooth
- Dietary factors
- Viral infection.

HISTOGENESIS OF AMELOBLASTOMA

Ameloblastoma develops from the odontogenic epithelial cells or their remnants but the exact cell of its origin is not very clearly known. According to different investigators, the possible cells or tissues from where ameloblastomas may arise are as follows:

- Enamel organ of the developing tooth germ.
- Cell rest of Serre (remnants of dental lamina).
- Epithelial lining of the odontogenic cysts, especially the dentigerous cyst.
- The basal cell layer of the oral epithelium (rarely).
- Reduced enamel epithelium.
- Cell rest of Malassez.

CLINICAL FEATURES

Incidence: Approximately one percent among all oral tumors and 18 percent of all odontogenic tumors are ameloblastomas.

Age: Second, third, fourth and fifth decade of life, the mean age of occurrence is about 32 years. This lesion occurs more commonly in blacks than whites. Women are generally 4 years younger than men when the tumor is first noticed.

Sex: Males are affected more often than females. Tumor size is usually larger in women.

Site: Ameloblastoma in most of the cases involve the mandible (80%), especially in the molar-ramus area (70%), although some lesions may develop in the premolar (20%) or symphysis (10%) regions.

Maxillary tumors also commonly involve its posterior part and the lesions often have a tendency to invade into the antrum (15%) or the nasal floor.

Extraosseous or peripheral ameloblastomas can rarely occur mostly in relation to the gingiva.

TYPES OF AMELOBLASTOMA

- Unicystic ameloblastoma
- Multicystic ameloblastoma
- Peripheral ameloblastoma
- Malignant ameloblastoma

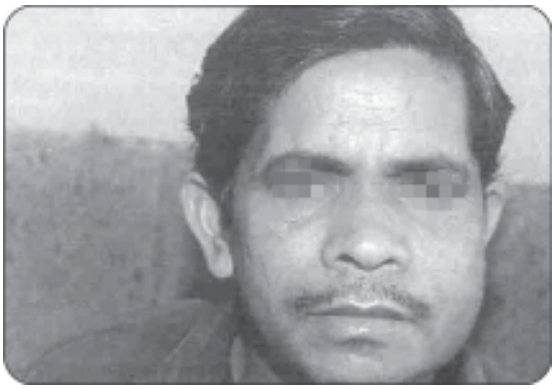

Fig. 5.1: Ameloblastoma developing from Lt. side of mandible

Fig. 5.2: Ameloblastoma of mandible causing large expansile swelling of the face

CLINICAL PRESENTATION (FIGS 5.1 AND 5.2)

- Clinically ameloblastoma commonly presents a slow enlarging, painless, ovoid or fusiform, bony hard swelling of the jaw.
- The lesion causes expansion and distortion of the cortical plates of the jawbone and displacement of the regional teeth, and these are often leading to gross facial asymmetry (Fig. 5.3).
- Pain, paresthesia and mobility of the regional teeth may be present only in few cases.
- Most of the patients report with a typical long time history of presence of an "**abscess**" or a '**cyst**" in the jaw bone that was operated on several occasions but has recurred after each attempt.

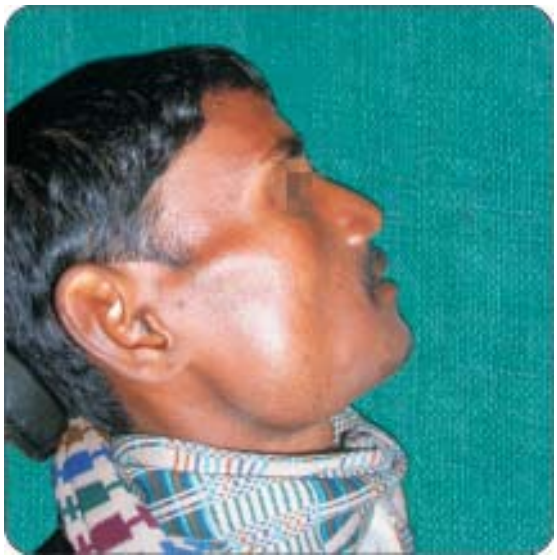

Fig. 5.3: Ameloblastoma-I

Fig. 5.4: Ameloblastoma-II

- Larger lesions of ameloblastoma often cause severe expansion, destruction and thinning of the cortical plates, which often result in '**fluctuations**" in the affected area.
- Expansion of the bony cortex occurs since slow growth rate of the tumor allows time for the periosteum to develop thin shell of bone ahead of the lesion. This thin shell of bone cracks under digital pressure and the phenomenon is called "**egg shell crackling**".
- "**Pathological fractures**", may occur in many such affected bones.
- The mucosa overlying the tumor appears normal and the regional teeth are usually vital.
- In some cases, smaller lesions may remain asymptomatic for a longer duration of time and are detected incidentally during routine radiographic examinations.
- Many untreated lesions may reach to an enormous size with time and cause extensive deformity of the jaws and face (Figs 5.4 to 5.6).
- Sometimes larger lesions may perforate the cortical plates and protrude outside the bone as a nodular soft tissue mass.
- Maxillary tumors can invade into the maxillary air sinus and extend further up to the orbit or the nasopharynx. Thereby leading to pressure sensation in the eyeball or nasal obstruction, etc.
- Some of the lesions may progress to ethmoidial air sinuses or even up to the cranial base.

Fig. 5.5: Ameloblastoma-III

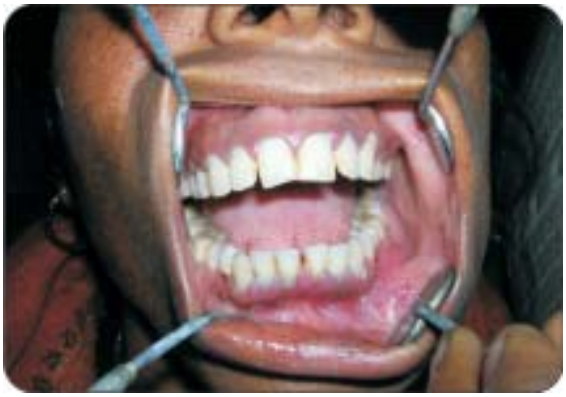

Fig. 5.6: Ameloblastoma-IV

- Extraosseous ameloblastoma often produces a small, nodular growth in the gingiva.
- Desmoplastic Ameloblastoma is a special variant, which unlike other lesions of ameloblastoma develops from the anterior part of the jaw, especially maxilla.

RADIOLOGICAL FEATURES (FIGS 5.7 TO 5.9)

- Radiographically ameloblastoma usually presents a well-defined, **multilocular**, radiolucent area in the bone with a typical "**honey-comb**" or "**soap-bubble**"appearance (Fig. 5.10). Few lesions can be **unilocular** too.
- For multilocular lesions, when the loculations are large the appearance will be 'soap bubble' type and when the loculations are small the appearance will be 'honey-comb' type.
- The larger lesions often cause expansion, distortion or even **perforation** of buccal and lingual cortical plates (Fig. 5.11).

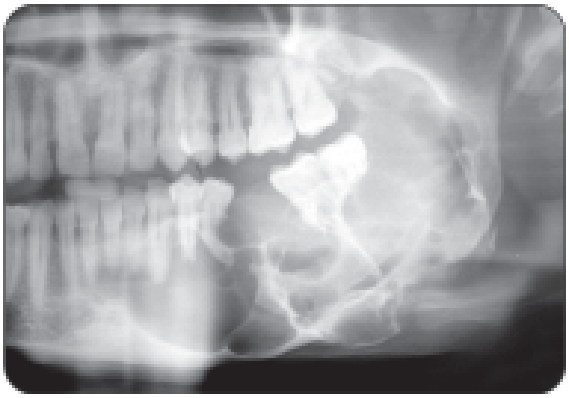

Fig. 5.7: Radiograph of ameloblastoma-I

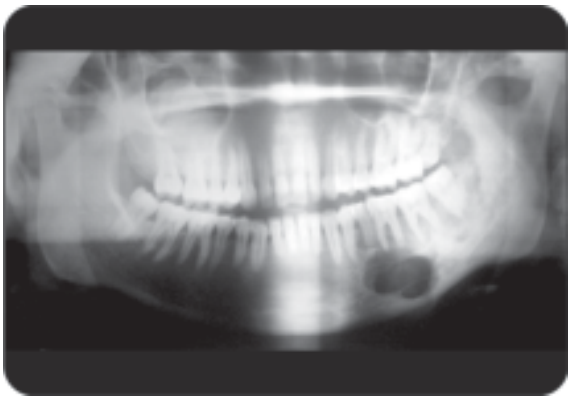

Fig. 5.8: Radiograph of ameloblastoma-II

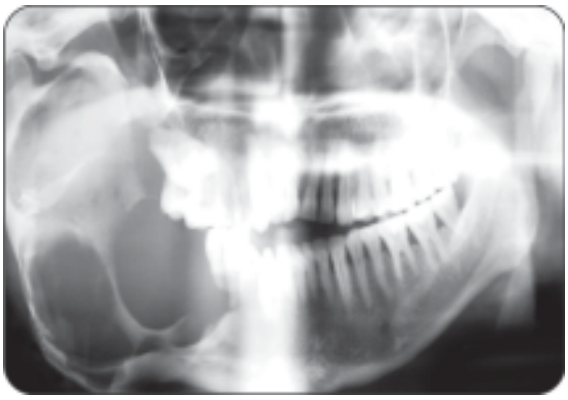

Fig. 5.9: Radiograph of ameloblastoma-III

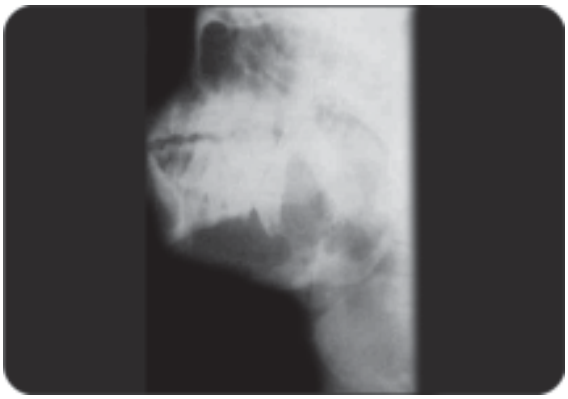

Fig. 5.10: A typical multilocular soap bubble appearance of ameloblastoma

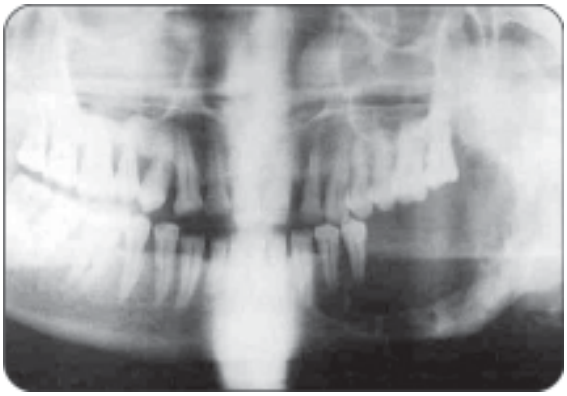

Fig. 5.11: Ameloblastoma causing large radiolucent lesion with expansion of the lower border of mandible

- In radiograph, the lesion typically exhibits an irregular and "**scalloped**" margin (Fig. 5.12).
- Resorption of roots of the adjoining normal teeth is often seen in rapidly growing lesions.
- Ameloblastoma can cause expansion of the lower border of mandible.

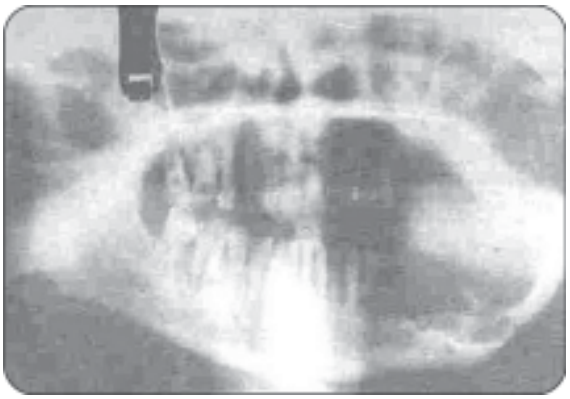

Fig. 5.12: Radiographically ameloblastoma producing large multilocular radiolucency with scalloped margin

- As the neoplasm progresses, it sometimes become associated with an impacted tooth (mostly the third molars) and in such cases the lesion may resemble a dentigerous cyst.
- Desmoplastic ameloblastoma presents a mixed radiolucent and radiopaque appearance, thus often resemble a fibrosseous lesion. It happens due to osseous metaplasia within the connective tissue (tumor cells, however do not produce any calcification in the lesion).

DIFFERENTIAL DIAGNOSIS

- Odontogenic keratocyst (primordial cyst)
- Dentigerous cyst
- Central giant cell granuloma
- Central hemangioma
- Aneurysmal bone cyst
- Pindborg's tumor
- Fibromyxoma.

MACROSCOPIC FEATURES

- On naked eye examination the tumor presents a cylindrical or fusiform swelling, which expands the bone, so severely that it can be broken by digital pressure (**egg-shell crackling**).
- Perforation of the bone with subsequent protrusion of the tumor mass outside the bony wall is often noticed.
- Cut section of ameloblastoma often appears as a "grayish-white" or "grayish-yellow" mass, which contains some 'cyst-like' spaces. However no calcified tissue is usually found within the tumor.
- Some lesions are made up entirely of solid tissue mass although most of them have some cystic spaces of varying size within them.
- Some intratumor cysts are large and contain either a straw colored fluid or a semisolid gelatinous material.
- Sometimes, one or two teeth may be present within the lesion.

HISTOPATHOLOGICAL FEATURES

Histologically ameloblastoma shows neoplastic proliferation of odontogenic epithelial cells (ameloblast-like cells), the cells exhibit their nucleus moved away from the basement membrane and this particular phenomenon is called '**reverse polarization**'.

Histologically ameloblastomas present two distinct patterns: (i) **Plexiform** and (ii) **Follicular** pattern, besides these two there are few other relatively uncommon histological patterns namely the acanthomatous pattern, basal cell pattern, granular cell pattern and desmoplastic pattern, etc.

Plexiform Ameloblastoma (Fig. 5.13)

- In this variant of ameloblastoma the neoplastic odontogenic epithelial cells proliferate in the form of "**long continuous anastomosing strands or cords**" hence the term plexiform has been given.
- This pattern of neoplastic cell proliferation is also often called a "fishnet like" pattern.
- The peripheral layer of cells of the epithelial cords are tall columnar in nature and they often resemble the **ameloblasts**.
- Reverse polarization of the nuclei of these bordering cells is indistinct.

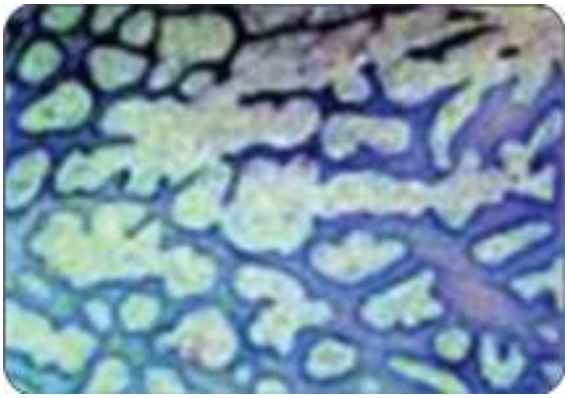

Fig. 5.13: Photomicrograph of plexiform ameloblastoma

- The triangular shaped cells situated at the center portion of the strands often resemble the **stellate reticulum** cells, while the cells located between the columnar cells and the stellate reticulum cells often resemble the **stratum intermedium**.
- The intervening connective tissue stroma is usually loose and vascular, with minimum cellularity.
- Although, much less common in comparison to the follicular type, cystifications do occur in the plexiform type of ameloblastoma, which may be either large or small in size.

Follicular Ameloblastoma (Fig. 5.14)

- In follicular type, the neoplastic odontogenic epithelial cells proliferate in the form of **multiple**, **discrete follicles** or **islands** within the fibrous connective tissue stroma.
- These follicles or islands of epithelium often resemble the enamel organ of the developing tooth germ.
- Each follicle-like structure is bordered on the periphery by a single layer of **tall columnar cells** resembling ameloblasts. These cells have well-defined nuclei, which are situated away from the basement membrane on the opposite pole, this type of nuclear positioning is called "**reverse polarization**".
- Sometimes these peripheral cells bordering the follicles are cuboidal in nature and resemble basal cells.
- The cells located at the center of the follicles are loosely arranged and are polyhedral or triangular in shape. These cells are widely separated from one another and they often resemble stellate reticulum cells (normally seen in the bell stage of odontogenesis).
- While the cells located in between the peripheral and the central group of cells, appear as the stratum intermedium.
- Occasionally, a distinctive zone of hyalinization is seen surrounding the follicles.
- Microcyst formation is often observed inside these follicles and the cysts sometimes may be large enough to occupy the entire inner part of the follicles.
- Microcyst formations can also be seen within the connective tissue stroma.
- Most of the follicular ameoloblastomas exhibit cyst formation particularly, if the lesion is large.
- The intervening connective tissue stroma is delicate in nature and it consists chiefly of collagen bundles, fibroblasts and blood vessels, etc.
- Extraosseous ameloblastomas also exhibit follicular structures as seen in the conventional intraosseous ameloblastomas, however the lining cells are often basaloid in nature.

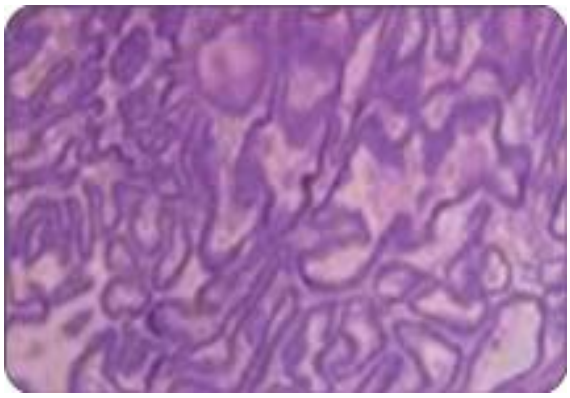

Fig. 5.14: Photomicrograph of follicular ameloblastoma

OTHER HISTOLOGICAL PATTERNS OF AMELOBLASTOMA

Besides the plexiform and the follicular patterns, some other histological types of ameloblastomas can occur and they are as follows:

Acanthomatous pattern of ameloblastoma: It occurs in relation to follicular ameloblastoma and in this type, the stellate reticulum-like cells at the center of the follicles undergo squamous metaplasia. Sometimes, the neoplastic epithelial cells can even produce "keratin pearls". Within the follicles the neoplastic cells may exhibit individual cell keratinization. Metaplasia does not indicate any aggressive nature of the tumor.

Granular cell pattern of ameloblastoma: In this type structurally resembles the follicular Ameloblastoma. However the cytoplasm of the stellate reticulum-like cells and even the ameloblast-like cells appear swollen and the cells are often densely packed with multiple, coarse, eosinophilic granules.

Key points of ameloblastoma

- Ameloblastoma is the most common odontogenic neoplasm of the oral cavity and it is a benign locally aggressive tumor arising from the odontogenic epithelium.
- It occurs between 2nd to 5th decade of life, more often in males.
- Ameloblastoma in most of the cases involve the mandible especially in the molar-ramus area, maxillary bone is also commonly affected by the disease.
- Clinically, ameloblastoma produces slow enlarging, painless, ovoid or fusiform, bony hard swelling of the jaw.
- Some lesions cause expansion and distortion of the cortical plates of the jawbone, pain, paresthesia, displacement and mobility of the regional teeth and gross facial asymmetry.
- Untreated lesions cause extensive destruction and thinning of bone, leading to 'egg-shell' crackling and pathological fracture, etc.
- Radiographically ameloblastoma usually presents a well-defined, multilocular, radiolucent area in the bone with a typical "honey-comb" or "soap-bubble" appearance. The border of the lesion is often scalloped.
- Histologically, the tumor shows neoplastic proliferation of odontogenic epithelial cells (ameloblast-like cells) in plexiform or follicular patterns.
- In plexiform pattern, the neoplastic odontogenic epithelial cells proliferate in the form of long continuous anastomosing strands cords.
- In follicular pattern, the neoplastic odontogenic epithelial cells proliferate in the form of multiple, discrete follicles or islands.
- Treatment is done by surgical enucleation of the tumor and through curettage.

Histologically this lesion often resembles "granular cell myoblastoma" and ultrastructural studies indicate that these granules are either lysosomal elements or residual bodies.

Basal cell pattern of ameloblastoma: This lesion shows excessive proliferation of uniform looking basaloid cells in several nests, with the absence of stellate reticulum or other centrally located cells. The cells bordering the nests are cuboidal in shape rather than columnar type and these tumor often resemble basal cell carcinomas.

Desmoplastic pattern of ameloblastoma: In this type the epithelial islands or the strands are small in size and the cells are cuboidal in shape and are darkly stained. The tall columnar ameloblast-like cells are scanty in this lesion.The cells of the epithelial components are widely separated by dense fibrous tissue and the neoplastic cells often infiltrate into the surrounding trabaecular bone.

TREATMENT

Surgical enucleation of the tumor and thorough curettage of the surrounding bone. Recurrence is common. Sometimes, radical surgical approach may have to be adopted in cases of repeated recurrences. Some tumors may cause distant metastasis also.

UNICYSTIC AMELOBLASTOMA

Unicystic ameloblastoma is separate entity from conventional ameloblastoma (Figs 5.15 to 5.19). It constitutes about 10 to 15 percent of all intraosseous ameloblastomas.

ORIGIN

The tumor arises either as a de novo lesion or it develops due to neoplastic transformation of the pre-existing cystic epithelium.

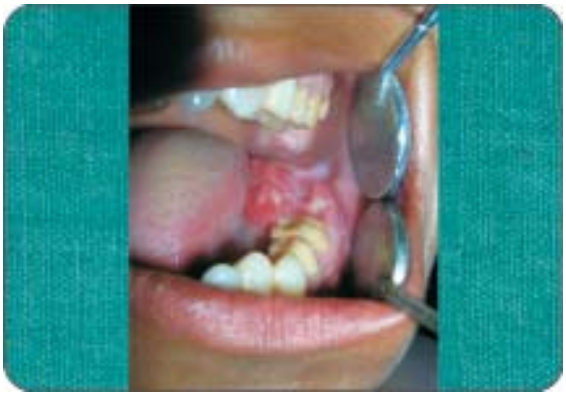

Fig. 5.15: Ameloblastoma turning into malignancy-I

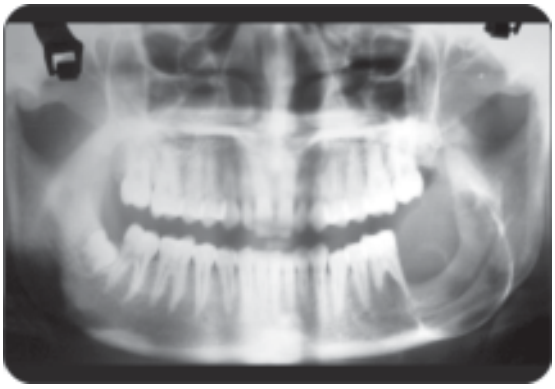

Fig. 5.16: Radiograph of ameloblastoma turning into malignancy

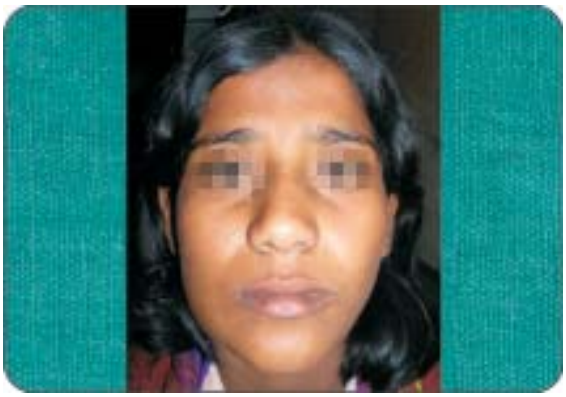

Fig. 5.18: Unicystic ameloblastoma

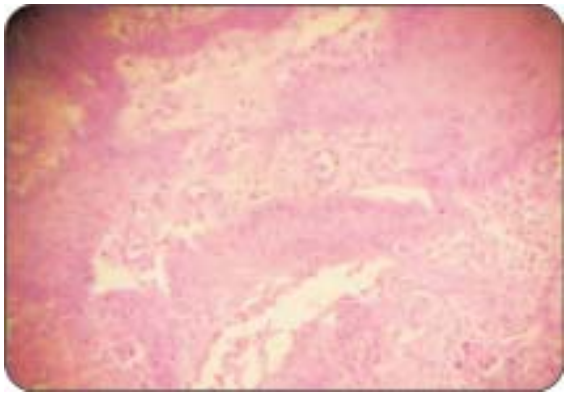

Fig. 5.17: Photomicrograph of ameloblastoma turning into malignancy

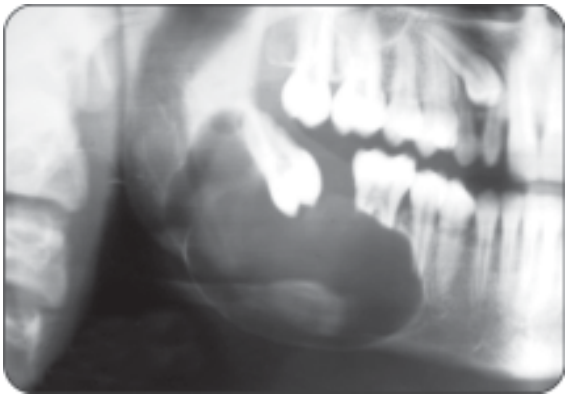

Fig. 5.19: Radiograph of unicystic ameloblastoma

CLINICAL FEATURES

Age: Young people are mostly affected (2nd decade of life).

Site: Mandible is predominantly involved.

CLINICAL PRESENTATION

Unicystic ameloblastoma produces painless swelling of the jaw with expansion of the cortical plates and disturbance in occlusion, etc (Fig. 5.18). Some lesions can be asymptomatic throughout the clinical course and are discovered incidentally during routine radiographic examination.

RADIOGRAPHIC FINDING

The lesion often exhibits a well-circumscribed radiolucent area in the bone that often surrounds the crown of an impacted 3rd molar tooth (Fig. 5.19).

HISTOPATHOLOGY

Histologically, unicystic ameloblastomas are of three distinct types—luminal type, intraluminal type and mural type.

***Luminal unicystic ameloblastoma*:** This type of unicystic ameloblastoma occurs on the luminal surface of a cyst, base of the tumor is made up of cystic epithelium, backed by a connective tissue wall. The lesion consists of a basal layer of columnar or cuboidal cells, which exhibit reverse polarity of the nuclei. The overlying cells are loosely arranged and resemble stellate reticulum.

Intraluminal unicystic ameloblastoma: This type of lesion produces several nodular growths; which project from the cyst lining into the cystic lumen. The lesion sometimes fill up the entire lumen and few lesions resemble plexiform ameloblastomas.

Mural unicystic ameloblastoma: In this lesion the neoplastic cells instead of projecting inside the cystic lumen infiltrates into the connective tissue wall of the cyst capsule.

TREATMENT

Enucleation and currattage, recurrence rate is low as compared to the conventional ameloblastomas.

ADENOMATOID ODONTOGENIC TUMOR (AOT)

DEFINITION

The adenomatoid odontogenic tumor is a relatively uncommon, well-circumscribed, odontogenic neoplasm characterized by the formation of multiple 'ducts-like' structures by the neoplastic epithelial cells.

The name 'adenomatoid' has been given to the neoplasm because histologically numerous duct-like structures are often interspersed throughout the lesion, which gives a **glandular** or **adenomatoid** appearance to it.

ORIGIN

The tumor probably arises from the **reduced enamel epithelium**, during the presecretory phase of enamel organ development. Some other investigators believe that it develops from either the dental lamina or from a pre-existing dentigerous cyst.

CLINICAL FEATURES

Age: The tumor usually occurs in the younger age (e.g. second and third decade of life). Rarely it occurs in the older age.

Sex: Females are more commonly affected in comparison to the males, with a ratio of 2:1.

Site: The lesion most typically occurs in the **maxillary anterior region** (upper lateral incisor-canine area). Sometimes it can occur in the premolar region. Rarely does it involve the mandible in the angle-ramus area. In about 70% cases, the neoplasms occur in association with an unerupted tooth. Some lesions develop extra-orally in relation to the gingiva (Figs 5.20 and 5.21).

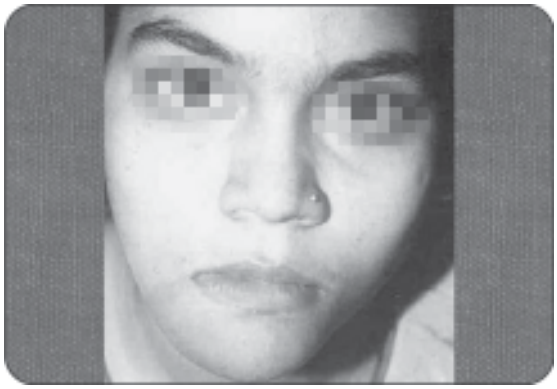

Fig. 5.20: Adenomatoid odontogenic tumor developing from the Rt. Side of mandible

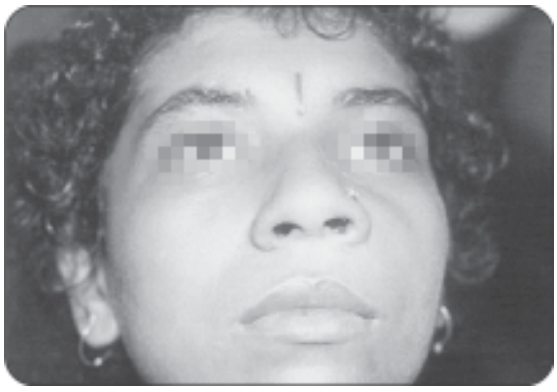

Fig. 5.21: Adenomatoid odontogenic tumor developing on the upper left canine region

CLINICAL PRESENTATION

- The tumor usually presents a slow enlarging, small, bony hard swelling in the maxillary anterior region (Figs 5.22 to 5.24).
- The lesion often causes elevation of the upper lip on the involved side, which often results in a change in the facial profile.
- Displacement of the regional teeth, mild pain and expansion of the cortical bones are usually present (Fig. 5.24A).
- If the lesion is very large it may cause severe expansion of the bone, which may sometimes elicit fluctuations.
- The tumor is often associated with an uperupted tooth (mostly the upper canine). Many lesions are asymptomatic in nature.
- Occasionally, adenomatoid odontogenic tumor may occur extra-osseously in the anterior maxillay gingiva.

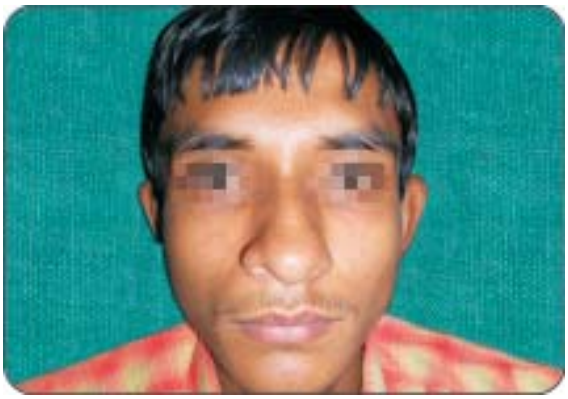

Fig. 5.22: Adenomatoid odontogenic tumor-I

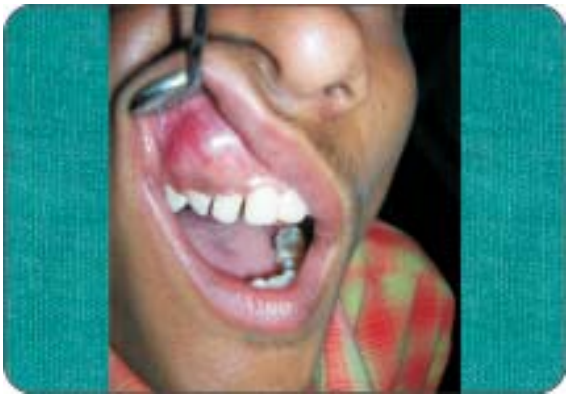

Fig. 5.23: Adenomatoid odontogenic tumor-II

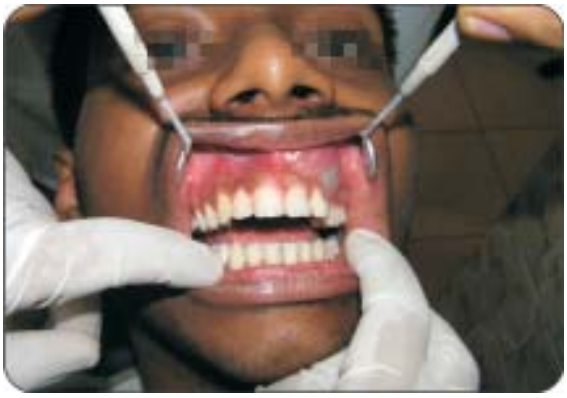

Fig. 5.24: Adenomatoid odontogenic tumor

- The extraosseous or peripheral tumor produces a solitary painless, asymptomatic nodular swelling on the gingiva predominantly on the facial surface.

RADIOLOGICAL FEATURES

- Radiographically, adenomatoid odontogenic tumor presents a well-circumscribed, unilocular, radiolucent area, which often encloses a tooth or tooth-like structure (mostly maxillary canine) (Fig. 5.25).
- Multiple small, radiopaque foci of varying radiodensity may be present inside the lesion and the finding is known as '**snow-flake**' calcifications.

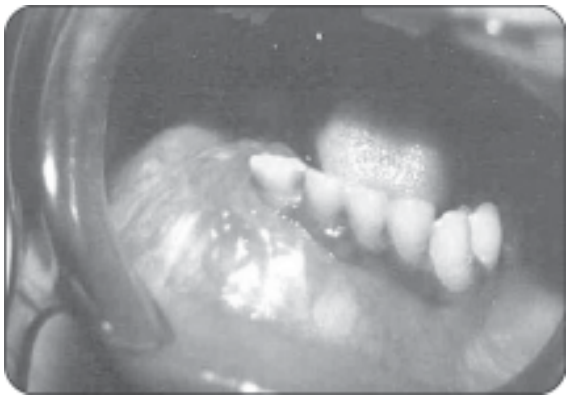

Fig. 5.24A: The lesion causing severe expansion of the bone

Key points of adenomatoid odontogenic tumor (AOT)

- The adenomatoid odontogenic tumor is a relatively uncommon, well-circumscribed, benign, odontogenic neoplasm.
- The tumor commonly occurs in the anterior part of maxilla (above the lateral incisor and canine tooth) and it has a definite female predilection.
- Clinically, AOT shows slow enlarging, small, bony hard swelling in the maxillary anterior region with elevation of the upper lip and facial asymmetry.
- Radiograph shows well-circumscribed, unilocular, radiolucent area, which sometimes contain few, small radiopaque foci.
- Microscopically, adenomatoid odontogenic tumor exhibits spindle shaped, neoplastic odontogenic epithelial cells proliferating in multiple "**duct-like**" patterns.
- The duct-like or tubular structures characteristically give the lesion an adenomatoid or glandular appearance, which are bordered on the periphery by tall columnar cells and the central lumen is often filled with an eosinophilic coagulum.
- Treatment is done by surgical enucleation.

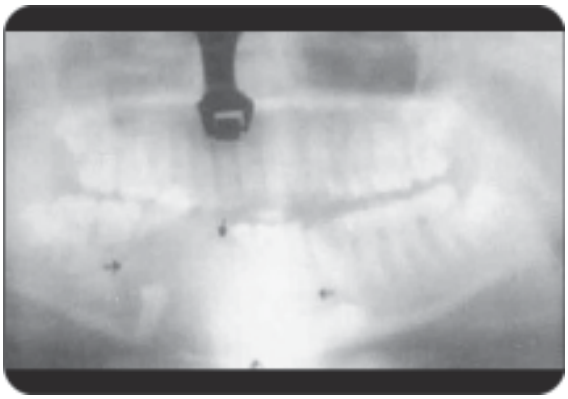

Fig. 5.25: Radiologically AOT producing a large irregular radiolucent lesion enclosing an entire tooth

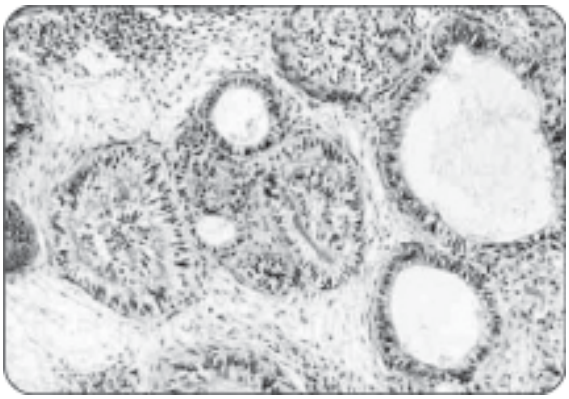

Fig. 5.26: Photomicrograph of adenomatoid odontogenic tumor-I

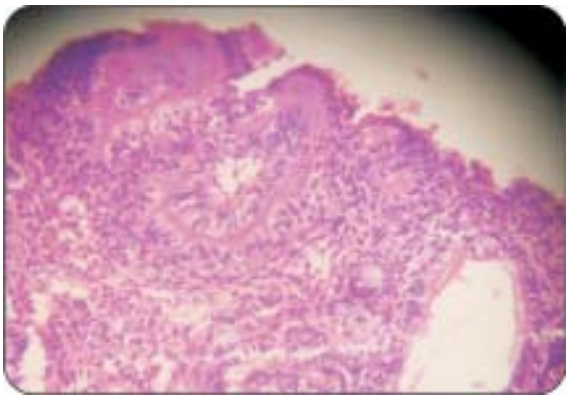

Fig. 5.27: Photomicrograph of adenomatoid odontogenic tumor-II

- Some lesions may present unilocular, well-defined radiolucencies between the roots of the erupted teeth and they do not enclose any tooth.
- Expansion and distortion of the cortical plates and displacement of the roots of the adjoining teeth are sometimes seen.
- The border of the lesion is not well corticated and it consistently engulfs the impacted tooth including its root. This feature differentiates adenomatoid odontogenic tumor from dentigerous cyst, since the later lesion encloses only the crown portion of an impacted tooth.

DIFFERENTIAL DIAGNOSIS

- Dentigerous cyst
- Globulomaxillary cyst
- Lateral periodontal cyst
- Odontome
- Unicystic ameloblastoma
- Ossifying or cementifying fibroma
- Calcifying epithelial odontogenic tumor
- Calcifying epithelial odontogenic cyst.

HISTOPATHOLOGICAL FEATURES (FIGS 5.26 AND 5.27)

- Microscopically, adenomatoid odontogenic tumor reveals spindle shaped, neoplastic odontogenic epithelial cells proliferating in multiple "**duct-like**" patterns, within a thin but well-vascularized stroma.
- The presence of these duct-like or tubular structures is very characteristic, which often give the lesion an adenomatoid or glandular appearance. However no actual glandular element is found in this tumor.
- Each duct-like structure exhibits a central space, which is bordered on the periphery by a single layer of tall columnar cells resembling ameloblasts or preameloblasts.
- Nuclei of these ameloblast like cells are often polarized away from the central space; Moreover sometimes these bordering cells can be cuboidal in nature.
- Serial sectioning reveals that the lumens are blind ended and they probably represent an abortive attempt at enamel organ formations.
- The lumen of the duct-like structures is generally filled with a homogenous **eosinophilic coagulum** (mostly amyloids). Although some lumens can be empty.
- Small foci of calcifications are often seen scattered throughout the lesion (sometimes even larger masses are found). This type of

calcification within the lesion probably indicates an abortive attempt towards formation of enamel, dentin or cementum by the tumor cells.
- In some cases, the neoplastic cells are arranged in solid nests, sheets or rosette-like patterns and these cells sometimes may even fill up the entire lumen of some of the ducts.
- Droplets of amorphous (PAS positive) eosinophilic materials are frequently found in between the neoplastic cells.
- In some adenomatoid odontogenic tumors, the neoplastic cells proliferate as narrow anastomosing cords within the loose, thin connective tissue stroma.
- The neoplasm is almost always well-encapsulated and the connective tissue stroma may occasionally contain diffuse areas of hyaline materials.

TREATMENT

By surgical enucleation. The associated tooth has to be removed and recurrence is rare.

CALCIFYING EPITHELIAL ODONTOGENIC TUMOR (CEOT)

The calcifying epithelial odontogenic tumor is a locally aggressive neoplasm, which is also known as Pindborg's tumor (named after Prof JJ Pindborg, who first reported it).

ORIGIN

The lesion arises from either the cells of the stratum intermedium of the enamel organ or the reduced enamel epithelium or even the remnants of the denral lamina.

Its biologic behavior is similar to that of ameoblastoma. However, it differs from ameloblastoma by the fact that it is composed of spherical cells and not the ameloblast-like cells as seen in ameloblastoma. Moreover calcifying epithelial odontogenic tumor always contains some calcified materials within it mass, which is never seen in ameloblastoma.

CLINICAL FEATURES

Incidence rate: The calcifying epithelial odontogenic tumor constitutes about one percent of all odontogenic neoplasms.

Age: The tumor commonly occurs in middle-aged adults (mean age 40 years).

Sex: Both sexes are almost equally affected.

Site: The mandible (two-third number of cases) is involved more often than the maxilla (one-third number of cases), the molar region is the most common site of occurrence followed by the premolar region. Rarely the tumor develops extraosseously from the gingiva as peripheral lesions. In about 50% cases the neoplasms are associated with impacted teeth.

CLINICAL PRESENTATION (FIGS 5.28 TO 5.31)

- The tumor usually presents a slow enlarging, painless swelling of the jaw with expansion and distortion of the cortical plates.
- The swelling is usually bony hard and clinically it can be either well defined or diffuse in nature.
- Displacement of regional teeth, with derangement of occlusion and facial asymmetry, etc. are commonly present.
- Pain, paresthesia and other related symptoms may develop on rare occasions, and few lesions may be even completely asymptomatic.
- Large maxillary lesions may invade into the antrum or the nasal floor and such lesions occasionally cause nasal airway obstruction, epistaxis and proptosis of the eyeball, etc.
- Extraosseous or peripheral lesions may cause nonspecific, sessile, superficial soft tissue swellings of gingiva either in the tooth bearing or the edentulous areas of the anterior jaw.

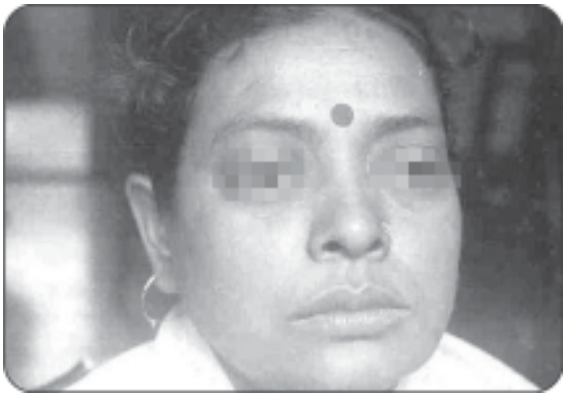

Fig. 5.28: Pindborg's tumor causing swelling of the Lt. sided mandible

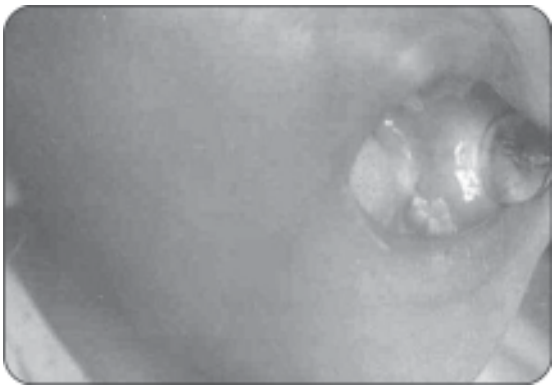

Fig. 5.29: Intraoral view of the same patient

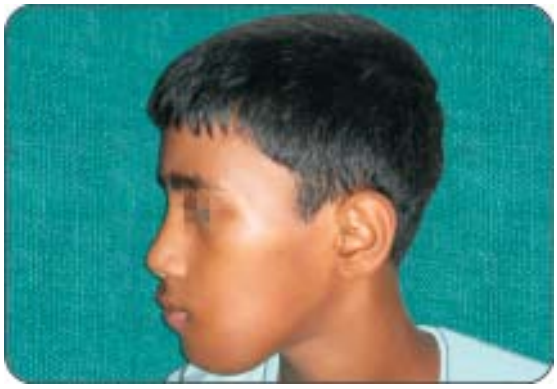

Fig. 5.30: Calcifying epithelial odontogenic tumor-I

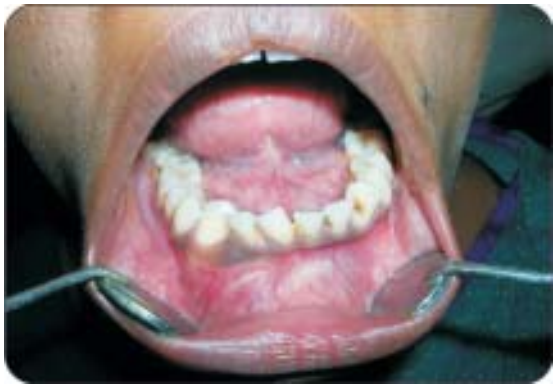

Fig. 5.31: Calcifying epithelial odontogenic tumor-II

RADIOLOGICAL FEATURES

- Radiographically calcifying epithelial odontogenic tumor usually presents a well-defined, **multilocular** (rarely unilocular) **radiolucent area** in the jaw.
- **Calcifications within the tumor** is a characteristic finding in the calcifying epithelial odontogenic tumors and radiographically it often exhibits **multiple, small, radiopaque foci** of varying radiodensity within the radiolucent zone produced by the tumor (Fig. 5.32).

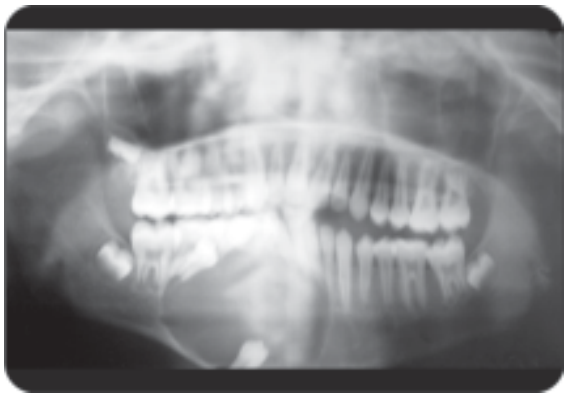

Fig. 5.32: Radiograph of calcifying epithelial odontogenic tumor

- This type X-ray of calcification within the tumor often produces a typical "**driven snow**" appearance.
- The border of the lesion is often scalloped and the lesion frequently causes expansion and destruction of the cortical plates of jawbones.
- In approximately half of the cases, an unerupted tooth (mostly mandibular third molar) may be seen within the tumor. Moreover the calcifications which occur within the tumor are seen mostly around the crown of this tumor associated tooth.
- Perforation of the cortical plates, pathological fractures and root resorptions, etc. are seen in few cases.
- Although larger lesions produce a mixed feature of radiolucency and radiopacity, smaller lesions of a calcifying epithelial odontogenic tumor often produce only unilocular radiolucencies (Fig. 5.33).
- The lesion may or may not be well-demarcated from the surrounding normal tissue.
- Peripheral (extraosseous) lesions sometimes cause superficial 'cupped out' erosion of the cortical bone.

DIFFERENTIAL DIAGNOSIS

- Calcifying epithelial odontogenic cyst
- Adenomatoid odontogenic tumor
- Poorly differentiated carcinoma

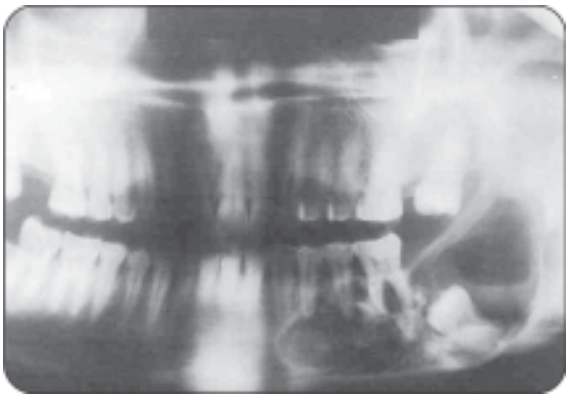

Fig. 5.33: Pindborg's tumor producing a large radiolucent area containing multiple radiopaque foci

- Ameloblastoma
- Ameloblastic fibro-odontome
- Dentigerous cyst
- Central ossifying or cementifying fibroma.

HISTOPATHOLOGICAL FEATURES (FIG. 5.34)

- Histologically, the tumor reveals sheets or islands of closely packed, **polyhedral epithelial cells,** in a noninflammed connective tissue stroma.
- Sometimes the neoplastic cells may have a '**cribriform**' arrangement and they enclose areas of hyalinized stoma.
- The tumor cells contain oval-shaped nuclei, with prominent nucleoli and a homogenious eosinophilic cytoplasm.
- Few cells may have multiple or a bizarre giant hyperchromatic nuclei (the later is not indicative of malignancy since mitotic activity is rare).
- **Prominent intercellular bridges** and distinct cell boundaries are characteristically seen in the tumor.
- Some amount of homogenous, hyaline materials is often deposited in between the tumor cells, which stain like "**amyloids**".
- One of the most distinctive histological characteristics of calcifying epithelial odontogenic tumor is the presence of **several calcified bodies or masses within the lesion**.
- These calcified masses are hematoxyphilic in nature and are present as concentrically laminated rings **(Liesegang rings)** in and around the degenerating tumor cells.
- Sometimes individual calcified structures are fused together to form a large complex mass within the tissue.
- Some tumors exhibit excessive cellularity and contain very little calcified mass within the tumor whereas other tumors may have diffuse large calcified areas with only small islands or nests of epithelial cells.
- In few tumors large numbers of **"clear cell"** are found and because of this, the tumor often

Key points of calcifying epithelial odontogenic tumor

- Calcifying epithelial odontogenic tumor is a locally aggressive, benign odontogenic tumor, whose biologic behavior is similar to that of amloblastoma.
- The tumor predominantly affects posterior part of the jaws, and clinically produces slow enlarging, painless swelling with expansion and distortion of the cortical plates.
- Radiographically, calcifying epithelial odontogenic tumor presents a well-defined, multilocular radiolucent area, which contains multiple, small, radiopaque calcified foci of varying radiodensity.
- This type calcification within the tumor often produces a typical "driven snow" appearance.
- Histologically, the tumor reveals sheets or islands of closely packed, polyhedral epithelial cells, in a noninflamed connective tissue stroma.
- The neoplastic cells have hyperchromatic nuclei and prominent intercellular bridges.
- Several calcified substances and amyloids are characteristically present in the lesion.
- Surgical enucleation is the treatment of choice.

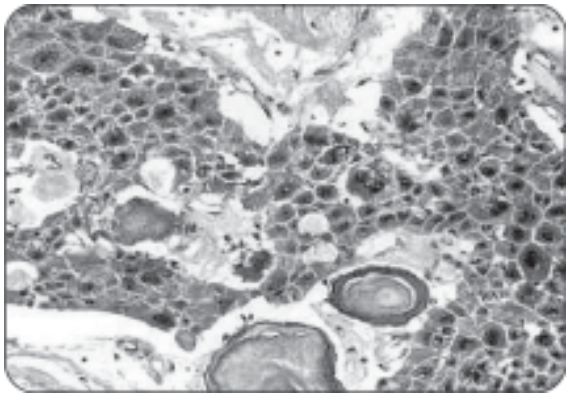

Fig. 5.34: Photomicrograph of Pindborg's tumor

resembles the clear cell variant of muco-epidermoid tumor.
- Calcifying epithelial odontogenic tumor is non encapsulated lesion and sometimes it is locally aggressive in nature.

TREATMENT

By surgical enucleation. Incomplete removal of the lesion is likely to be followed by recurrences.

SQUAMOUS ODONTOGENIC TUMOR

DEFINITION

Squamous odontogenic tumors are rare, sometimes multifocal, potentially aggressive neoplasms derived from the odontogenic epithelium.

ORIGIN

This neoplasm was first reported in the year 1975 and it probably originates from the following tissue remnants found on the lateral root surfaces of the erupted teeth:
- Remnants of dental lamina.
- Cell rests of Malassez.

CLINICAL FEATURES

Age: It occurs more commonly among young adults.

Sex: Female predilection.

Site: Maxillary incisor-canine area and mandibular molar area. Sometimes the neoplasm can be multicentric.

PRESENTATION

- Initially, there can be a painless swelling on the gingival areas of the jaw with mobility and looseness of the regional teeth (Fig. 5.35).
- Intraosseous lesions are usually small and slow enlarging.
- There can be local tenderness in the area upon palpation.
- Many lesions are asymptomatic and are discovered incidentally during radiographic examinations.

RADIOGRAPHIC FEATURES (FIG. 5.36)

- Radiographically, squamous odontogenic tumor presents a well-circumscribed, often

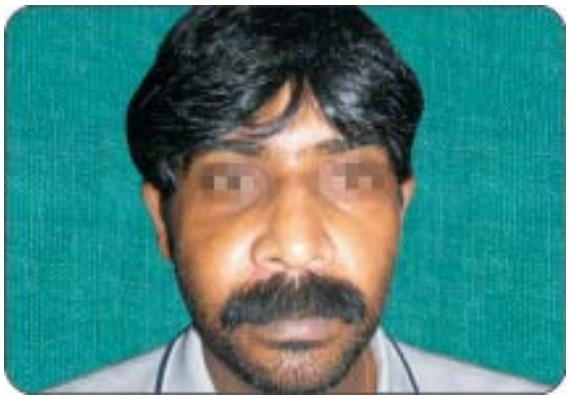

Fig. 5.35: Squamous odontogenic tumor

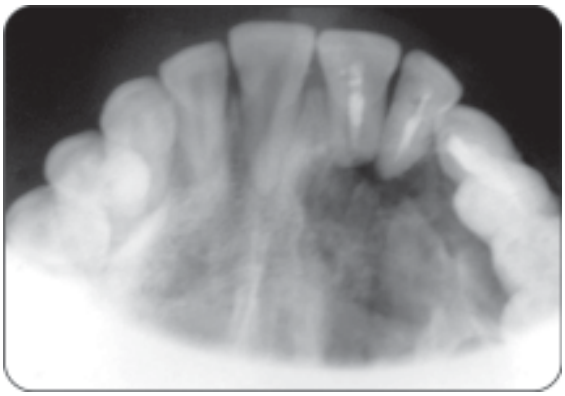

Fig. 5.36: Radiograph of squamous odontogenic tumor

semilunar or triangular shaped, unilocular radiolucent area with sclerotic border.
- These lesions are interspersed between contagious teeth near their roots.
- Some lesions can be multilocular.
- Resorptions of root are usually absent.
- Some lesions of squamous odontogenic tumors mimic chronic periodontitis due to similar type of extensive bone loss.

HISTOPATHOLOGY

- Microscopically, squamous odontogenic tumor presents **irregularly-shaped, islands of well-differentiated squamous epithelium** in a mature fibrous connective tissue stroma (Fig. 5.37).
- The islands can be of round or oval in shape and there is absence of peripheral palisaded or polarized basal cells.
- **Individual cell keratinization** is often seen in this tumor, moreover focal areas keratin or parakeratin formation by the neoplastic epithelial cells is also sometimes noticed.

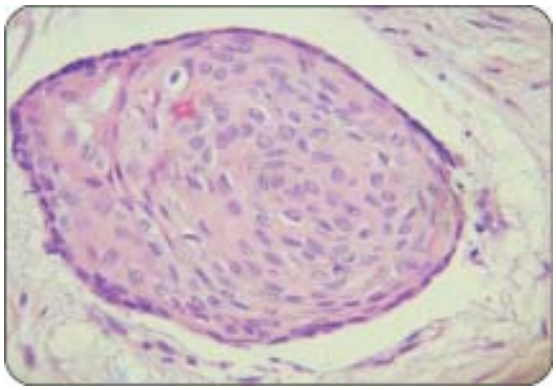

Fig. 5.37: Photomicrograph of squamous odontogenic tumor

- The basal cell layer in squamous odontogenic tumor is usually made up of inactive looking cuboidal cells.
- The remaining epithelial cells of the islands are composed of mature intermediate type of cells with prominent desmosomal bridges.
- Many epithelial islands reveal central areas of microcyst formations.
- Some of the epithelial islands contain spherical or irregularly shaped calcified structures, indicating dystrophic calcifications within the tumor.
- Similar calcifications can also be found within the connective tissue stroma as well.
- Although the tumor is benign, the tumor cells sometimes invade into the adjacent tissues (it is more often seen in maxillary tumors).

DIFFERENTIAL DIAGNOSIS

- Acanthomatous ameloblastoma
- Lateral periodontal cyst
- Squamous cell carcinoma
- Central ossifying or cementifying fibroma
- Histiocytosis-X
- Collateral type of keratocyst.

TREATMENT

Surgical enucleation with thorough curettage.

AMELOBLASTIC FIBROMA

Ameloblastic fibroma is a true benign odontogenic tumor in which both the epithelial and the mesenchymal elements are neoplastic (In ameloblastoma only the epithelium is neoplastic).

CLINICAL FEATURES

Age: It occurs usually below the age of 20 years (average age 14 years).

Sex: More often in males than females.

Site: Mandibular posterior (premolar-molar) region is the most common site, maxillary tumors are usually rare.

CLINICAL PRESENTATION (FIGS 5.38 TO 5.41)

- A slow growing, painless, bony hard swelling of the jaw.
- Few lesions can be completely asymptomatic and discovered accidentally during routine examinations.
- There may be mobility of the regional teeth, with obvious facial asymmetry.
- The tumor develops predominantly above the impacted or unerupted molar teeth as a pericoronal lesion.
- Over 90 percent cases it is associated with an impacted tooth.
- Untreated lesions can be exceptionally large.

RADIOLOGICAL FEATURES (FIGS 5.42 AND 5.43)

On radiograph, the tumor usually presents a well-defined, unilocular or multilocular radiolucent area that often resembles ameloblastoma or dentigerous cyst.

Lesions are well corticated and they vary considerably in size.

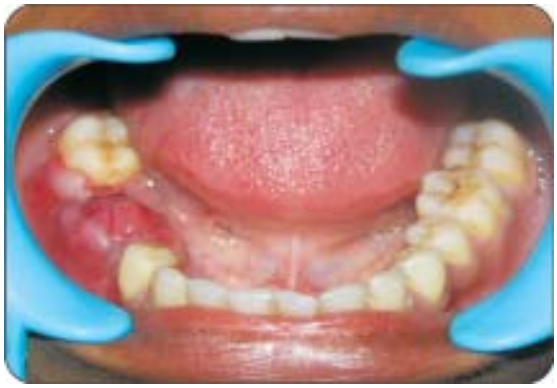

Fig. 5.38: Ameloblastic fibroma-I

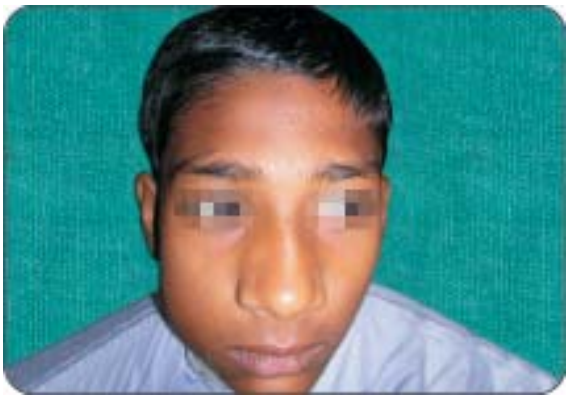

Fig. 5.39: Ameloblastic fibroma-II

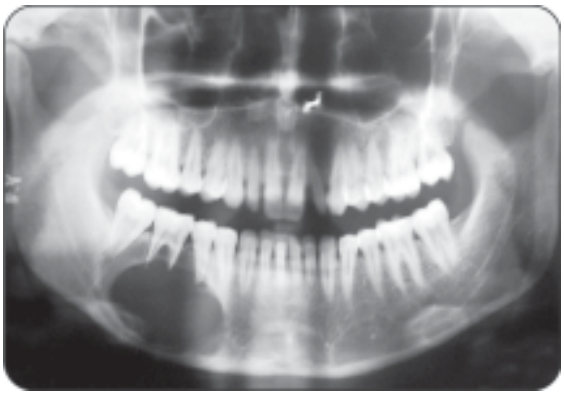

Fig. 5.42: Radiograph of ameloblastic fibroma-I

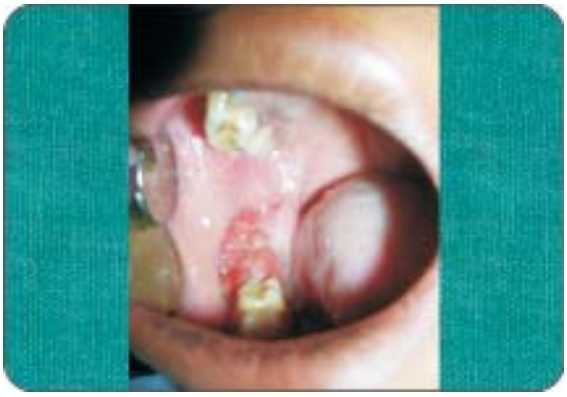

Fig. 5.40: Ameloblastic fibroma-III

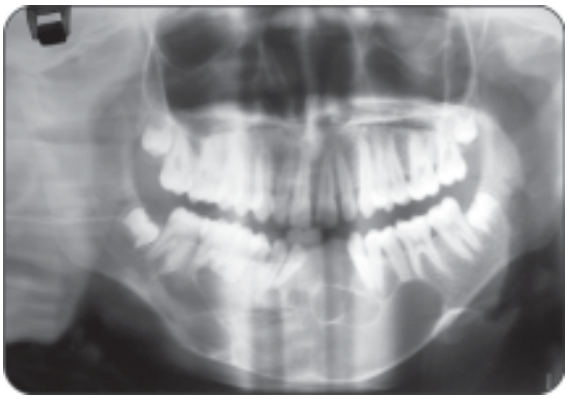

Fig. 5.43: Radiograph of ameloblastic fibroma-II

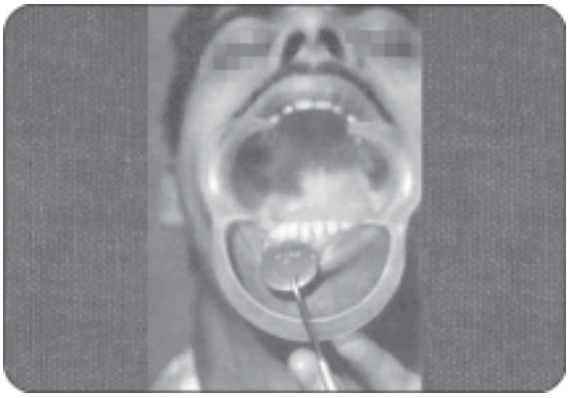

Fig. 5.41: Ameloblastic fibro-odontome of Rt. maxillary posterior region

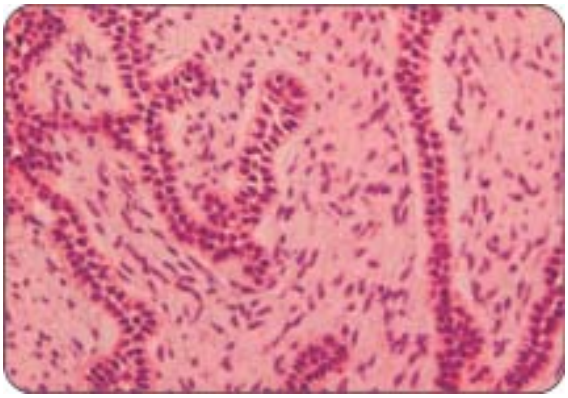

Fig. 5.44: Photomicrograph of ameloblastic fibroma-I

HISTOPATHOLOGICAL FEATURES (FIGS 5.44 AND 5.45)

- Ameloblastic fibroma histologically consists of neoplastic epithelial as well as mesenchymal components of odontogenic tissue.
- The epithelial components of the tumor consist of multiple sharply defined, strands, islands or narrow cords.
- Sometimes the tumor cells exhibit a 'mushroom' proliferation within a loose connective tissue stroma.
- The epithelial cords may be as thin as only few cells thickness, the epithelial islands are small and discrete, and they resemble the follicular stage of a developing enamel organ.
- The epithelial components are circumscribed by a basal membrane and at the periphery

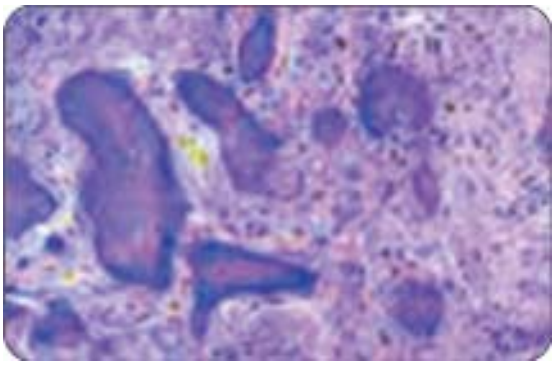

Fig. 5.45: Photomicrograph of ameloblastic fibroma-II

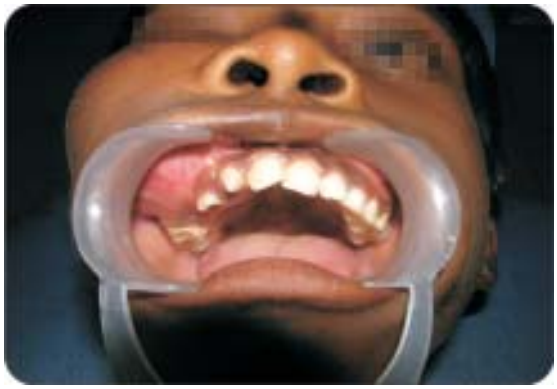

Fig. 5.46: Ameloblastic fibro-odontome

these are bordered by tall columnar cells resembling ameloblasts.

- The cells, which are located at the center of the islands or strands, resemble the stellate reticulum cells.
- Although the epithelial components of this neeplasm resemble ameloblastoma but the stellate cells are much less abundant and cyst formation is rare.
- There may be a narrow cell free zone of hyaline connective tissue bordering the epithelial component.
- The mesenchymal component of the tumor consists of plump stellate or ovoid cells with a loose fibroblastic stroma that often resembles the dental papilla of the developing tooth.
- Diffuse area of hyalinized acellular tissue is also found in the tumor.

TREATMENT

By surgical excision with thorough curettage of the bone. Recurrence is uncommon.

AMELOBLASTIC FIBRO-ODONTOME

It is a benign neoplasm of odontogenic origin and is characterized by the presence of combined features of ameloblastic fibroma along with the presence of calcified enamel or dentin like tissues.

CLINICAL FEATURES

Age: Children and young adults.

Sex: No predilection.

Site: Posterior region of jaw, more common in mandible.

CLINICAL PRESENTATION

- Most of the lesions are asymptomatic.
- Lesions are often associated with an impacted or missing tooth (Fig. 5.46).
- Larger lesions cause progressive, painless swelling of the jaw with expansion of the cortical plates.
- Untreated lesions can result in severe facial deformity.

RADIOLOGICAL APPEARANCE

Radiographs show unilocular radiolucent area (rarely multilocular) containing multiple radiopaque foci having radiodensity similar to that of tooth. Sometimes, a solid conglomerated mass is seen inside the lesion, unerupted tooth is often present near the lesion or sometimes the crown of the tooth is included in the lesion. Early lesions may be comparatively radiolucent as the calcified tissues were yet to form.

HISTOPATHOLOGY (FIG. 5.47)

- Histologically the tumor exhibits neoplastic odontogenic epithelial cells proliferating in the form of small discrete islands or narrow cords as may be seen in ameloblastic fibromas.
- Connective tissue stroma is loose, primitive looking and it often resembles the dental papilla.
- Multiple calcified foci of enamel and dentin matrix are found near the epithelial components.

TREATMENT

Surgical excision and curettage.

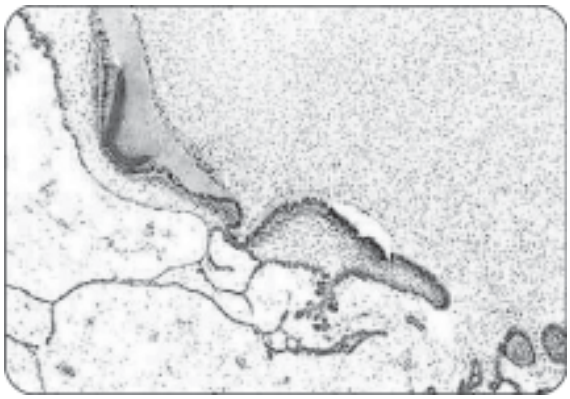

Fig. 5.47: Photomicrograph of ameloblastic fibrodontome

ODONTOMES

DEFINITION

Odontomes are a group of common hamartomatous odontogenic lesions with limited growth potential. These lesions are capable of producing normal appearing enamel, dentin, cementum and pulp, etc. in an unorganized fashion.

The tumor probably occurs during the development of teeth at a point after the stage of histodifferentiation but prior to the stage of morphodifferentiation.

TYPES

Two types of odontomes are commonly recognized:

A. Compound odontome, and
B. Complex odontome (both these lesions are closely related malformation).

Complex odontome: It consists of a completely disorganized and diffuse mass of odontogenic tissue with haphazardly arranged enamel, dentin and cememtum.

Compound odontome: Compound odontome presents collections of numerous small, discrete, tooth-like structures. Most odontogenic tissues in compound odontome bear superficial anatomical resemblance to normal teeth.

CLINICAL FEATURES

Frequency: Odontomes represent about 7% of all odontogenic neoplasms.

Age: These lesions usually occur among children or young adults (preferably in their second decade of life).

Sex: Both sexes are almost equally affected or there may be a slight male predominance.

Site: Maxilla is more commonly affected than the mandible. Odontomes are most commonly seen in the pericoronal area of the permanent teeth.

Compound odontomes usually involve the anterior part of the maxilla (intercanine area).

Complex odontomes often involve the posterior (premolar-molar) region of the jaw and are slightly more common in mandible. Some lesions may occur extraosseously in the gingival soft tissues.

CLINICAL PRESENTATION

- Odontomes generally produce small, asymptomatic lesions, which are detected incidentally.
- The lesions vary in size greatly, it can be as small as a tooth or it may be as large as six centimeters in diameter.
- In few cases, they may produce large, bony hard swellings of the jaw, with expansion of the cortical plates and displacement of the regional teeth (Figs 5.48 to 5.51).
- A tooth may be often missing from the dental arch as the odontome can block the eruption path of the tooth.
- The lesions are often associated either with an impacted tooth or a retained deciduous tooth.
- If the odontomes are located high in the alveolus, they may tend to erupt in the oral cavity by resorbing the overlying bone and as a result there may be pain, inflammation, ulceration or fistula formation, etc.
- Multiple odontomes can occur in the jaw simultaneously in some patients.
- Some odontomes may exhibit cyst formation around the tumor mass (mostly dentigerous cyst).

RADIOLOGICAL FEATURES (FIG. 5.50)

Odontomes usually produce pericoronal radiolucencies with well-defined and well-corticated

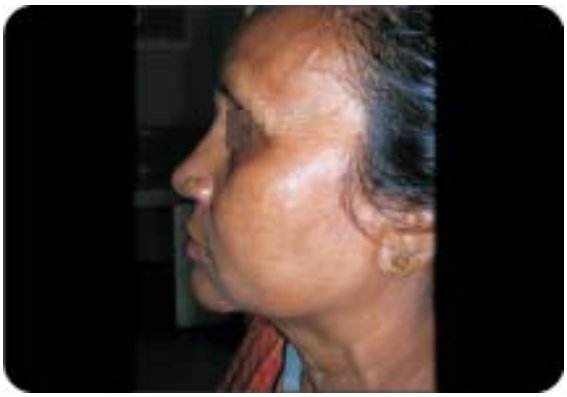

Fig. 5.48: Odontome-I

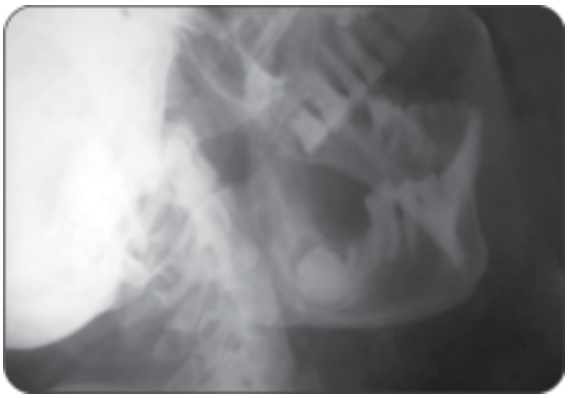

Fig. 5.50: Radiograph of odontome

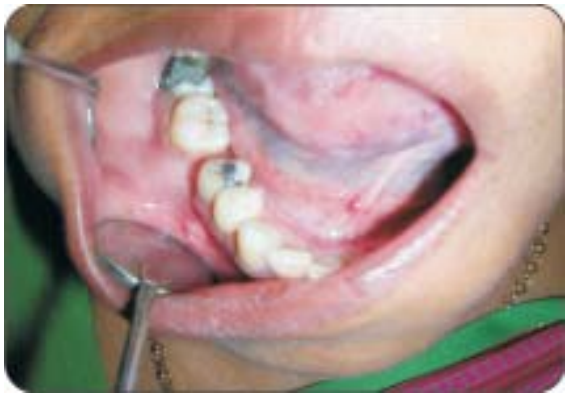

Fig. 5.49: Odontome-II

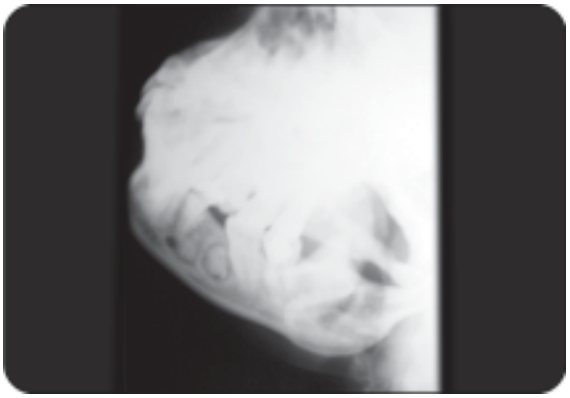

Fig. 5.51: Odontome-III

borders. A developing odontome may look completely radiolucent as the calcified elements do not form in the initial stages.

The compound odontome: The compound odontomes radiographically appear as numerous, small, miniature teeth or tooth-like structures, which are projecting from a single focus.

- Apparently they look like "**a bag of teeth**" and are commonly located between the roots of the erupted permanent teeth or above the crown of an impacted tooth.

The complex odontome: The complex odontomes radiographically appears as round or oval or **'sunburst-like'**, conglomerated radiopaque mass within the jawbone.

- They do not produce any morphologically identifiable tooth or tooth-like structures.
- Both types of odontomes are usually surrounded by a thin radiolucent zone at their periphery, which represents the capsule.
- When odontomes are associated with any impacted tooth, they are usually mandibular molars.
- Small odontomes may be located between the roots of the erupted teeth.

DIFFERENTIAL DIAGNOSIS

- Calcifying epithelial odontogenic tumor (CEOT)
- Ameloblastic fibrodentinoma
- Ameloblastic fibro-odontome
- Osteoma
- Odontoameloblastoma
- Focal sclerosing osteomyelitis.

HISTOPATHOLOGY (FIG. 5.52)

- Fully developed compound odontome histologically reveals the presence of an encapsulated mass of multiple separate denticles, embedded in a fibrous tissue stroma (Fig. 5.51A).
- Morphologically most of the denticles do not resemble the tooth of the normal dentition.

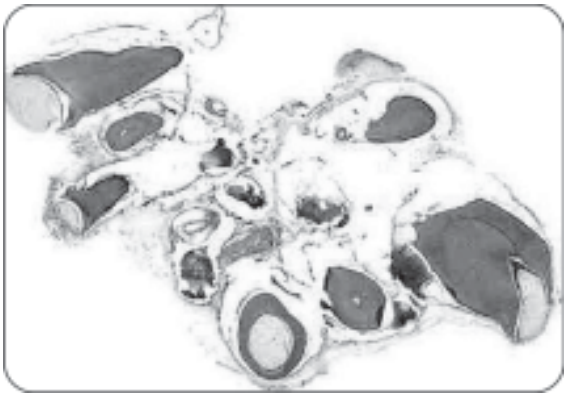

Fig. 5.51A: Photomicrograph of compound odontome

- However in each one of them, there is presence of enamel, dentin, cementum and pulp tissues, which are arranged in a similar fashion as seen in a normal tooth.
- The number of denticles in a compound odontome varies from as few as 2 to 3 or as many as 20 to 30.
- Histologically, the fully developed complex odontome presents an irregularly arranged but well-formed mass of enamel, dentin, cementum and pulp, etc. which is surrounded by a fibrous tissue capsule (Fig. 5.53).
- Mature tubular dentin forms the bulk of the tissues and on the surface it is neither covered by enamel nor by cementum.
- The dentinal tissue lies in direct contact with a connective tissue that resembles dental pulp.
- Most of the enamel tissues are fully calcified and on decalcified sections, they appear as small clefts or circular empty spaces.
- If the enamel is not fully calcified then the empty spaces contain fibrilar enamel matrix or immature enamel.
- A thin layer of cementum may be present about the periphery of the tumor.
- Small islands of epithelial ghost cells are seen in the tumor, which are remnants of the odontogenic epithelium.
- The developing complex and compound odontomes contain appreciable amount of soft tissues, which include odontogenic epithelium, secretory ameloblasts, developing enamel organs, reduced enamel epithelium, odontoblasts and cementoblasts, etc.

TREATMENT

By surgical enucleation. Recurrence is rare.

Key points of odontomes

- Odontomes are benign hamartomatous odontogenic lesions, capable of producing normal appearing enamel, dentin, cementum and pulp, etc. in an unorganized fashion.
- Two types of odontomes are found—**compound odontome** and **complex odontome.**
- Compound odontomes usually involve the anterior part of the maxilla (intercanine area).
- Complex odontomes often involve the posterior (premolar-molar) region of the jaw.
- Clinically, small odontomes produce painless, asymptomatic lesions, which are detected incidentally.
- The larger lesions however can be as large as 6 centimeter, in diameter and they cause expansion and distortion of cortical plates, displacement of teeth and malocclusion, etc.
- Odontomes are often associated either with an impacted tooth or a retained deciduous tooth.
- The compound odontomes radiographically appear as numerous, small, miniature teeth or tooth-like structures, projecting from a single focus and thus apparently look like "**a bag of teeth".**
- The complex odontomes radiographically appears as round or oval or **'sunburst-like'**, conglomerated radiopaque mass within the jawbone (Fig. 5.53).
- Fully developed compound odontome histologically presents an encapsulated mass of multiple separate denticles, embedded in a fibrous tissue stroma.
- Histologically, fully developed complex odontome presents an irregularly arranged mass of well formed enamel, dentin, cementum and pulp, etc.
- Treatment is done by surgical enucleation.

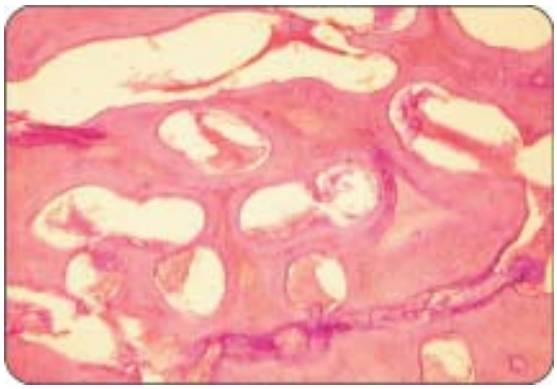

Fig. 5.52: Photomicrograph of odontome (complex)

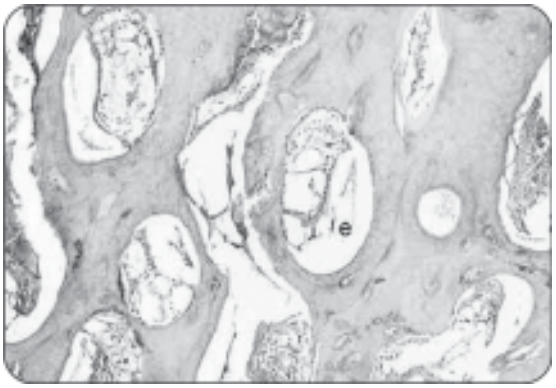

Fig. 5.53: Photomicrograph of complex odontome

ODONTOGENIC FIBROMA

DEFINITION

Odontogenic fibroma is a rare benign neoplasm derived from connective tissue of odontogenic origin and it can be either a peripheral lesion or a central (intraosseous) lesion.

PERIPHERAL ODONTOGENIC FIBROMA

DEFINITION

Peripheral odontogenic fibroma is the most common form of the disease, which develops extraosseously from the tooth bearing areas of the jaw.

ORIGIN

The lesion probably arises from the overlying gingival epithelium or the cell rests of the dental lamina.

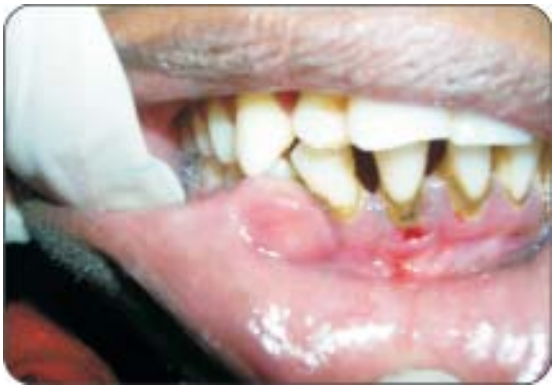

Fig. 5.54: Peripheral odontogenic fibroma

CLINICAL FEATURES

- Peripheral odontogenic fibroma clinically appears as a slow enlarging, exophytic, well-circumscribed, sessile growth of the gingiva (Fig. 5.54).
- The lesion is usually firm in consistency, it is painless and the overlying epithelium is of normal color.
- Most of the lesions occur on the facial gingiva (Fig. 5.55) and their size ranges between 0.5 to 1.5 centimeter in diameter.
- Sometimes, more than one lesion can occur in the oral cavity but rarely.
- In some cases, there can be erythematous changes or even ulcerations on the surface epithelium, which result from trauma.
- Interdental lesions may cause separation of the teeth.
- Consistency of the lesion often varies, since lesions may occur with ossification or without ossification (Fig. 5.56).

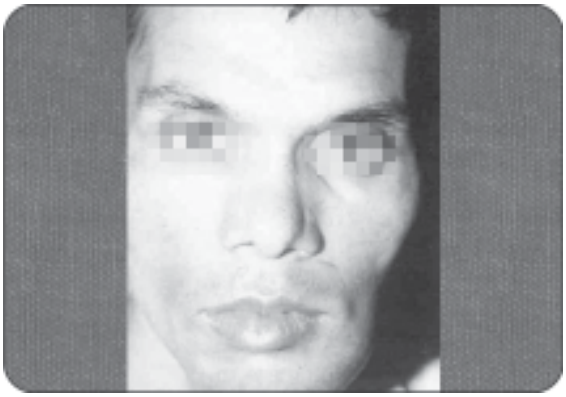

Fig. 5.55: Central odontogenic fibroma causing swelling of the Lt. sided mandible

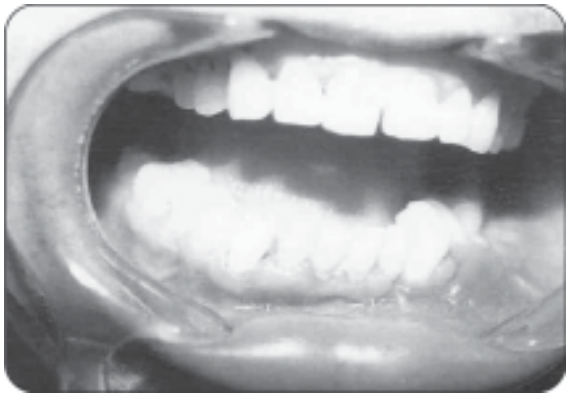

Fig. 5.56: Odontogenic fibroma causing expansion of bone on Lt. sided mandible

RADIOGRAPHIC FEATURES

- Since peripheral odontogenic fibromas are small lesions and they occur extraosseously within the gingiva, radiographic changes in the bone are not apparently found.
- However in certain cases saucerization of the cortical bone or widening of the periodontal ligament space at the cervical region may be seen.
- Numerous foci of small radiopaque masses are sometimes found within few lesions of peripheral odontogenic fibroma, which indicate calcifications within the tumor (Fig. 5.57).

HISTOPATHOLOGY

- Histologically peripheral odontogenic fibroma reveals a mass of dense connective tissue with few spindle-shaped fibroblasts, which is separated from the adjacent normal loose connective tissue.
- Surface epithelium shows long, slender rete-pegs projecting deep into the connective tissue.
- Small islands of odontogenic epithelium are present near the rete-pegs or deep within the connective tissue.
- Epithelial islands often contain few clear cells.
- Areas of hyalinized tissue with calcification can be present within the lesion.

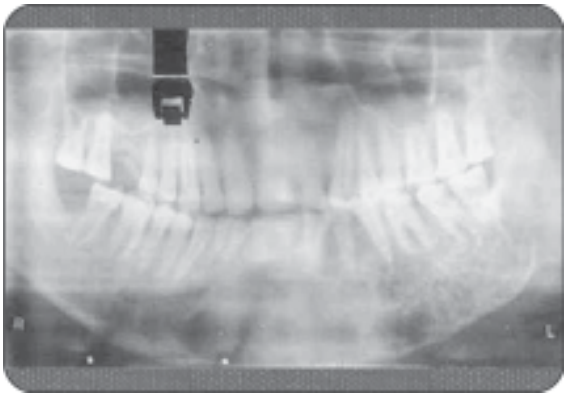

Fig. 5.57: Odontogenic fibroma producing a large irregular radiolucent area containing numerous radiopaque foci

DIFFERENTIAL DIAGNOSIS

- Peripheral ossifying fibroma
- Peripheral giant cell granuloma
- True fibroma
- Neurofibroma
- Fibroepithelial polyp.

TREATMENT

Surgical excision.

CENTRAL ODONTOGENIC FIBROMA

DEFINITION

Central odontogenic fibroma is a relatively uncommon odontogenic neoplasm arising within the jawbone.

CLINICAL FEATURES

Age: Wide age range (mean age is 20 years).

Sex: Female predilection is seen.

Site: It occurs more often in relation to mandible than maxilla. Maxillary lesions mostly occur anterior to the first molar tooth (Fig. 5.58). Mandibular lesions generally occur in the posterior part of the jaw, in the tooth bearing areas.

- Central odontogenic fibroma produces a slow enlarging, non-descript, painless swelling of the jaw.
- Displacement of teeth or formation of space or gap between teeth is common.
- Cortical expansion is often minimum, however larger lesions can cause localized bony expansion and loosening of teeth (Fig. 5.59).

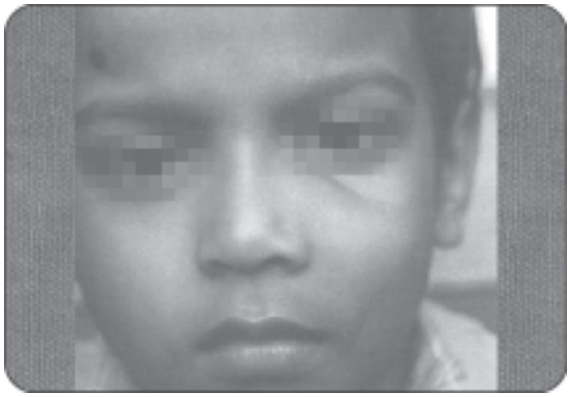

Fig. 5.58: Odontogenic fibroma involving Lt. sided maxilla

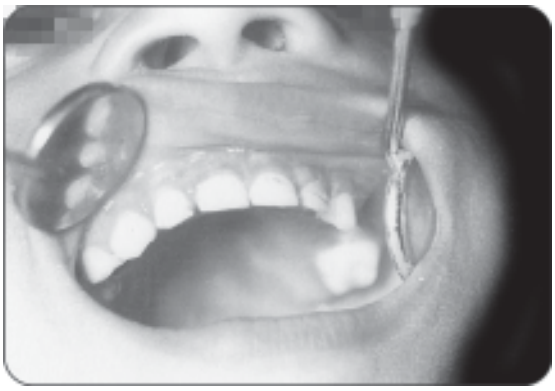

Fig. 5.59: The tumor causing swelling of the bone in upper premolar region

- A large number of lesions can occur in association with unerupted teeth and moreover some smaller lesions often remain asymptomatic.

RADIOGRAPHIC FEATURES

- Radiographically, the lesion presents a well-circumscribed, rounded, unilocular radiolucent area in the jaw.
- Some lesions are multilocular with sclerotic borders.
- Lesions often contain several small radiopaque flecks of varying radiodensity.
- Resorption of roots of the adjoining teeth is often seen in this tumor.

HISTOLOGICAL PRESENTATION

- Histologically central odontogenic fibroma presents a cellular connective tissue, containing numerous thin strands of odontogenic epithelium.
- The epithelial component closely resembles dental lamina and it often contains some clear cells.
- The connective tissue exhibits stellate fibroblast cells, which are often arranged in 'whorled' pattern.
- Areas of spherical or diffuse calcifications are often present in the lesion.
- Some lesions may contain giant cells.

DIFFERENTIAL DIAGNOSIS

- Calcifying epithelial odontogenic tumor (CEOT)
- Ameloblastoma
- Cementifying fibroma
- Calcifying epithelial odontogenic cyst
- Central giant cell granuloma.

TREATMENT

Surgical excision and curettage.

ODONTOGENIC MYXOMA

DEFINITION

Odontogenic myxomas are aggressive, intraosseous neoplasms derived from embryonic odontogenic mesenchyme.

ORIGIN

Odontogenic myxomas probably arise from the dental papilla or follicular mesenchyme.

CLINICAL FEATURES

Age: Young and middle aged adults.

Sex: Both sexes are equally affected.

Site:

- Nearly all lesions are found in the tooth bearing areas of maxillary and mandibular bone.
- Mandibular lesions are commonly found in the premolar-molar area. Some lesions may be found in the ramus of the mandibular bone or other non tooth-bearing areas.

PRESENTATION

- Odontogenic myxomas are slow growing but locally aggressive lesions, which often cause painless swellings in the jaw (Fig. 5.60).

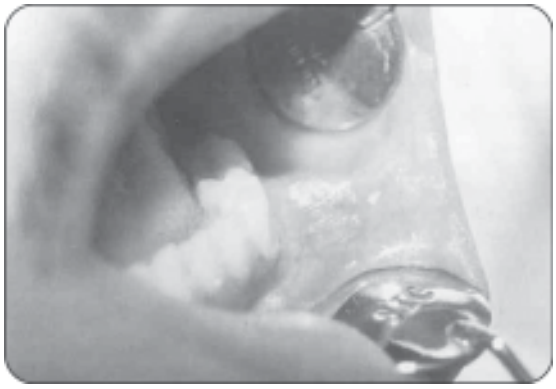

Fig. 5.60: Odontogenic myxoma producing a large swelling of Lt. sided mandible

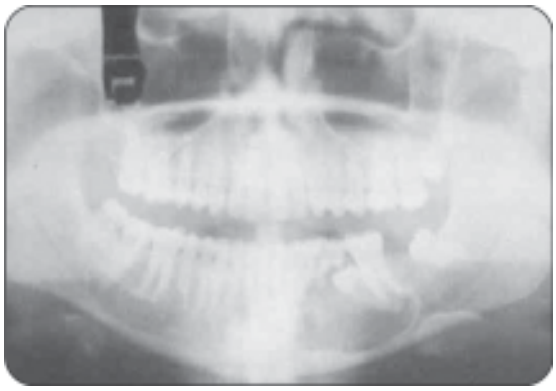

Fig. 5.61: Odontogenic myxoma producing a large radiolucent area in the Lt. sided mandible

- Sometimes they cause displacement of the regional teeth.
- If left untreated, their size can be huge and that may cause considerable expansion of the jaws with facial asymmetry.
- Maxillary lesions can perforate the bone and spread into the sinus. Afterwards they can cross the midline septa and invade into the opposing sinus cavity.
- Mandibular lesions also often extend into the ramus area.
- Few lesions are asymptomatic and are detected only during routine radiographic examinations.

RADIOGRAPHIC FEATURES

- The lesions often produce multilocular radioluency with a "soap bubble" or "honey comb" appearance in the bone.
- Thin and extremely delicate septa of residual bone are often seen to course through the radiolucent area (Fig. 5.61).
- These wispy trabeculae of thin bones are often arranged at right angles to one another and thus they produce a **"spider-web"** like or **"tennis racket"** like appearance.
- Displacement of teeth is common and often there is root resorption in the adjacent teeth.
- Border of the lesion is mostly ill-defined, irregular and scalloped.
- Smaller lesions of myxoma often appear as unilocular nonspecific radiolucent areas in the jawbone.

Key points of odontogenic myxoma

- Odontogenic myxomas are aggressive, intraosseous neoplasms, derived from embryonic odontogenic mesenchyme.
- Clinically, the lesions produce slow growing but locally aggressive growths, which often cause painless swellings in the jaw.
- Sometimes the lesions assume huge size and cause displacement of the regional teeth, malocclusion and gross facial deformity.
- The lesions often produce multilocular radioluency in the X-ray and characteristically exhibit a "spider-web" like or "tennis racket" like appearance.
- The cut surface of the tumor presents a loose gelatinous mass of tissue.
- Histologically, myxomas present widely separated, stellate shaped cells within a loose mucoid, non-fibrilar, basophilic ground substance.
- The myxomatous tissue often invades widely into the surrounding normal bony trabeculae.
- Radical surgery is the treatment of choice.

MACROSCOPIC APPEARANCE

On necked eye examination the tumor appears as a loose gelatinous mass of tissue.

HISTOLOGICAL PRESENTATION (FIG. 5.62)

- Microscopically, odontogenic myxomas present widely separated, undifferentiated, spindle or angular or stellate shaped cells with long fine anastomosing processes.

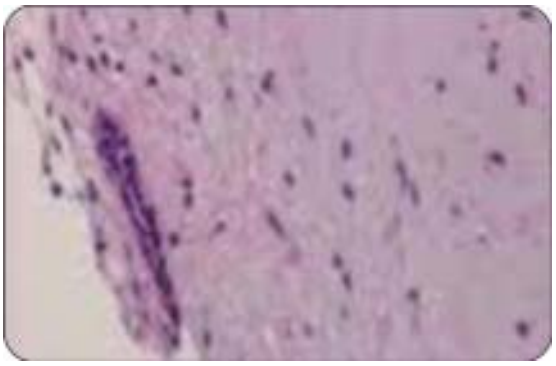

Fig. 5.62: Photomicrograph of odontogenic myxoma

- These cells are dispersed in a loose mucoid, non-fibrilar, basophilic ground substance.
- There is often presence of focal areas of delicate immature collagen fibrilar strands and as a whole the ground substance represents a myxomatous tissue.
- The blood vessels in the area often exhibit hyalinization at the periphery.
- The myxomatous tissue often invades widely into the surrounding normal bony trabaculae.
- Oval shaped islands of odontogenic epithelial cell rests are sometimes present within the lesion.
- Some lesions may also have areas of calcification.

DIFFERENTIAL DIAGNOSIS

- Central giant cell granuloma.
- Aneurysmal bone cyst.
- Chondromyxoid fibroma
- Ameloblastoma
- Calcifying epithelial odontogenic tumor
- Hyperparathyroidism
- Central neurilemmoma.

TREATMENT

Since myxomas consist of a grossly gelatinous or mucoid material, which often penetrate the surrounding trabacular spaces of bone, surgical excision of the lesion and curettage is not always successful and hence resection of the jaw should be done in larger lesions.

PERIAPICAL CEMENTRAL DYSPLASIA (CEMENTOMA)

Cementoma is a relatively uncommon odontogenic neoplasm, occurring in relation to the periapical bone and cementum at the root apex of vital teeth.

CLINICAL FEATURES

Age: Usually third and fourth decade of life.

Sex: Females are affected far more commonly than males.

Site: Mostly in relation to the mandibular anterior teeth, maxillary teeth are also affected in some cases.

CLINICAL PRESENTATIONS

The lesions are mostly asymptomatic and are detected only during routine radiographic examinations. These are usually small and multiple in number and the associated teeth are always vital.

RADIOLOGICAL FEATURES

The radiographic appearance of cementoma varies in different stages of the disease.

- In the initial **osteolytic stage**, the lesion presents a small, well-defined, radiolucent area near the apex of the involved tooth. The radiolucency is always found to be in continuation with the periodontal ligament space.
- In the second or the **cementoblastic stage**, the lesion appears as a radiolucent area containing multiple small radiopaque foci.
- In the third or the **mature stage**, cementoma presents a well-defined radiopaque mass at the root apex, being surrounded by a thin radiolucent zone.

HISTOPATHOLOGY

- In the initial stage of the disease, the cemental tissue at the apex of the involved teeth as well as the periapical alveolar bone are destroyed and are replaced by a fibrous connective tissue.
- During the cementoblastic stage, small amorphous masses of immature cementum form within the fibrous tissue stroma.

- In the mature stage cementoma, the entire fibrous tissue is replaced by a large mass of mature cemental tissue at the apex of the teeth.

DIFFERENTIAL DIAGNOSIS

- Periapical granuloma
- Periapical cyst
- Condensing osteitis
- Bony artifacts.

TREATMENT

No treatment is required for cementoma, periodic observation and time-to-time vitality test of the involved teeth are to be done.

FAMILIAL GIGANTIFORM CEMENTOMA

DEFINITION

Familial gigantiform cementoma is a rare benign condition, which appears to represent a dysplastic or hamartomatous malformation of the cementum forming tissues.

ORIGIN

The disease seems to be inherited as an autosomal dominant trait with variable expression and its often shows a familial tendency for occurrence.

CLINICAL FEATURES

Age: The condition develops during childhood.

Sex: Females are affected more often then males.

Site

- Both jaws are affected and it can be bilateral.
- Initially familial gigantiform cementoma presents slow growing painless expansile jaw swelling.
- Multiple lesions often develop simultaneously at different sites involving all the four quadrants of the jaw.
- Lager lesions cause obvious facial asymmetry.
- Secondary infection in the lesion may produce pain and even formation of intraoral or extra-oral pus discharging sinuses.

RADIOGRAPHY

- Radiograph reveals a large, sometimes massive expansile lesion of the jaw with well-defined margins.
- The lesion presents features of mixed radiolucency and radiopacity, however, it becomes more radiopaque with time.

HISTOLOGICAL PRESENTATION

- Histologically, the lesion presents a loose vascular tissue stroma consisting of delicate collagen fibers and numerous monomorphic fibroblasts.
- Large irregular masses of dense mineralized tissue resembling acellular cementum are scattered throughout the stroma.
- Small ovoid calcifications are also common.
- There can be variable degree of chronic inflammatory cell infiltrations especially in those lesions, which are secondarily infected.

DIFFERENTIAL DIAGNOSIS

- Florid osseous dysplasia
- Garre's osteomyelitis
- Paget's disease of bone.

TREATMENT

Surgical recontouring of bone.

CEMENTOBLASTOMA

Cementoblastoma is a rare benign odontogenic neoplasm arising from the cementoblast cells. The tumor develops as an irregular rounded mass in continuity with the apical cemental layer of a vital molar or premolar tooth.

CLINICAL FEATURES

Age: Usually second and third decade of life (Peak age of incidence is about 19 years).

Sex: Seen more frequently among males.

Site: Mandible is affected more often (75 percent cases) than the maxilla and posterior part of the jaw is usually the site of choice for this tumor.

ORIGIN

Cementoblastoma or "true cementoma" is a true neoplasm of the cemental tissue. It arises from

the cementoblast cells of the cemental layer of the apical third of a vital tooth.

CLINICAL PRESENTATION

- Cementoblastoma often produces a slow enlarging, bony hard swelling of the jaw that only rarely causes expansion of the jaw and displacement of the regional teeth (Figs 5.63 and 5.64).
- Both buccal and lingual cortical plates are expanded uniformly.
- In most of the cases, low-grade intermittent pain may be present, which is felt more often, when the area is palpated.
- The lesion is often attached to the apical third of a vital premolar or molar tooth. Mandibular first molar is predominantly involved (50 percent cases).
- A dull sound is produced when the tooth percussed.

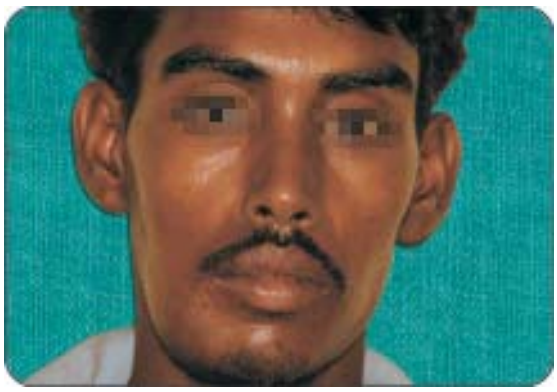

Fig. 5.63: Benign cementoblastoma

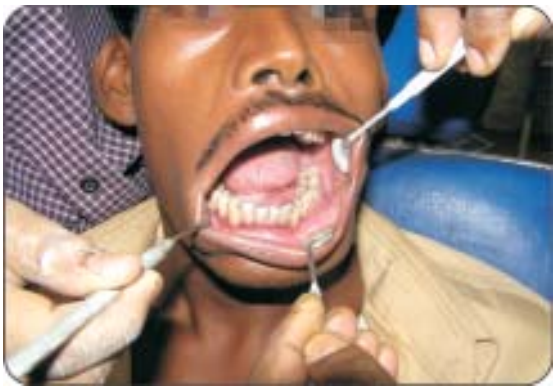

Fig. 5.64: Intraoral view of the same patient

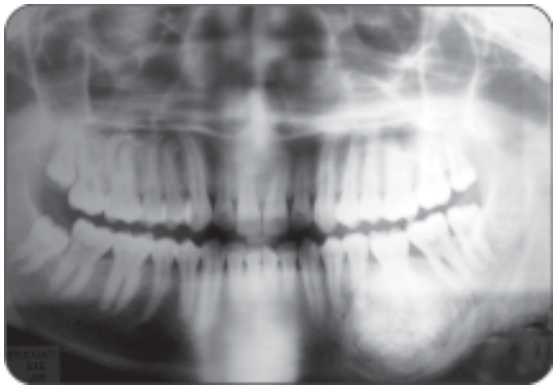

Fig. 5.65: Radiograph of benign cementoblastoma

RADIOLOGICAL FEATURES (FIG. 5.65)

- Radiographically the tumor often presents a **large, dense, radiopaque mass** that is often attached to one or more vital tooth roots. The early lesions may be radiolucent.
- Resorption and subsequent fusion of the tumor to the roots of the tooth often make them (roots) completely obscured, when seen in the radiograph.
- The lesion is surrounded by a thin zone of radiolucency at the periphery.
- Roots adjacent to the growing lesion often exhibit resorption of their apical third.

HISTOPATHOLOGY (FIG. 5.66)

- Histologically, cementoblastoma presents a large mass of amorphous cemental tissue that often shows irregularly placed lacunae.
- The lesion also shows the presence of multiple basophilic reversal lines.
- On histologic sections, the tumor characteristically shows its fusion with the roots of the tooth.
- A fibrovascular connective tissue stroma is present between the individual mineralized trabeculae.
- Individual trabeculae are often bordered at the periphery by cementoblast or cementoblast-like cells.
- The periodontal ligament that is adjacent to the normal cementum becomes integrated with capsule and separates the neoplasm from the surrounding normal bone.
- The peripheral area of the lesion is relatively acellular while the central zone is composed of

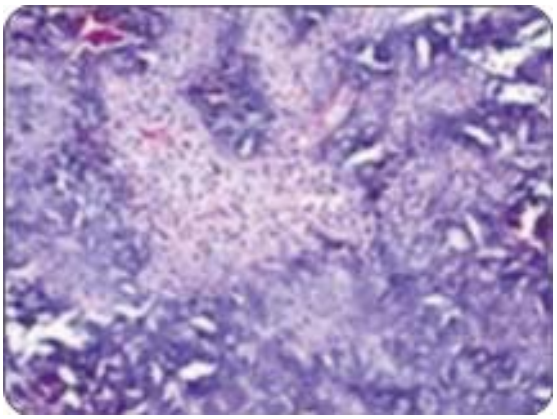

Fig. 5.66: Photomicrograph of cementoblastoma

a highly mineralized tissue with intervening areas of loose, very cellular tissue with increased vascularity.

- Multinucleated cells are present in large numbers in the central area and are associated with active resorption.
- The root of the involved tooth may extend up to the center of the lesion and the neoplastic cemental tissue is seen, continuation with the normal cementum of tooth.

DIFFERENTIAL DIAGNOSIS

- Osteoblastoma
- Osteoid osteoma
- Paget's disease of bone
- Osteosarcoma
- Focal sclerosing osteomyelitis

TREATMENT

By surgical excision.

MALIGNANT ODONTOGENIC NEOPLASMS

MALIGNANT AMELOBLASTOMA

DEFINITION

Malignant ameloblastomas are lesions with the histological features of common ameloblastoma in which metastasis has occurred.

In many cases, these lesions are recurrent, although metastasis can occur from a primary lesion.

Metastasis usually occurs to the distant regional lymph nodes moreover, metastasis to the distant sites, e.g. lung can also occur.

In all the cases malignant ameloblastoma lesions appear cytologically benign.

AMELOBLASTIC CARCINOMA

DEFINITION

Ameloblastic carcinoma is a true malignant neoplasm of odontogenic epithelial tissue origin, in which the epithelial components of the lesion are cytologically malignant.

These lesions are clinically more aggressive and metastasis occurs very often. The lesions can affect both maxilla and mandible (Figs 5.67 and 5.68).

Cytologically the epithelial components of the lesion exhibit cellular pleomorphism and nuclear hyperchromatism.

Radical surgical intervention should be undertaken.

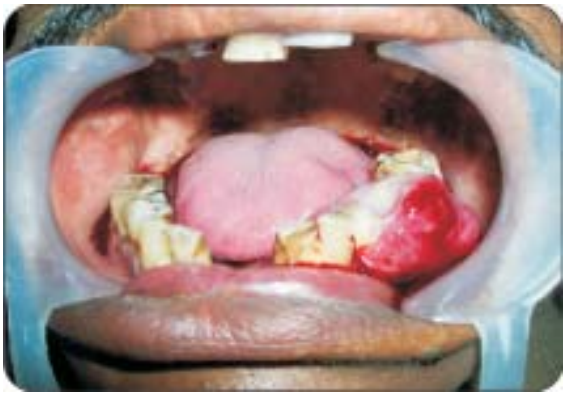

Fig. 5.67: Ameloblastic carcinoma

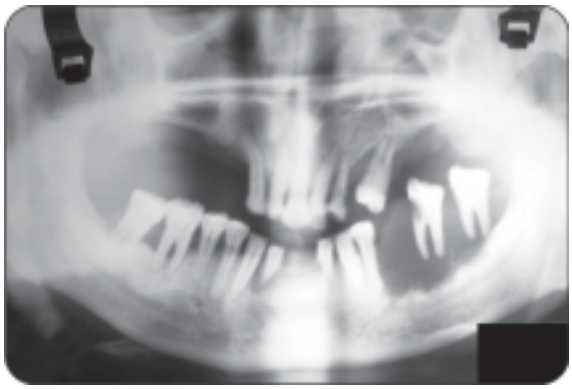

Fig. 5.68: Radiograph of ameloblastic carcinoma

ODONTOGENIC CARCINOMA

DEFINITION

These are aggressive and destructive intraosseous lesions consisting of poorly differentiated epithelial cells and clear cells in a pattern that is reminiscent of early odontogenesis.

CLINICAL FEATURES

Age: About 50 years.

Sex: More prevalent among females.

Site: These are uncommon lesions, which can affect both maxilla and mandible.

Clinical feature is not pathgnomonic, there can be large swelling of the jaw with expansion of the cortical plates. Mobility of the teeth is very common.

RADIOGRAPHIC FEATURES

Radiographically, the neoplasm appears as a diffuse radiolucent area with a "honey comb" appearance.

Considerable amount of bone destruction is often evident.

HISTOPATHOLOGY

The lesion is composed of islands or strands of clear cells, which are scattered throughout the fibrous tissue stroma. The clear cells are glycogen rich. The non-clear cells often resemble cells of dental lamina. The epithelial components are often surrounded by a zone of myxomatous connective tissue.

The cellular features of malignancy in the epithelial cells are minimum.

TREATMENT

Radical surgical excision.

ODONTOGENIC SARCOMAS

Odontogenic sarcomas are exceedingly rare lesions occurring in maxilla and mandible. The histological features exhibit a fibrosarcoma like appearance. The epithelial components are non-neoplastic in nature and there may be presence of few dental hard tissues.

CLEAR CELL ODONTOGENIC CARCINOMA

DEFINITION

Clear cell odontogenic tumor is a locally aggressive, rare odontogenic neoplasm of epithelial cell origin.

CLINICAL FEATURES

Age: Above 50 years of age.

Sex: More prevalent among females.

Site: Both maxilla and mandible can be affected.

CLINICAL PRESENTATION

Clinical features are not pathognomonic and both jaws can be affected by the tumor. Clinically there can be mild pain and swelling of the jawbone with expansion of the cortical plates and mobility of the teeth.

RADIOLOGICAL FINDING

The tumor produces irregular radiolucent area in the bone with a ragged border.

HISTOLOGICAL PRESENTATION

- Histologically this neoplasm is poorly circumscribed and it consists of sheets of odontogenic epithelial cells with clear cytoplasms and centrally placed nuclei.
- The cells are glycogen rich and are distributed through out a fibrous connective tissue stroma.
- In the connective stroma inflammatory cells are scanty, areas of hemorrhage are often seen in the tumor.
- The tumor cells frequently invade into the adjacent tissues, metastasis to the regional lymph nodes and to the distant organs is also common.

TREATMENT

Surgical excision and curettage.

PRIMARY INTRA-ALVEOLAR CARCINOMA

Ref. Chapter 2 (Neoplasms of neural tissue)

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CHAPTER 6

Cysts of the Oral Region

DEFINITION

Cyst is a pathological cavity containing fluid, semifluid or gas, which is usually lined by epithelium and is not formed by the accumulation of pus.

The above mentioned definition of the cyst requires some clarifications:

- ***Pathological cavity:*** Means any cystic lesion in the body must arise as a result of some pathologic processes. Unlike the normal anatomical cavities in the body, e.g. gallbladder or plural cavity or pericardial cavity or urinary bladder, etc. which are also cyst like cavities but these are normal anatomical structures of the body. On the other hand, a cyst is not normal to the body but a pathological or a disease entity.
- ***Contents of the cyst:*** Generally cystic cavities are filled with a variety of materials. For example the dentigerous, the radicular or the globulomaxillary cyst, etc. are normally filled with some fluid.

  The primordial cyst is usually filled with a thick, keratin-rich semifluid mass.

  On the contrary, some of the cysts like the solitary bone cyst or aneurysmal bone cyst, etc. are usually filled with gas.
- ***Regarding cyst lining:*** Most of the cystic cavities are lined by an epithelium, but the lining epithelium may be absent in few cysts, e.g. traumatic bone cyst or aneurysmal bone cyst or mucous extravasation cyst, etc.

  True cyst: If the lining epithelium is present in a cyst it known as a true cyst.

  Pseudo or false cyst: If the lining epithelium is absent in a cyst it called a false or pseudo cyst.
- ***Question of pus:*** Unlike an abscess, a cyst is never formed by the accumulation of pus. However, in few cases a cyst may be secondarily infected, resulting in the formation of pus within it. This type of abscess developing in a pre-existing cyst is known as "cyst abscess".

CLASSIFICATION OF CYSTS

ODONTOGENIC

Developmental

- Gingival cyst of infants
- Odontogenic keratocyst (primordial cyst)
- Dentigerous (follicular) cyst
- Eruption cyst
- Lateral periodontal cyst
- Gingival cyst of adults
- Botryoid odontogenic cyst
- Glandular odontogenic (*sialo-odontogenic*) cyst
- Calcifying odontogenic cyst.

Inflammatory

- Radicular cyst, apical and lateral
- Residual cyst
- Paradental cyst and mandibular infected buccal cyst.
- Inflammatory collateral cyst.

NON-ODONTOGENIC

- Nasopalatine duct (incisive canal) cyst
- Nasolabial (nasoalveolar) cyst
- Midpalatal raphe cyst of infants
- Median palatine, median alveolar and median mandibular cysts
- Globulomaxillary cyst.

NON-EPITHELIAL

- Solitary bone cyst (traumatic, simple, hemorrhagic bone cyst)
- Aneurysmal bone cyst

Clinical significance of jaw cysts

- Cystic lesions occur at a higher frequency in relation to the jawbones as compared to any other bone in the skeleton, because of the typical embryology of the facial skeleton and also because of the presence of teeth.
- The teeth are always associated with some epithelium or epithelial residues, which are potentially capable of forming a cyst.
- The widely varying clinical and biological behavior of different cystic lesions comprise a significant clinical problem in oral pathology.
- Jaw cysts generally present as well-defined radiolucent lesions, which may or may not be associated with erupted or unerupted teeth, or with other features such as expansions of the cortical bone and occlusal disharmony, etc. These features are not pathognomonic of a cyst and may be shared by other forms of cystic or noncystic pathology.
- The border of the lesion in mostly smooth, well-delineated and well corticated.
- Cystic lesions grow slowly in the jaw and displace the regional teeth but generally do not cause root resorptions. Therefore, a cystic lesion of the jaw should always be differentiated from other forms of pathology before any definitive treatment is done.
- Cystic fluids can be aspirated from the cysts and its biochemical nature among different cystic lesions.
- Moreover, different types of cysts must be clearly differentiated from one another during making the diagnosis, because the treatment protocols for various large cysts can vary significantly.
- Biologically, most of the cystic lesions of the jaw are slow growing and they maintain a relatively *innocuous* character for a considerable period of time.
- A fluctuant or compressible swelling often develops if the cyst is present in the soft tissue or if the intrabony cyst has completely resorbed the overlying bone.
- However, few cystic lesions could cause severe bone destruction and involve a large part of the jaw without actually being noticed clinically during the initial stages, e.g. primordial cyst.
- A cyst may look bluish in color, if it is lying close to the overlying epithelial surface.
- Large cystic lesions eventually cause bone expansion and manifest with pain and discomfort in the jaw.
- Cystic lesions especially the odontogenic cysts may become infected, which can result in abscess formation and cellulites, etc.
- Rarely large cysts may cause considerable amount of bone destruction and weaken the bone, which may result in pathological fracture.
- Cystic epithelium sometimes can undergo neoplastic changes and gives rise to the development of benign or malignant tumors.

CYSTS ASSOCIATED WITH THE MAXILLARY ANTRUM

- Benign mucosal cyst of the maxillary antrum
- Postoperative maxillary cyst (surgical ciliated cyst of the maxilla).

CYST OF THE TISSUE OF THE MOUTH, FACE AND NECK

- Dermoid and epidermoid cysts
- Lymphoepithelial (branchial cleft) cyst
- Thyroglossal duct cyst
- Anterior median lingual cyst (intralingual cyst of foregut origin)
- Oral cysts with gastric or intestinal epithelium (oral alimentary tract cyst)
- Cystic hygroma
- Nasopharyngeal cysts
- Thymic cyst
- Cysts of the salivary glands: Mucous extravasation cyst, mucous retention cyst, ranula
- Parasitic cysts: Hydatid cyst, cysticercus cellulosae, trichinosis.

ODONTOGENIC CYSTS

ODONTOGENIC KERATOCYST (PRIMORDIAL CYST)

DEFINITION

Odontogenic keratocyst is a common cystic lesion of the jaw, which arises from the remnants of the dental lamina; it has distinctive clinicopathologic character and a higher tendency for recurrence after treatment. Odontogenic keratocysts often have a more aggressive curse than any other cystic lesion of jaw and for this reason these are sometimes known as "benign cystic neoplasms.

This cyst often occurs as a solitary lesion in the angle of the mandible, however in some cases multiple such cysts may occur in association with a syndrome called "nevoid basal cell carcinoma syndrome".

PATHOGENESIS

Odontogenic keratocyst arises mainly from the:

- Dental lamina or its remnants.
- . Primordium of the developing tooth germ or enamel organs.
- . Sometimes from the basal layer of the oral epithelium.

It is mostly believed that the keratocyst develops due to the cystic degeneration of the cells of the stellate reticulum in a developing tooth germ (before its calcification starts). The daughter cysts, a common finding in this lesion, probably develop from the remants of the dental lamina.

Nevoid basal cell carcinoma syndrome is a hereditary condition and since odontogenic keratocysts develop in association with this syndrome, a strong correlation is believed to exist between genetic influence and the development of this cyst.

CLINICAL FEATURES

Incidence: Nearly one percent among all types of jaw cysts.

Age: Mostly second and third decade of life.

Sex: Males are affected slightly more often than females.

Site

- Majority of the cases develop in relation to mandible (75%) as compared to maxilla.
- Among the mandibular lesions, 50% of the cases occur at the angle of the mandible, which extend for varying distances into the ascending ramus and the body of the mandible.
- Few cysts absolutely occur in the body of the mandible and some of these lesions can even cross the midline of the jaw.
- Maxillary lesions more frequently involve the anterior part of the jaw, however some lesions can develop from the posterior region. Few lesions can even develop in relation to the maxillary air sinus.
- On rare occasions, this cyst may occur in the gingiva (extraosseous type).

PRESENTATION

- In the initial stages (Figs 6.1 and 6.2) odontogenic keratocyst does not produce any signs or symptoms and the lesion may be discovered only during routine radiographic examinations.
- Larger lesions of odontogenic keratocyst however produce swelling of the jaw with facial asymmetry (Fig. 6.3).
- Pain in the jaw along with mobility and displacement of the teeth are frequently seen.
- There is often one tooth missing from the dental arch on clinical examination, which means that the cyst has developed from the developing tooth germ of that particular tooth.
- Bony expansion is minimum in odontogenic keratocyst because in most of the cases, the

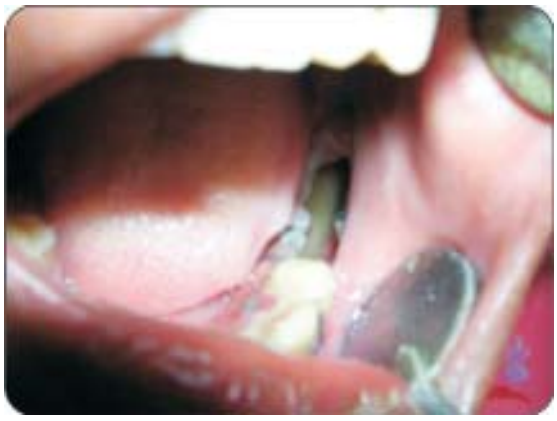

Fig. 6.1: Keratocyst

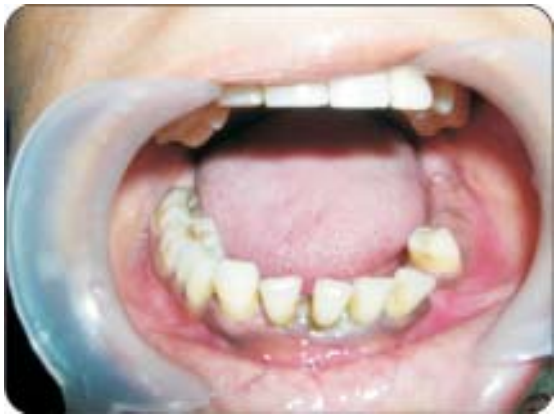

Fig. 6.2: Odontogenic keratocyst

Fig. 6.3: Odontogenic keratocyst involving the right sided mandible

cyst spreads via the medullary spaces of bone and therefore, remarkable bony swelling is usually absent despite the cyst being very large.

- Expansion of bone occurs in about 60% cases in odontogenic keratocyst. One-third of the maxillary lesions cause expansion of the buccal cortical plate while expansion of the palatal cortical plate is rarely seen.
- Mandibular lesion exhibits buccal expansion in about 50% cases, while lingual expansion occurs in over 30% cases.
- In some cases, completely extraosseous lesions may develop in relation to the gingiva.
- Some patients may have multiple odontogenic keratocysts in the jaw.
- Multiple lesions may also develop in the jaw as a manifestation of the nevoid basal cell carcinoma syndrome.
- Paresthesia of the lower lip and teeth may be present occasionally.
- Excessive expansion and thinning of bone may result in pathological fracture in some cases.
- Discharge of pus may be seen in case the cyst is secondarily infected.
- Larger odontogenic keratocysts of the maxillary sinus often cause displacement or destruction of the floor of the orbit and protrusion of the eye-ball.

Nevoid basal cell carcinoma syndrome

Nevoid basal cell carcinoma syndrome is a hereditary disease and is inherited as an autosomal dominant trait.

The features of this syndrome include the following:

- Multiple nevoid basal cell carcinomas of skin.
- Multiple odontogenic keratocyst of the jaws.
- Bifid ribs and abnormalities in vertebrae.
- Ocular hypertelorism and broad nasal root.
- Frontal and parietal bossing with enlarged head circumference.
- CNS disturbances with calcification of falx cerebri and abnormal shape of sella turcica, etc.
- Epidermal cyst of the skin.
- Cleft lip and cleft palate in few cases.

RADIOLOGICAL FEATURES (FIGS 6.4 AND 6.5)

- Keratocysts often radiographically present multilocular radiolucent areas, with a typical "**soap-bubble**" appearance.
- In many cases, the lesion can be unilocular with a well-corticated margin.
- On many occasions, the mandibular lesions enlarge and extend to the other side of the

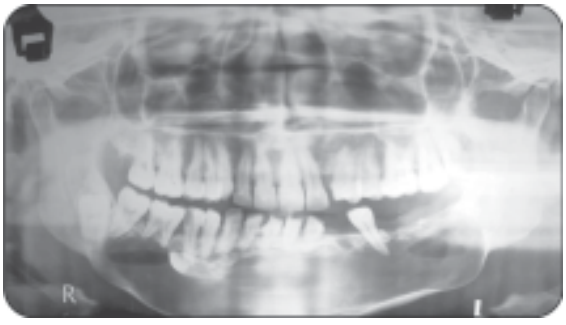

Fig. 6.4: Radiograph of odontogenic keratocyst

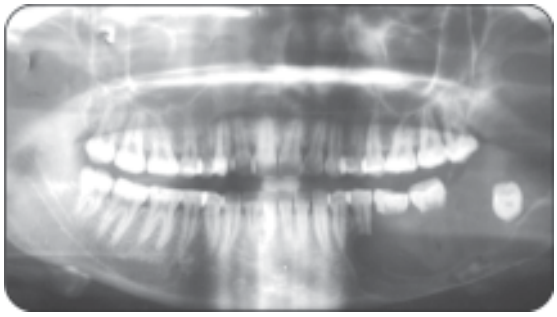

Fig. 6.5: Radiograph of keratocyst

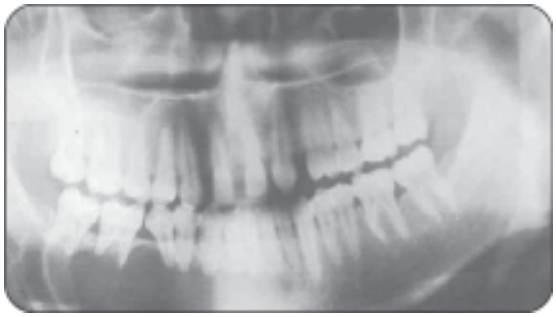

Fig. 6.6: Radiograph of odontogenic keratocyst producing a multilocular radiolucent area with expansion of bone

bone by **crossing the midline**. This is an important characterisric of odontogenic keratocyst.

- Sometimes the border of the cyst is smooth (slow growing lesions) and sometimes it is scalloped.
- Lesions in the angle of mandible often spread to the body as well as the ascending ramus up to the condyle and the coronoid process.
- Displacement of unerupted teeth and deflection of their roots are often seen.
- Sometimes multiple cysts may be seen in the jaw.
- Occasionally, there may be presence of an unerupted tooth in relation to the cyst. In such cases the cyst might have arisen from the 'cell rests of Sarre' from around the unerupted tooth and later on had encircled the tooth itself.
- Some lesions cause **pathological fracture** or **perforation** of the cortical plates of the jaw.
- Root resorption rarely occurs in association with odontogenic keratocysts.
- Expansion and distortion of the cortical plates are common and radiological size of the lesion is almost always significantly large than the clinical size of the lesion (Fig. 6.6) (Clinically, the cyst appears much smaller than its actual size).

Radiological types of keratocyst

Replacement type	When a keratocyst develops in place of a developing normal tooth, it is called the replacement type. In such cases, there will be absence of a normal tooth in the dental arch.
Envelopmental type	When a cyst entirely encloses an impacted tooth within the bone, it is called the envelopmental type of keratocyst.
Extraneous type	When a keratocyst develops away from the tooth bearing areas of the jaws, it is called extraneous type of keratocyst.
Collateral type	When a cyst develops between the roots of a tooth, it is called collateral type of keratocyst.

DIFFERENTIAL DIAGNOSIS

- Ameloblastoma
- Dentigerous cyst
- Aneurysmal bone cyst
- Odontogenic myxoma
- Stafine bone cyst
- Lateral periodontal cyst.

MACROSCOPIC FINDINGS OF KERATOCYST

- On naked eye examination, the odontogenic keratocyst presents a cystic cavity, which is filled with a thick cheesy material (keratin debris).
- Some cysts are filled with a clear fluid
- The cystic wall is thin and friable; and is difficult to separate from the bone wall.

CYSTIC FLUID

Aspiration of the cystic content reveals a straw colored fluid, which contains about 3.5 gm percent of soluble protein. Paper electophoresis of the cystic fluid is useful in determining this protein level.

PAPER ELECTROPHORESIS

Electrophoretic analysis reveals that the cystic fluid of odontogenic keratocyst has soluble protein levels, which is below 3 to 5 gram/100 ml whereas in case of nonkeratinizing cysts, the level is about 5 to 11 gram/100 ml. It is therefore, concluded that if the soluble protein level in a cyst is less than 4.5 gram/100 ml it should be considered a keratocyst and if the level is more than 5.0 gram/100 ml, it should be a non-keratinizing cyst.

HISTOPATHOLOGY (FIGS 6.7 AND 6.7A)

Histologically, odontogenic keratocyst reveals the following features:

- A cystic cavity, which is lined by an uniform looking keratinized stratified odontogenic epithelium having 6 to 8 cell layers thickness.
- The lining epithelium and connective tissue interface is flat and no rete-peg formation is seen in the lining epithelium of cyst.
- In about 80 to 90% cases the cystic epithelium is keratinized and the epithelium uniform in thickness.
- Sometimes the epithelium shows "V" shaped rete pegs formation with areas of acanthosis.
- In almost 80 to 90% cases the cystic epithelium exhibits parakeratinization and on few occasions there can orthokeratinization in the epithelium.
- Sometimes both forms of keratinization may be present in different areas of the lining.
- The basal layer of the epithelium is made up of tall columnar cells or cuboidal cells.
- Columnar cells are often associated with parakeratinized epithelium and they exhibit a palisading arrangement.
- The cells contain intensely basophilic nuclei, which are situated away from the basement membrane. Reverse polarity of basal cell nuclei could be seen in some cases.
- Sometimes the basal layer of the epithelium is made up of cuboidal cells and these cells are more often seen in association with orthokeratotic linings.
- The orthokeratotic cysts often exhibit abundant orthokeratin formations and a well-defined granular layer.
- The cells of the suprabasilar layer of the epithelium are polyhedral in nature and these cells often exhibit intercellular edema.
- Mitotic activity is seen in both basal as well as suprabasal layers but it is more frequent in suprabasal layers.
- Mitotic activity is higher in odontogenic keratocysts occurring in association with nevoid basal cell carcinoma syndrome.
- Large amounts of desquamated keratin is often found within the cystic lumen.
- The cystic lining often shows a folded or corrugated appearance, which could be due to unequal growth pattern of the lining at different places.
- The junction between the cystic lining and the connective tissue capsule is weak and in many cases the cystic epithelium may be detached from the underlying connective tissue.

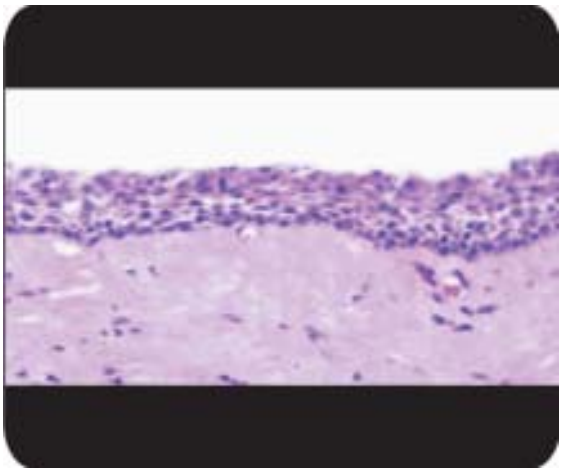

Fig. 6.7: Photomicrograph of odontogenic keratocyst-I

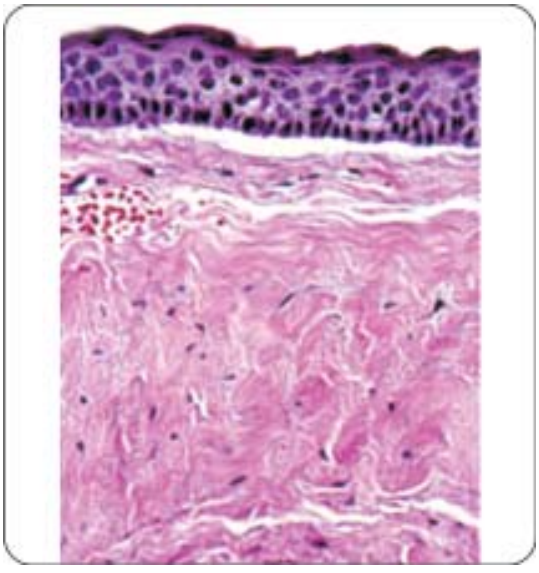

Fig. 6.7A: Photomicrograph of odontogenic keratocyst-II

- One of the most interesting histopathological features of odontogenic keratocyst is the presence of multiple small micro cysts within the connective tissue wall of this cyst. These small cysts are often known as "**daughter cysts**" or "**satellite cysts**".
- Besides "satellite cysts" the connective tissue wall may also exhibit proliferating remnants of dental lamina.
- In syndrome associated odontogenic keratocyst, the lining epithelium is considerably thicker and exhibits nests of basaloid cells budding-off from the cystic lining.
- The cystic epithelium of odontogenic keratocyst sometimes shows dysplastic changes and on rare occasions the lining epithelium may undergo malignant transformation.
- The fibrous capsule is usually thin and is devoid of inflammatory cells.
- Hyalinization may sometimes occur in the cyst capsule.
- Melanin pigmentation, mucous metaplasia and hyaline bodies may sometimes be seen in the wall of the keratocysts.
- In cases of intense secondary inflammation, the epithelial lining of the cyst often looses its characteristic features and therefore looks like the lining of a radicular cyst.

SPECIAL INVESTIGATIONS

Computed tomographic scan (CT scan): CT scan helps in making the accurate diagnosis of odontogenic keratocyst in the following ways:

- It helps in understanding the exact size of the lesion.
- It can help in assessing the exact extent of the lesion by showing the boundary. It is an excellent technique in determining the involvement of cortical plates particularly in localizing the point of perforation in the cortical plate.
- It helps in the assessment of soft tissue involvement.
- In maxillary lesion, particularly where it is extending towards the base of the skull, CT scan can effectively determine the position of the cyst.

PROBLEMS

CT scan involves a very high dose of radiation (1000 times more than general X-rays) and has more radiation induced hazards, for this reason it is risky particularly for the lens of the eye.

ALTERNATIVES TO CT SCAN

- Ultrasound.
- MRI—Magnetic Resonance Imaging.

DNA ANALYSIS OF THE LINING CELLS OF THE CYSTIC EPITHELIUM

- DNA analysis in odontogenic keratocyst can help in determining the dysplastic or malignant potential of the cystic epithelial cell.
- HPV virus is sometimes detected in the cystic epithelial cells (by DNA analysis) and it is suggested that the virus can be responsible for dysplastic or malignant transformation of the cystic epithelial cells.
- Ultrastructural analysis of keratinizing pattern of the cystic epithelium reveals that cysts with orthokeratinized epithelium do have a lower rate of recurrence than the cyst with parakeratinized epithelium.

SCANNING ELECTRON MICROSCOPY (SEM)

Scanning electron microscopy reveals a complex series of depressions and elevation on the cell surface in case of parakeratinized epithelium. Whereas in case of orthokeranitized epithelium, uniform, flat surface covered with layer of orthokeratin is found with no evidence of surface corrugations.

TRANSMISSION OF ELECTRON MICROSCOPY (TEM)

Analysis of the surface of parakeratinized epithelium reveals the presence of cytoplasmic interdigitations and desmosomal junctions, which result in the complex surface morphology. The analysis of orthokeratinized cystic epithelium shows an attachment between superficial shreds of orthokeratin and component layers of underlying keratin.

Key points of odontogenic keratocyst

- Odontogenic keratocyst is a common aggressive type of cystic lesion of the jaw; which arises from the remnants of the dental lamina.
- The cyst commonly occurs in 2nd and 3rd decade of life and it frequently develops in mandible near the angle.
- Clinically, the smaller lesions are slow growing, painless and asymptomatic; however the larger lesions of odontogenic keratocyst often produce extensive swelling of the jaw with facial asymmetry.
- Paresthesia in the jaw along with mobility and displacement of the teeth are frequently seen.
- On many occasions a very large cyst can produce little bony expansion; because the cyst spreads via the medullary spaces of bone.
- Keratocysts often radiographically present multilocular radiolucent areas with typical "soap-bubble" appearance.
- Occasionally the mandibular lesions cross the midline and extend from one side of body of mandible to the other side.
- Odontogenic keratocyst has four radiological types: Replacement type, envelopmental type, extraneous type and collateral type.
- The cystic fluid is generally straw colored and contains about 3.5 gm percent of soluble protein.
- Microscopically, the lesion presents a cystic cavity lined by an uniform looking keratinized stratified odontogenic epithelium having 6 to 8 cell layers thickness.
- The lining epithelium and connective tissue interface is flat and no rete-peg formation is seen in the lining epithelium of cyst.
- The cyst characteristically exhibits the presence of multiple small microcysts within the connective tissue wall; which are known as "daughter cysts" or "satellite cysts".
- Odontogenic keratocysts have a tremendous tendency for recurrence after treatment.
- Treatment is done by surgical enucleation; resection of jaw done in case of repeated recurrence.

IMMUNOHISTOCHEMISTRY

Immunohistochemical study using monoclonal antibodies indicates that the epithelial cells in odontogenic keratocyst appear to undergo a gradual maturation as they migrate to the upper cell layers. However, in dentigerous and radicular cyst, this type of basal to surface differentiation is absent.

ENLARGEMENT OF CYST

The odontogenic keratocyst always tends to spread via the cancellous bone and clinically noticeable bone expansion is evident only in the later stages. Generally the expansion of the cyst occurs through the following mechanisms.

Mechanism of cyst enlargement

- *Cell proliferation*
- *Osmolarity of cyst fluid*
- *Enzymatic mechanisms*

Cell Proliferation

As odontogenic keratocyst is made up of preformative cells of dental lamina they have an increased tendency for mitotic divisions. Increase mitotic activity of the cystic epithelial cells may contribute to the greater expansion or enlargement of the cyst.

Osmolarity of Cyst Fluid

The average concentration of the cystic fluid is usually higher than that of the blood serum, which could be due to the presence of large amounts of soluble protein and cell break down products within the cystic fluid.

Because of this there is a significant osmotic difference between the serum and the cystic fluid, which helps to draw more and more fluid towards the cystic lumen through the process of diffusion (osmotic).

Thus, there is an increased hydrostatic pressure in the cyst, which causes resorption of bone and results in more and more expansion of the cyst.

It is to be noted that continuous shedding of the cells of the cystic lining and incorporation of their break down products (mainly proteins) into the cystic fluid always maintains the higher Osmolarity of the fluid in comparison to the blood serum. This results in a continuous tendency for the cyst to enlarge itself with time.

Enzymatic Mechanisms

Increased collagenase activity: It is believed by some investigators that odontogenic keratocysts can release considerable amount of collagenese enzyme, which causes destruction of collagen in the bone (collagenolysis). This results in increased bone resorption and subsequent expansion of the cyst.

TREATMENT

Treatment is done by either "**surgical enucleation**" or "**marsupialization"** of the cyst. The oral epithelium, which is overlying the cystic lesion, has to be excised to eliminate the possibility of further recurrence (because some cysts may develop from the basal layer of the oral epithelium). Usually, the recurrence rate is very high in odontogenic keratocyst and in case of repeated recurrence of the cystic lesion, jaw resection is recommended.

Key points in recurrence

- Satellite cyst
- New cyst formation
- Keratinization pattern
- Nature of cyst lining
- Basal layer of oral epithelium
- Conservative surgical approach.

CAUSES OF RECURRENCE

Odontogenic keratocysts may recur after treatment in about 60% cases, the causes of this higher rate of recurrence are as follows:

- ***Satellite cyst:*** The satellite cyst or daughter cyst are common entities in odontogenic keratocysts and these small cysts often remain undetected within the tissue during treatment. The higher rate of recurrence in keratocysts could be due to the enlargement of the satellite cysts following treatment.
- ***New cyst formation:*** The cells of the odontogenic keratocysts have an aggressive potential for multiplication (since these are preformative group of cells of the dental lamina) and this tendency may often cause formation of newer cysts in the jaw, which often appears to be a case of recurrence.

  Moreover, if any part of the cyst capsule remains within the bone during surgery, the retained part of the capsular tissue of the cyst (containing remnants of epithelial islands) may lead to recurrence due to multiplication and subsequent cystification of those epithelial remnants.
- ***Keratinization pattern of the cyst epithelium:*** Odontogenic keratocysts which have parakeratinized epithelium often have more possibility of recurrence.
- ***Nature of cyst lining:*** The lining of the odontogenic keratocyst is thin and fragile and therefore, it is very difficult to enucleate the entire lining of a large cyst during surgery. Thus, if some portion of the lining is left behind within the bone, it could result in further cyst formation.

  Moreover, the odontogenic keratocysts grow very fast but as the bony expansion is too little, the size of the cyst is always smaller than what is expected; as a result the cystic epithelium often folded. These narrow infoldings or finger-like projections extend deep into the cancellous bone up to a variable depth and during surgery these narrow infoldings are easily left behind, therefore increasing the risk recurrence.
- ***Basal layer of oral epithelium:*** New keratocysts may sometimes develop from the basal layer of oral epithelium.
- ***Conservative surgical approach:*** In an attempt to save a vital structure (a tooth, a nerve or a blood vessel, etc.) adjacent to the cyst, sometimes conservative surgical approach is undertaken. This may result in incomplete removal of the cyst leading to recurrence.

DENTIGEROUS CYST

DEFINITION

Dentigerous cyst is a common odontogenic cystic lesion, which encloses the crown of an impacted

tooth at its neck portion. The cyst develops due to abnormal dilatation of the dental follicle.

PATHOGENESIS

- Dentigerous cyst is derived from the cells of the **reduced enamel epithelium**, which surrounds the crown of the impacted or unerupted tooth.
- The cyst enlarges due to accumulation of fluid in between the reduced enamel epithelium and the tooth crown.
- When the cyst develops around the crown of an impacted permanent tooth, periapical inflammation in the overlying deciduous tooth may be the triggering factor.
- However, in many cases the stimulus, which separates the reduced enamel epithelium from the enamel surface and thereby creates a space for fluid accumulation around the crown of the tooth and eventual cystification, is not known.
- A strong association is seen between failure of eruption of tooth and the development of dentigerous cyst. That's why this cyst often develops in relation to lower third molars and the upper canines.
- Regardless of the size, dentigerous cyst always remains attached to the cervical margin (cementoenamel junction) of the involved tooth.
- The crown of the tooth is located within the lumen of the cyst while the root remains outside.

CLINICAL FEATURES

Incidence: Incidence rate of dentigerous cyst is about 16 percent among all intraoral cysts.

Age: Mostly second and third decade of life.

Sex: It is seen more commonly in males in comparison to females.

Site: This cyst occurs twice as common in mandible as in maxilla.

Mandibular third molar area is the most common site of occurrence of dentigerous cyst, although the maxillary canine, mandibular second premolar and maxillary third molar areas are also commonly affected. The cyst also frequently occurs in relation to the supernumerary teeth or odontomes, etc. Although rare, dentigerous cyst can develop in relation to an unerupted deciduous tooth.

CLINICAL PRESENTATION (FIGS 6.8 TO 6.10)

- In many cases, smaller cysts remain asymptomatic and are detected incidentally during the routine radiographic examinations for a missing tooth in the dental arch.
- A cyst can also be found occasionally during radiographic examination of a retained deciduous tooth.
- Dentigerous cyst normally presents a slow enlarging bony hard swelling of the jaw with expansion of the cortical plates of bone (Figs 6.8 and 6.9).
- Massive facial swelling, derangement of occlusion and development facial asymmetry,

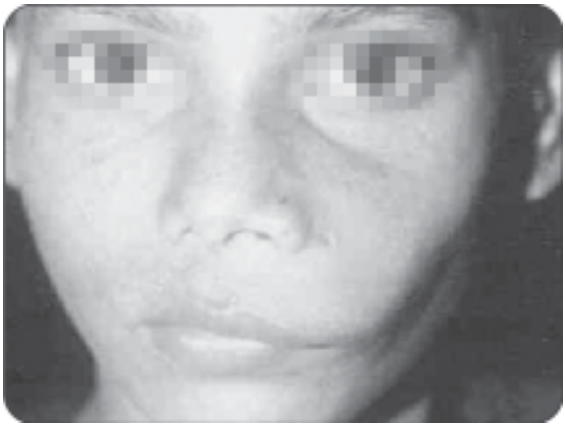

Fig. 6.8: Dentigerous cyst involving the left side of maxilla

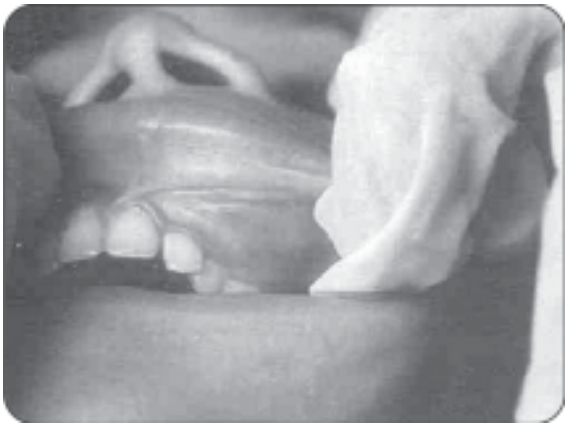

Fig. 6.9: Dentigerous cyst causing a large swelling of the bone

etc. are seen in extremely large lesions.

- Severe expansion of bone results in thinning of the cortical plates and on palpation the affected area of bone gives a "**crepitus-like**" sensation. Moreover, if the overlying bone is completely lost due to a growing cyst, "**fluctuations**" may be felt in the area.
- Occasionally, pain and accelerated swelling may be noticed if the cyst gets secondarily infected and besides this, there may be formation of pus discharging sinuses on the mucosa overlying the cyst.
- Paresthesia and anesthesia on the affected part of the jaw often develop. In few lesions pathological fractures of the jawbone may occur.
- As the cyst develops around the crown of an impacted or embedded tooth; clinically often there is a missing tooth in the dental arch.

RADIOLOGICAL FEATURES (FIGS 6.11 TO 6.14)

- Radiograph of dentigerous cyst reveals a well-defined, unilocular rounded, radiolucent area, enclosing the crown of an impacted tooth.
- The tooth associated with the cyst is often displaced from its normal position in the jaw, e.g. the involved lower third molar is often pushed to the lower border of mandible or to the ramus area. Likewise the upper tooth may be pushed to the maxillary sinus or to the floor of the orbit.
- Exceedingly large cysts may look multilocular due to the persistence of several residual bony trabeculae within the cystic space.

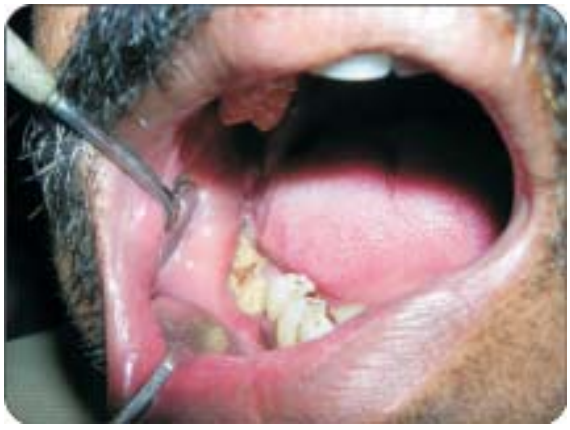

Fig. 6.10: Dentigerous cyst

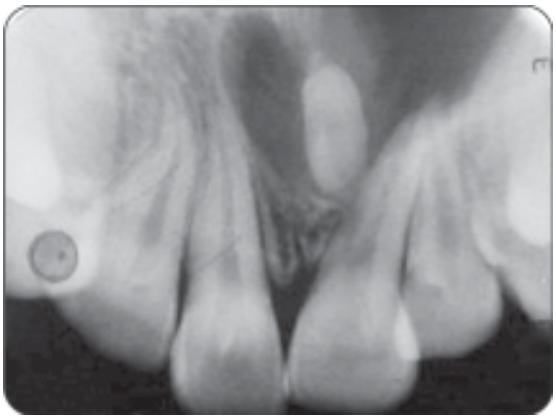

Fig. 6.11: Dentigerous cyst in relation to a supernumerary tooth

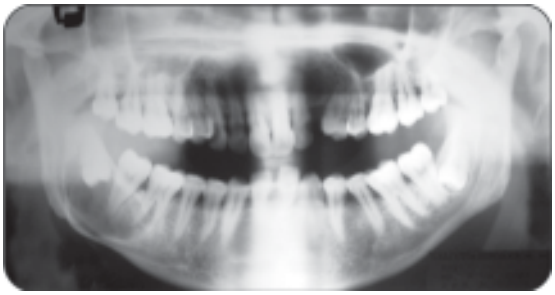

Fig. 6.12: Radiograph of dentigerous cyst

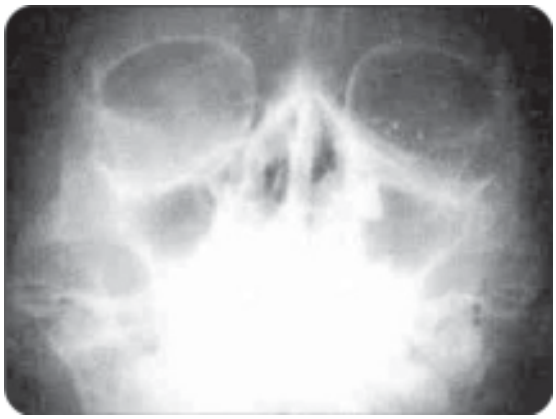

Fig. 6.13: X-ray reveals dentigerous cyst developing in relation to maxillary antrum

- Expansion and distortion of the cortical plates of bone occurs commonly and the periphery of the cyst is often bordered by well-corticated or sclerotic margin.
- The cyst occurs in association with an impacted tooth of regular series in the dentition or an impacted supernumerary tooth or even an odontome (Fig. 6.11).

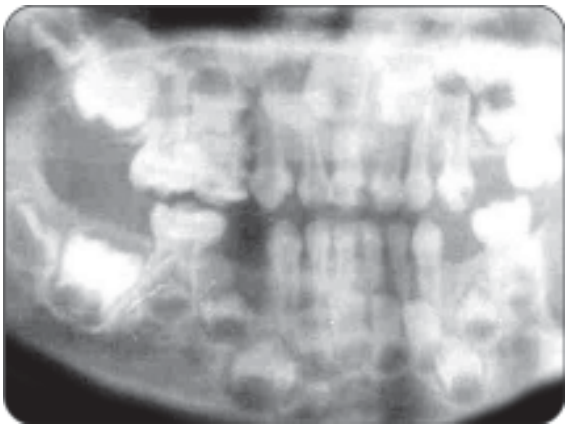

Fig. 6.14: X-ray reveals dentigerous cyst developing in relation to lower first molar tooth

- Interestingly, the dentigerous cyst in most of the cases shows **resorption of the roots** of the neighboring erupted teeth. In long standing lesions, the tooth which is enclosed within the cyst may also become resorbed.
- Chronically infected dentigerous cysts may have hazy or ill-defined borders.

RADIOLOGICAL TYPES OF DENTIGEROUS CYST

On the basis of the 'cyst' to 'the associated tooth crown' relationship, dentigerous cysts are divided into three types:

Central type: When the cystic cavity envelops or surrounds the crown of the impacted tooth symmetrically from all sides. This is the most common radiographic type found and this type of cyst may push the involved tooth away from its direction of eruption.

Lateral type: In this case, the cystic cavity is located on one side of the involved crown. It results from deflection of the dental follicle on one side of the crown during the eruption of the tooth. This type is mostly seen when the cyst develops in relation to a partially erupted, mesioangular type of mandibular third molar.

Circumferential type: When the cystic cavity radiolographically appears to enclose the entire tooth. This type of radiographic appearance is found when the impacted tooth is seen in a two-dimentional picture in the background of a very large cyst (although the cyst never encloses the tooth completely).

Cystic Fluid in Dentigerous Cyst

The cyst is usually filled with a straw colored fluid that contains about 5 gm percent of soluble protein.

DIFFERENTIAL DIAGNOSIS

- Adenomatoid odontogenic tumor (AOT)
- Compound odontome
- Unilocular ameloblastoma
- Odontogenic keratocyst
- Ameloblastic fibro-odontome
- Ameloblastic fibroma
- Calcifying epithelial odontogenic cyst.

HISTOPATHOLOGY (FIGS 6.15 TO 6.17)

- Histologically, dentigerous cyst reveals the presence of a cystic cavity, which is lined by a **thin layer of nonkeratinized, odontogenic epithelium (about 2 to 3 cell layer thickness).**
- The lining epithelium is supported by a loosely arranged connective tissue stroma that often resembles the **odontogenic ectomesenchyme**.
- The stroma consists of young fibroblast cells, which are widely separated by a ground substance rich in mucopolysaccharides and collagen bundles.
- The cystic epithelial cells are usually flat or cuboidal in nature and the epithelium often exhibits pseudostratifications.
- The epithelium is mostly nonkeratinized and has relatively uniform orientation of the cell layers.
- Sometimes superficial layer of the cystic epithelium may be low columnar in nature

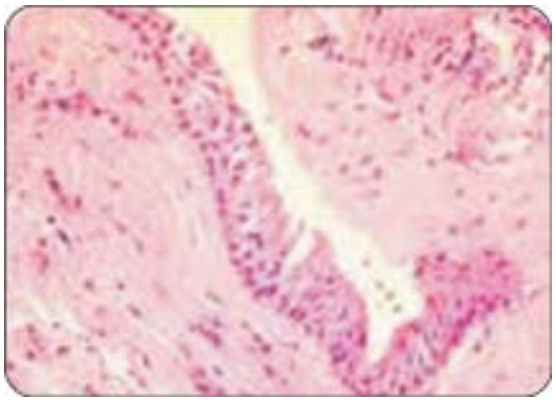

Fig. 6.15: Photomicrograph of dentigerous cyst-I

Key points of dentigerous cyst

- Dentigerous cyst is a common odontogenic cystic lesion, which encloses the crown of an impacted tooth at its neck portion.
- The cyst develops from the reduced enamel epithelium which surrounds the crown of the impacted or unerupted tooth.
- Dentigerous cyst commonly develops from the mandibular third molar area. The other common sites include the maxillary canine, mandibular second premolar and maxillary third molar areas, etc.
- Clinically, the cyst often presents a slow enlarging bony hard swelling of the jaw with expansion of the cortical plates of bone.
- Massive facial swelling, derangement of occlusion and development facial asymmetry, etc. are seen in extremely large lesions.
- Expansion and severe thinning of the bone may produce fluctuations in the area.
- Radiographically, the cyst reveals a well-defined, unilocular rounded,radiolucent area enclosing the crown of an impacted tooth.
- Dentigerous cyst often exhibits resorption of roots of the adjoining teeth.
- The cyst has three radiological types: Central type, lateral type and circumferential type.
- The cyst is usually filled with a straw colored fluid that contains about 5 gm percent of soluble protein.
- Histologically, dentigerous cyst reveals the presence of a cystic cavity, which is lined by a thin, non-keratinized epithelium of 2 to 3 cell layer thickness.
- The lining epithelium of the cyst is supported by a loosely arranged connective tissue stroma that resembles the odontogenic ectomesenchyme.
- Localized areas of "bud-like" proliferations of cystic epithelial cells may be seen in few areas of the cyst wall, which are known as "**mural proliferations**".
- Treatment is done by enucleation.

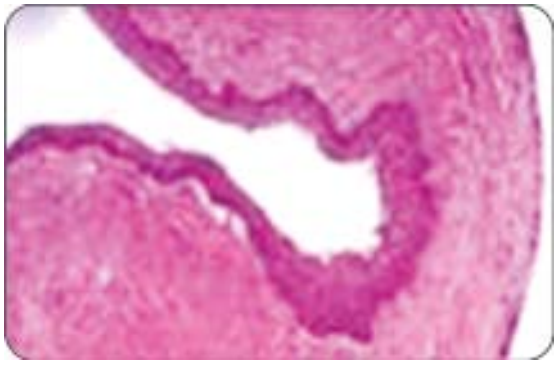

Fig. 6.16: Photomicrograph of dentigerous cyst-II

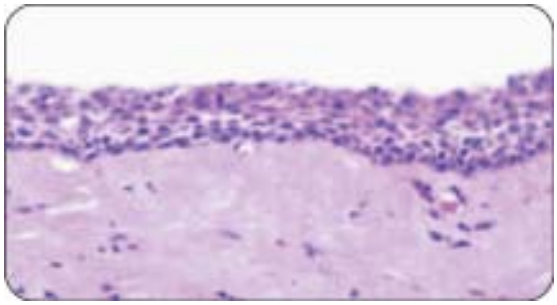

Fig. 6.17: Photomicrograph of dentigerous cyst-III

and the cells partly resemble ameloblasts cells of the developing tooth germ.

- Nests, islands and strands of odontogenic epithelium are sometimes seen within the capsule.
- Long standing dentigerous cysts may occasionally exhibit areas of keratinization or dysplastic changes in the epithelial lining.
- Localized areas of "bud-like" proliferations of cystic epithelial cells may be seen in few areas of the cyst wall, which are known as "**mural proliferations**" and they indicate the neoplastic change in the cystic epithelium towards the development of "ameloblastoma" from the lining of the dentigerous cyst.
- Besides ameloblastoma, many other tumors, e.g. squamous cell carcinoma and intraosseous mucoepidermoid carcinoma, etc. can develop from the dentigerous cyst lining.
- Chronic inflammatory cell infiltration is rarely seen in the connective tissue stroma.

- Discontinuities in the epithelial lining may be seen due to secondary infections in the cyst.
- Cystic epithelium may undergo **mucous metaplasia** and thus, the lining epithelium may exhibit the presence of numerous mucous producing cells.
- In some cases the cystic epithelium may be keratotic, hyperplastic, atrophic or ulcerated in nature and such changes may occur in response to either pericystic or intracystic inflammations.

ENLARGEMENT

Osmolarity

Increased osmolarity of the cystic fluid (in comparison to the blood serum) often cases more and more fluid accumulation in its lumen. Thus, the increased intracystic hydrostatic pressure may result in bone resorption with subsequent expansion of the cyst.

Chemical Mediators

- The cystic epithelium often releases chemical mediators, e.g. interleukin -1, prostaglandins (PGE_2, PGE_3 and PGI_2) and collagenase, etc.
- These chemical agents cause bone resorption at the periphery of the cyst and eventually help in its expansion.
- The prostaglandins also cause activation of the osteoclast cells, which in turn cause increased bone resorption.
- The interleukin-1 may produce osteolytic bone resorption with subsequent cyst expansion in the following pathways:
  - It causes stimulation of the osteoclast cells to resorb bone.
  - It stimulates the connective tissue cells to produce prostaglandins, which can cause resorption of bone by stimulating the osteoclastic activity.
  - It also stimulates the connective tissue cells to produce collagenase enzyme, which causes destruction of bone matrix (collagen).

CAUSES OF ROOT RESORPTION IN DENTIGEROUS CYST

The dentigerous cyst often shows resorption of root(s) of the adjacent normal teeth. The possible reasons for this could be the presence of reduced enamel epithelium in dentigerous cyst.

- During the normal physiologic shedding of primary teeth, the reduced enamel epithelium actively participates in the root resorption of these deciduous teeth.
- This inherent tendency for root resorption may be retained by the cells of dentigerous cyst, which are also derived from the reduced enamel epithelium.
- The cystic epithelial cells release some chemicals substances, which can cause resorption of roots similar to that of the normal reduced enamel epithelial cells in a developing permanent tooth.

TREATMENT

Treatment of dentigerous cyst is done by "marsupialization" (if the involved tooth is to be preserved). In other cases, the treatment can be done by surgical enucleation of the cyst.

RADICULAR CYST

DEFINITION

Radicular or periapical cyst is the most common odontogenic cystic lesion of inflammatory origin, which occurs in relation to the apex of a nonvital tooth.

In a radicular cyst if the involved tooth is exfoliated or extracted and the cystic lesion remains within the bone, the condition is known as residual cyst.

PATHOGENESIS

The radicular cyst develops due to the proliferation and subsequent cystic degeneration of the "**epithelial cell rests of Malassez**", in the periapical region of a nonvital tooth. The entire process of development of this cyst occurs in several phases.

- Phase of initiation
- Phase of proliferation
- Phase of cystification
- Phase of enlargement.

Phase of initiation: During this phase, the bacterial infection of the dental pulp or direct inflammatory effect of necrotic pulpal tissue, in a nonvital tooth causes stimulation of the "cell rest of Malassez" which are present within the bone near the root apex of teeth.

Phase of proliferation: The stimulation to the cell rests of Malassez leads to excessive and exuberant proliferation of these cells, which leads to the formation of a large mass or island of immature proliferating epithelial cells at the periapical region of the affected tooth.

Phase of cystification: Once a large bulk of the cell rest of Malassez is produced, its peripheral cells get adequate nutritional supply but its centrally located cells are often deprived of proper nutritional supply. As a result the central or innermost group of cells undergo ischemic liquefactive necrosis while the peripheral group of cells survive. This eventually gives rise to the formation of a cavity that contains a hollow space or lumen inside the mass of the proliferating cell rest of Malassez and a peripheral lining of epithelial cells around it.

Phase of enlargement: Once a small cyst is formed, it enlarges gradually by the following mechanisms:

- Higher osmotic tension of the cystic fluid causes progressive increase in the amount of fluid inside its lumen and this causes increased internal hydrostatic tension within the cyst. The process results in cyst expansion due to resorption of the surrounding bone.
- The epithelial cells of the cystic lining release some bone resorbing factors like prostaglandins and collagenase, etc. which destroy the bone and facilitate expansion of the cyst.
- It has been observed that some people are more prone to develop radicular cyst as compared to others who do not develop radicular cyst despite having grossly carious nonvital teeth in the jaws. It is, therefore, believed that some kind of immune mechanisms may prevent the cyst formation in few people while on the other hand defective immunity may cause the development of cyst in other persons. Sometimes the process of cyst formation can be genetically determined.

CLINICAL FEATURES

Incidence: Radicular cyst constitutes about 50 percent or more among all types of jaw cysts.

Age: Mostly third, fourth and fifth decade of life.

Sex: More common among males.

Site: The cyst can occur in relation to any tooth of either jaw, but maxilla (60%) is usually more commonly affected than mandible (40%). The occurrences of more caries in the upper anterior teeth and the occasional presence of dense–in–dente in the upper lateral incisors are usually responsible for the higher incidence of this cyst in the maxilla. Moreover, people tend to save the anterior teeth more often as compared to the posterior teeth even if those are grossly carious. This can be a cause for the occurrence of more periapical cysts in anterior part of the jaws.

CLINICAL PRESENTATION (FIG. 6.18 TO 6.21)

- The involved tooth is always nonvital and it can be easily detected by the presence of caries, fractures or discolorations, etc. Moreover, the affected tooth does not respond to thermal or electric pulp testing.
- Radicular cyst may occur rarely in association with nonvital deciduous tooth (mostly molars).
- The cyst becomes more symptomatic when there is acute exacerbation of the periapical inflammation.
- The smaller cystic lesions are usually asymptomatic and are detected only when a radiograph is taken.

Fig. 6.18: Radicular cyst

- The larger lesions on the other hand, often produce a slow enlarging, bony hard swelling of the jaw with expansion and distortion of the cortical plates or disturbance in occlusion mostly of the regional teeth.
- Maxillary lesions may cause either buccal or palatal cortical expansions whereas the mandibular lesions often cause buccal or labial expansions and rarely the lingual expansions (Fig. 6.19).
- Severe bone destruction by the cystic lesion results in thinning of the cortical plates and it may produce a "**springiness"** of the jawbone when digital pressure is applied.
- There may be presence of fluctuations in case the bone is completely eroded by a large cyst. These lesions clinically appear **blue** as they lie close to the overlying epithelium since the bone has been completely resorbed.
- Pain may be present in the cyst, if it is secondarily infected and it may result in the development of either intraoral or extraoral pus discharging sinuses.
- On rare occasions, there may be occurrence of paresthesia or pathological fractures in the bone, etc.
- Occasionally, radicular cysts can be multiple in numbers, occurring in relation to several teeth or in relation to several roots of a multi-rooted tooth.
- A radicular cyst may persist in the jaw after the attached tooth has been extracted; such cyst is often called a '**residual cyst'**. These cysts frequently cause of swelling in the edentulous jaws and they regress slowly and spontaneously (Fig. 6.21).
- In some cases, radicular cysts may develop at the opening of a large accessory pulp canal on the lateral aspect of the tooth root; and these cysts are often termed as '**lateral radicular cysts**'.
- If the cyst is secondarily infected it leads to the formation of an abscess, which is called "**cyst abscess"**.

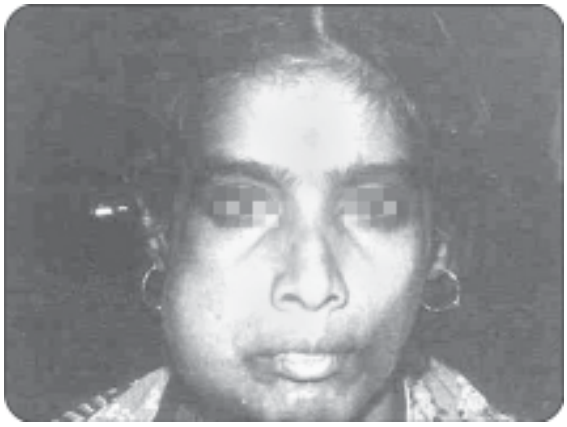

Fig. 6.19: Radicular cyst developing from the right side of mandible

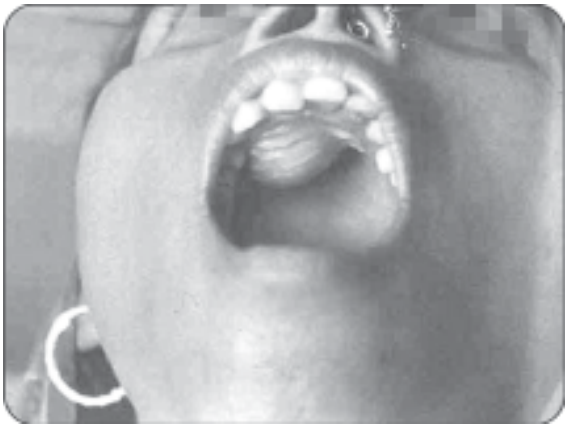

Fig. 6.20: Radicular cyst developing from the right upper lateral incisor

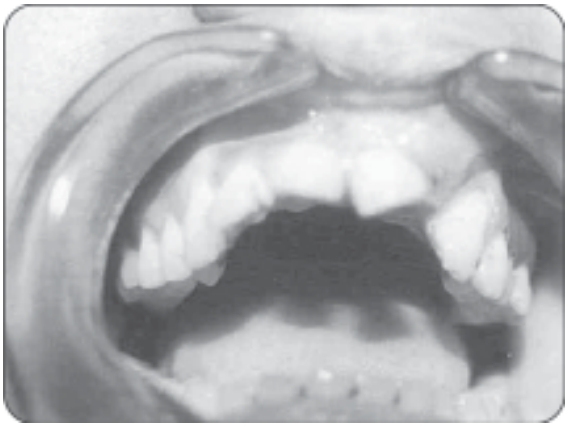

Fig. 6.21: A residual cyst at the left maxillary lateral incisor region

RADIOLOGICAL FEATURES (FIGS 6.22 TO 6.24)

- On radiographs, radicular cysts present well-defined, unilocular, round shaped radiolucent areas of variable size (few millimeters to several centimeters in diameter) (Fig. 6.23).

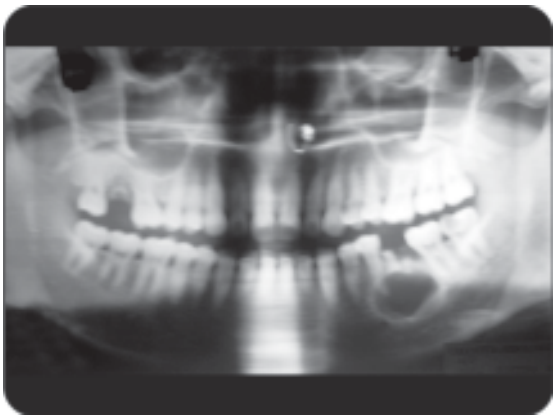

Fig. 6.22: Radiograph of radicular cyst

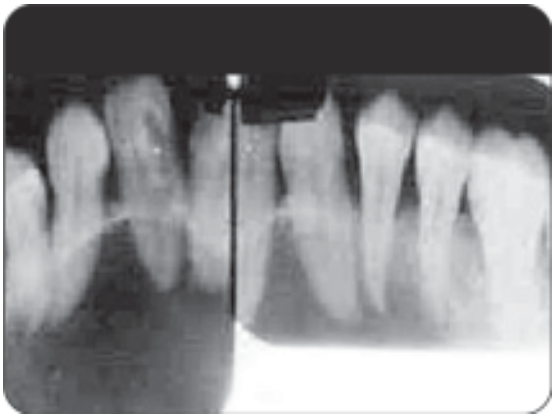

Fig. 6.23: Radiograph of radicular cyst producing a unilocular radiolucency in relation to right upper lateral incisor

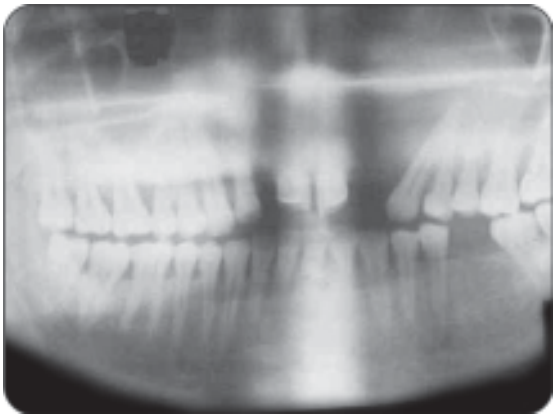

Fig. 6.24: Radiograph of residual cyst causing displacement of the root of the neighboring teeth

- The cyst is always found in contact with the root apex of a nonvital tooth and it is bordered on the periphery by a well-corticated margin. The infected cysts often have hazy or an ill-defined border.
- The adjacent teeth are often tilted or displaced and often there is loss of lamina dura of these adjacent tooth roots.
- The nonvital tooth with which the cyst is attached, often have a large carious cavity or a fracture on the crown.
- The lateral radicular cysts appear as semi-circular radiolucency on the lateral aspect of the root with loss of lamina dura.
- Root resorption is often seen in the associated nonvital tooth.
- Residual cyst appears as a round or oval radiolucent area in the alveolar ridge where from a tooth was extracted previously (Fig. 6.24).

MACROSCOPIC APPEARANCE

- Macroscopic examination of radicular cyst reveals a round or ovoid soft tissue sack, which is attached to the root apex of a nonvital tooth.
- On cutting, a thin straw colored fluid or a thick, paste like, yellow-brown coagulum is found within the lumen.
- Cholesterol crystals may be present within the cyst content, which appear as glistening particles.
- The cyst capsule is usually several millimeters thick and the internal luminal contour of the cyst may be smooth or corrugated.

Cystic Fluid

Aspiration of the cystic contents often reveals a straw colored fluid, which may be sometimes blood-tinged. Sometimes the cystic fluid may be watery and opalescent. The cystic fluid may also contain cholesterol crystals; which can be seen under microscope once a smear of the fluid is prepared.

Paper electrophoresis indicates the presence **of about 5 gm percent of soluble protein in it.**

HISTOPATHOLOGY (FIGS 6.25 AND 6.26)

- Histologically, radicular cyst shows the presence of a cystic cavity, which is lined by a nonkeratinized, stratified squamous epithelium of **about 6 to 20 cell layers thickness** and the lining epithelium is backed by a well-vascularized, connective tissue stroma.

Key points of radicular cyst

- Radicular or periapial cyst is the most common odontogenic cystic lesion of inflammatory origin, which occurs in relation to the apex of a non-vital tooth.
- The radicular cyst develops from the "epithelial cell rests of Malassez"
- Clinically smaller cystic lesions are usually asymptomatic and are detected only when a radiograph is taken.
- The larger lesions however produce a slow enlarging, bony hard swelling of the jaw with expansion and distortion of the cortical plates, displacement of teeth and malocclusion, etc.
- On radiograph radicular cyst presents a well-defined, unilocular, round shaped radiolucent area at the root apex.
- The cystic fluid is often straw colored and contains about 5 gm percent of soluble protein.
- Histologically radicular cyst presents of a cystic cavity lined by thick, nonkeratinized, stratified squamous epithelium of about 6 to 20 cell layers thickness.
- The proliferating cystic epithelium may sometimes grow in a peculiar "arcading pattern".
- The cyst capsule is made up of vascular connective tissue, which is often infiltrated by many chronic inflammatory cells.
- The cyst also contains many other important structures, e.g. cholesterol clefts, Russell body and Rushton body ,etc
- Treatment is done by enucleation and marsupialization.
- In radicular cyst, if the associated tooth is removed but the cyst remains inside the jaw, the condition is called 'residual cyst'.

- Sometimes discontinuities in the epithelial lining may be seen in the areas of inflammation.
- The epithelium is **non-keratinized** and it often shows localized areas of increased cell proliferation and edema.
- The thickness of the lining is not same everywhere, in some areas it is thin while in some other areas it is very thick. This entirely depends upon the presence of inflammatory stimulus within the cyst.
- Ciliated columnar epithelium or respiratory epithelium may also be present in radicular cyst on rare occasions due to metaplastic change in the cystic lining.

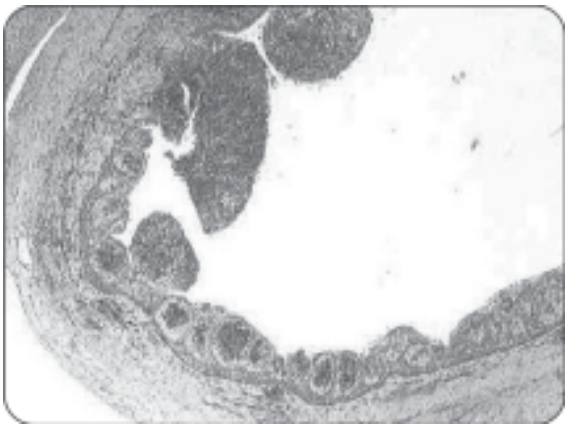

Fig. 6.25: Photomicrograph of radicular cyst-I

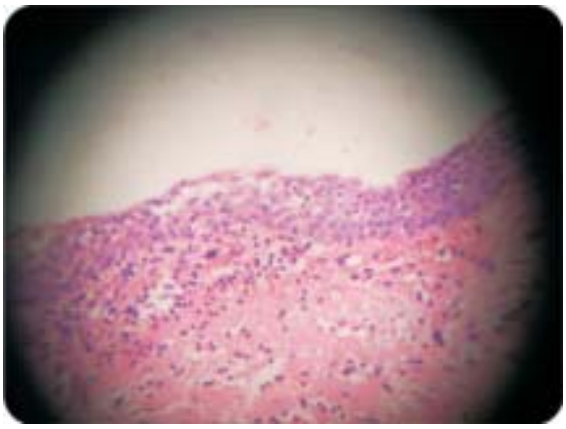

Fig. 6.26: Photomicrograph of radicular cyst-II

- Occasionally, there may be presence of mucous secreting goblet cells in the lining of the cyst (these cells form also as a result of metaplasia in the cystic lining).
- Focal or generalized keratinization may be seen in some cases in the cysts lining.
- The proliferating cystic epithelium may sometimes grow in a peculiar fashion, by enclosing or encircling a mass of connective tissue capsule from all sides. This pattern of growth is called "**arcading pattern**".
- Presence of inflammatory cell infiltration and edema is often seen the cystic lining.
- The cyst capsule is made up of vascular connective tissue, which is often infiltrated by chronic inflammatory cells (predominantly plasma cells).
- Multiple small, ribbon-shaped or needle-shaped, cleft-like spaces are seen either in the

cystic lumen or in the connective tissue capsule of the cyst; these are known as "**cholesterol clefts**". Normally, cholesterol is derived from breakdown of blood cells and is present in the cyst wall; only the cholesterol clefts are left out in the cyst, when cholesterol is dissolved during chemical processing of the tissue for sectioning.

- In some cases, multiple laminated "crescent" shaped or "hairpin" shaped hyaline structures are also present in the cyst.
- "**Rushton bodies**" are also found within the cystic lining or in the connective tissue.
- "**Russell bodies"** are sometimes seen in the cyst, which are nothing but a plasma cell being surrounded by immunoglobulines.
- The cystic epithelium may sometimes undergo malignant transformation.
- Round or irregular shaped squamous epithelial islands are sometimes seen within the capsule.
- Multinucleated foreign body type of giant cells may be seen within the connective tissue.

DIFFERENTIAL DIAGNOSIS

- Periapical granuloma
- Central giant cell granuloma
- Periapical abscess
- Cementoma (Stage I)
- Traumatic bone cyst
- Bony artifact.

SCANNING ELECTRON MICROSCOPY

- SEM study of the inner surface of the radicular cyst shows that the surface epithelium is sometimes fairly smooth with shallow foldings or ridges.
- Sometimes, it is irregular and ruffled.
- Irregular shaped intraepithelial spaces are found, which can permit the penetration of WBC or RBC cells.

TREATMENT

Small cysts are treated by root canal treatments of the affected teeth and apical curettage. The larger cysts are treated either by enucleation and marsupialization.

ERUPTION CYST

DEFINITION

Eruption cyst is an odontogenic cyst, which surrounds the crown of a tooth that has erupted through the bone, but not the soft tissue.

The eruption cyst develops due to the accumulation of fluid within the follicular space of an erupting tooth and hence can be called the **soft tissue variant of dentigerous cyst**.

ORIGIN

The cyst is derived from the reduced enamel epithelial cells.

CLINICAL FEATURES

- Clinically, the cyst presents a small, rounded, soft and fluctuant swelling on the alveolar ridge, immediately superior to an erupting tooth.
- This soft tissue cyst is obviously common among the children and it can develop in relation to a deciduous or a permanent tooth.
- The cyst contains either a clear fluid or a blood-tinged fluid and it often has a translucent hue.
- Masticatory trauma may induce hemorrhage within the cyst, which gives rise to the formation of "**eruption hematoma**" and the lesion often appears **bluish-purple** or red in color.

HISTOPATHOLOGY

Histologically, the cyst is similar to the dentigerous cyst and exhibits a thin lining of non-keratinized squamous epithelium.

The cyst may also have numerous epithelial ghost cells within the lumen of the cyst and these cells are derived from the exfoliating lining epithelial cell of the cyst.

TREATMENT

No treatment is required for eruption cyst as it disappears spontaneously once the tooth erupts into the oral cavity. Sometimes in long standing lesions, the roof of the cyst is excised to allow the tooth to erupt in the oral cavity.

LATERAL PERIODONTAL CYST

DEFINITION

The lateral periodontal cyst is an uncommon developmental odontogenic cyst that develops in immediate association with the **lateral root surface of an erupted vital tooth**. It is considered to be the intrabony counterpart of gingival cyst of adults.

CLINICAL FEATURES

- Lateral periodontal cyst represents about 0.7% of all jaw cysts and it commonly occurs in adult males.
- Maxillary and mandibular anterior region is the common site.
- Clinically, the lesion is mostly asymptomatic and detected during routine radiographic examinations.
- In few cases there may be a small, painless soft tissue swelling within or just anterior to the interdental papillae.
- The overlying mucosa is generally normal in color, but in few cases, there may be a bluish discoloration.
- The tooth, with which the cyst is associated, is vital.
- The cyst is usually less than 1 cm in diameter and it never causes resorption of the root of the affected tooth.

RADIOLOGICAL FEATURES

Radiographically, lateral periodontal cyst presents a small, unilocular, "teardrop-shaped" radiolucent area, on the lateral aspect of the root (near the crest of the alveolar ridge).

The lesion is often surrounded by a thin, delicately corticated margin at the periphery.

PATHOGENESIS

Mainly controversial, but it is generally believed that the cyst arises from the reduced enamel epithelial cells or from the cell rest of Malassez or from the cell rests of Serre, all these cells could be present within the periodontal ligament tissue.

DIFFERENTIAL DIAGNOSIS

- Lateral periodontal abscess or granuloma
- Radicular cyst
- Early ameloblastoma
- Collateral type of primordial cyst
- Lateral dentigerous cyst
- Globulomaxillary cyst.

Key points of lateral periodontal cyst

- The lateral periodontal cyst is a developmental odontogenic cyst of the jaw.
- It develops in relation to the **lateral root surface of an erupted vital tooth** mostly in the mandibular anterior region.
- The cyst originates from the reduced enamel epithelial cells or from the cell rest of Malassez
- It is considered to be the intrabony counterpart of gingival cyst of adults.
- Clinically, lateral periodontal cyst presents a small, painless soft tissue swelling within or just anterior to the interdental papillae.
- Radiographically, it shows a small, unilocular, "**teardrop-shaped**" radiolucent area, on the lateral aspect of the root
- The cyst is lined by nonkeratinized stratified squamous epithelium of 2 to 3 cell layers thickness.

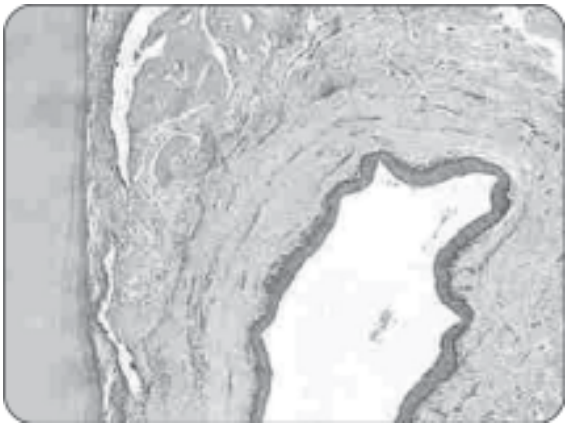

Fig. 6.27: Photomicrograph of lateral periodontal cyst

HISTOPATHOLOGY

- Lateral periodontal cyst microscopically presents a small cystic cavity, backed by a thin, noninflammed connective tissue wall (Fig. 6.27).
- The cavity in lined on the inner aspect by non-keratinized stratified squamous epithelium of 2 to 3 cell layers thickness.

- The lining epithelial cells appear flattened and they often resemble the reduced enamel epithelial cells.
- Focal areas of thickening of the lining epithelium (plaques) as well as some papillary infoldings of the wall are commonly seen in the cyst.
- The cystic epithelium often contains cluster of glycogen–rich, clear cells, with vacuolated cytoplasm (these cells resemble the cells of dental lamina).
- The epithelial cells are sometimes separated by the intercellular fluid and these cells have small pyknotic nuclei.

TREATMENT

Treatment of lateral periodontal cyst is done by surgical excision along with the tooth. Sometimes the related tooth can be saved if healthy.

DENTAL LAMINA CYST (GINGIVAL CYST) OF THE NEWBORN

DEFINITION

Gingival cysts of the newborn are multiple small, nodular, keratin-filled, cystic lesions seen in the oral cavity of newborns or very young infants (from birth up to 3 months of age).

Depending upon their locations in the oral cavity, these cysts are divided into several types.

Cysts of the dental lamina: These lesions are mostly found **along the alveolar ridge** and are odontogenic in origin (arising from the remnants of dental lamina).

Epstein's pearls: These small creamy colored cystic lesions are **found linearly along the midpalatine raphe** and are probably derived from the epithelium, entrapped along the line of fusion of the palate during embryogenesis.

Bohn's nodules: In this case, small cysts are usually found along the **junction of the hard** and **soft palate** and on the buccal and lingual aspects of **alveolar ridge**. These types of cysts are derived from remnants of the mucous glands.

Gingival cysts of newborn

Types of cyst	Location
Cysts of the dental lamina	Along the alveolar ridge
Epstein's pearls	Found linearly along the midpalatine raphe
Bohn's nodules	Along the junction of the hard and soft palate, and buccal and lingual aspects of alveolar ridge.

CLINICAL FEATURES

- All these types of cysts in the newborn usually appear as multiple, asymptomatic, small discrete, white nodules, which develop in several parts of the oral cavity.
- Once formed the dental lamina cysts may discharge the contents by fusion with the overlying alveolar mucosa or they may undergo spontaneous regression.
- The size of these cysts are very small and do not exceed 2 to 3 millimeters in maximum diameter.
- The gingival cysts of newborn involve the maxillary arch more often than mandibular arch.

HISTOPATHOLOGY

Microscopic section exhibits a small keratin–filled cystic cavity, which is lined by a thin and flattened squamous epithelium.

TREATMENT

No treatment is required.

GINGIVAL CYSTS OF THE ADULT

DEFINITION

Gingival cysts of the adult are small developmental odontogenic cysts of the gingival soft tissue. These are mostly derived from the cell rests of the dental lamina (cell rest of Serre).

CLINICAL FEATURES

Age: Fifth and sixth decade of life (after 40 years of age).

Sex: It is more prevalent among females.

Site: It is more common in relation to mandible in comparison to maxilla, particularly in the canine-premolar region. Facial side of the gingiva is more commonly affected.

PRESENTATION

- The cyst is located in the gingival tissue outside the bone.
- It clinically presents a firm but compressible, fluid filled, 'dome-like' swelling on the mandibular or maxillary facial gingiva around the canine-premolar area.
- The swelling is often well-circumscribed, usually less than 1 cm in diameter and it occurs in the attached gingiva or the interdental papilla.
- The surface of the lesion is smooth and is of the normal color of gingiva or bluish.
- The adjacent teeth are vital and the cyst is almost always vital unless it is secondarily infected.

PATHOGENESIS

The gingival cyst of adult arises from the cell rest of the dental lamina, interestingly it is the same cell from which the lateral periodontal cyst also develops. For this reason, it is often believed that gingival cysts of adult and lateral periodontal cysts, represent the extraosseous and intraosseous manifestations of the same entity.

RADIOGRAPHIC FINDINGS

Since gingival cysts of adult are entirely extraosseous lesions they do not reveal any radiographic change in the bone. However, in some cases there may be a pressure induced faint round superficial depression (cupping out) in the underlying alveolar bone.

HISTOPATHOLOGY

- Histologically, gingival cysts of adult present a cystic cavity, which is lined by a thin epithelial lining made up of flat or cuboidal cells having 2 to 3 cell layer thickness (Fig. 6.28).
- Many of the lining epithelial cells exhibit pyknotic nuclei with perinuclear cytoplasmic vacuoles.

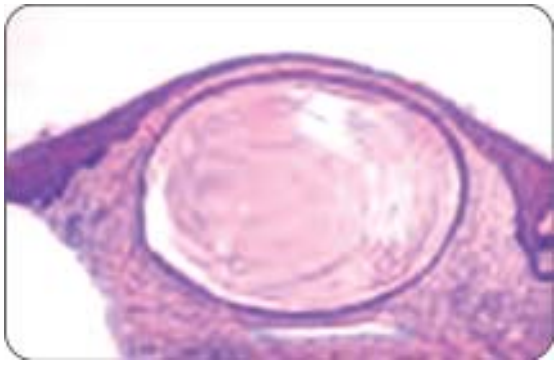

Fig. 6.28: Photomicrograph of gingival cyst of adults

- Layers of keratin may be present in the cystic lumen.
- Sometimes localized areas of epithelial thickening (plaque) are observed in which the epithelial cells are arranged in a whorled manner.
- Like lateral periodontal cysts, some clear cells may also be present.

TREATMENT

Surgical enucleation.

SIALO-ODONTOGENIC CYSTS (GLANDULAR ODONTOGENIC CYST)

DEFINITION

These are large intraosseous odontogenic cysts, which often exhibit an aggressive course. The cysts consist of stratified squamous epithelium and areas of numerous mucus secreting cells. The mucus secreting cells often produce pools of mucin within the cyst.

ORIGIN

The cysts arise from the remnants of dental lamina and are **capable of glandular differentiation**.

CLINICAL FEATURES

- Sialo-odontogenic cysts are extremely rare and are usually seen among adults.
- There is no sex predilection.
- Mandible is more often affected than maxilla.
- Anterior part of the mandible is the most common site for the cyst.

- Clinically the sialoodontogenic cysts appear as slow enlarging, asymptomatic, central jaw lesions.
- Some aggressive lesions may attain a very large size and many of them cross the mandibular midline.
- Larger lesions often cause expansion and distortion of the cortical plates of bone, displacement of teeth; with pain and paresthesia of the affected area.

RADIOGRAPHIC FEATURES

The radiographic appearances of sialo-odontogenic cysts are nonspecific; most of the cysts present unilocular or sometimes multilocular, radiolucent areas with well-demarcated, sclerotic border.

HISTOPATHOLOGY

Histologically, sialo-odontogenic cysts present the following features:

- The cyst is lined by a thin squamous epithelial lining, which may be of uniform thickness or there can be focal areas of thickening (plaque).
- Several small glandular structures or microcysts are found within the lining epithelium.
- Organization of the glandular elements (occurs due to metaplasia of the cystic epithelium) may result in the formation of acinar-like clusters.
- There may be large collection of mucin in the cystic lumen.
- Occasionally, mucous cells resembling goblet cells of the intestinal mucosa are present.
- The superficial layer of the lining epithelium is made up of cubiodal or columnar cells.

DIFFERENTIAL DIAGNOSIS

- Odontogenic keratocyst
- Ameoblastoma
- Aneurysmal bone cyst
- Central giant cell granuloma
- Intraosseous mucoepidermoid tumor.

TREATMENT

Surgical excision, the cyst has a strong tendency to recur.

BOTRYOID ODONTOGENIC CYSTS

DEFINITION

Botryoid odontogenic cysts are rare odontogenic cystic lesions, which resemble cluster of grapes. It is probably a variant of lateral periodontal cyst.

CLINICAL FEATURES

- Adults over 50 years of age are commonly affected and mandibular canine-premolar region is the most favorite site for this cyst.
- Clinically, the cyst presents a well-defined, painless, expansile central jaw lesion.

RADIOGRAPHIC FINDING

Radiographically, there can be presence of a unilocular or multilocular radiolucent area with well-corticated margin.

HISTOPATHOLOGY

- Histologically, botryoid odontogenic cyst reveals multiple cystic cavities separated from one another by fine fibrous septa.
- The cystic cavities are lined by nonkeratinized cuboidal or squamous epithelium, which are of 1 to 2 cell layer thickness.
- Focal areas of glycogen containing clear cell clusters are often found along the lining.
- Sometimes bud-like proliferations of the lining epithelial cells protrude into the cystic lumen.

TREATMENT

Treatment by enucleation, this cyst has a strong tendency to recur.

CALCIFYING EPITHELIAL ODONTOGENIC CYST (CEOC)

Calcifying epithelial odontogenic cyst (Gorlin's cyst) is a relatively uncommon odontogenic cystic lesion of the jawbones and in many instances it is considered as a tumor.

CLINICAL FEATURES

Age: Mostly the cyst develops in the second decade of life.

Sex: Both sexes are equally affected.

Fig. 6.29: Calcifying epithelial odontogenic cyst-I

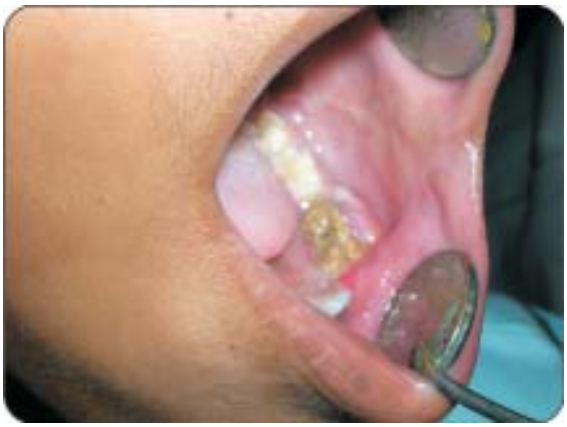

Fig. 6.30: Calcifying epithelial odontogenic cyst-II

Site: Both jaws are affected but the most favored site is the mandibular premolar region. The other common sites of cyst are the anterior parts of maxilla and mandible, occasionally extraosseous lesions develop from the gingiva too.

CLINICAL PRESENTATION

- Clinically, the cyst presents a bony hard swelling of the jaw; the average size of the tumor is about 2 to 3 centimeters in diameter but sometimes it can be extensive (Figs 6.29 and 6.30).
- Expansion and distortion of cortical plates and displacement of regional teeth, etc. are usually common.
- Large bony lesions can cause perforation of the cortex.
- Extraosseous lesions produce circumscribed, sessile or pedunculated gingival swelling; the associated tooth is vital.

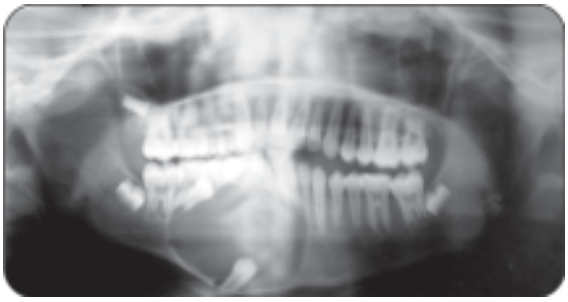

Fig. 6.31: Radiograph of calcifying epithelial odontogenic cyst

- Pain is rarely present in the cyst and most of the smaller cysts are completely asymptomatic.
- Some cysts can develop in association with an odontome.

RADIOLOGICAL FEATURES (FIG. 6.31)

- Radiograph usually shows a unilocular radiolucent area with a typical cystic appearance; but sometimes it can produce a multilocular radiolucency with well-corticated margin.
- Within the lesion, multiple small, irregular radiopaque calcified foci of varying radiodensity are often found. Sometimes miniature tooth-like structures may also found within the cyst.
- Some cysts may be associated with an unerupted tooth (mostly canines). Root resorption in the adjacent teeth is occasionally seen.
- The extra osseous lesion causes indentation on the overlying bone.

PATHOGENESIS

The cyst probably develops from the reduced enamel epithelial cells or remnants of odontogenic epithelium in the dental follicle, gingiva or bone.

HISTOPATHOLOGY

- Microscopically calcifying epithelial odontogenic cyst presents a cystic cavity, lined by an odontogenic keratinized epithelium of about 6 to 8 cell layer thickness.
- The cystic epithelium in some areas is thick and these areas exhibit some cells, which closely resemble the stellate reticulum of the developing tooth germ.
- The basal cells of the lining epithelium are columnar or sometimes cuboidal in nature,

Key points of calcifying epithelial odontogenic cyst

- Calcifying epithelial odontogenic cyst (Gorlin's cyst) is a relatively uncommon odontogenic cystic lesion of the jawbone.
- In many instances, it is considered as a tumor.
- The cyst probably develops from the reduced enamel epithelial cells or remnants of odontogenic epithelium.
- It frequently develops from the mandibular premolar region. Some lesions are extraosseous.
- Clinically smaller lesions ate asymptomatic. However the larger lesions cause expansion and distortion of bone and displacement of regional teeth.
- Extraosseous lesions produce circumscribed, sessile or pedunculated gingival swelling.
- Radiographically, the cyst presents unilocular or multilocular radiolucent area with well-corticated margin.
- Within the lesion, multiple small, irregular radiopaque calcified foci of varying radiodensity are often found.
- Histologically, calcifying epithelial odontogenic cyst presents a cystic cavity, lined by an odontogenic keratinized epithelium of about 6 to 8 cell layer thickness.
- The luminal surface epithelium often shows the presence of many "**ghost cells**".
- These are swollen, eosinophilic, abnormally keratinized cells devoid of nuclei; which gradually become paler, leaving only a faint outline and hence are called ghost cells.
- The connective tissue capsule contains many "satellite" microcysts and moreover, there may be presence of multiple multinucleated giant cells.

and they often exhibit a palisading arrangement (these cells resemble ameloblasts).

- The luminal surface epithelium often shows the presence of many "**ghost cells**". These are swollen, eosinophilic, abnormally keratinized cells devoid of nuclei.
- These cells gradually become paler, leaving only a faint outline and hence are called ghost cells.
- Sometimes multiple number of ghost cells fuse together to form large cellular mass. Occasionally such masses can fill up the entire cystic lumen.
- The ghost cells often undergo calcification and for this reason there may be presence of multiple, small, basophilic calcified bodies within the lumen of the cyst.
- The spinus cell layer of the cystic lining often resembles reduced enamel epithelium.
- The connective tissue capsule contains many "**satellite" microcysts** and in addition to this, there may be presence of **multiple multinucleated giant cells**.
- Melanin pigmentation may be occasionally present in the cyst.

DIFFERENTIAL DIAGNOSIS

- Calcifying epithelial odontogenic tumor
- Adenomatoid odontogenic tumor
- Dentigerous cyst
- Ameloblastoma.

TREATMENT

By surgical enucleation.

PARADENTAL CYST

DEFINITION

Paradental cyst is an inflammatory odontogenic cyst, which occurs in association with the root surface of an impacted or partially erupted vital tooth, usually the mandibular third molar.

ORIGIN

The cysts probably arises from the cell rest of Malassez or the reduced enamel epithelium. Inflammation is considered to play an important role in the development of this cyst.

CLINICAL FEATURES

- The cyst commonly occurs in males preferably in the third decade of life.
- It is commonly seen on the facial or distal aspect of a vital mandibular third molar tooth.
- In all the cases the involved tooth had an associated history of pericoronitis.

RADIOGRAPHIC FEATURES

- Paradental cyst occurring on the distal aspect of the mandibular third molar presents a well-circumscribed radiolucent area.
- The radiolucency may sometimes extend apically.

MACROSCOPY

Macroscopically, paradental cyst presents an adherent soft tissue lesion in a tooth covering the buccal aspect of the roots including the bifurcation areas.

HISTOPATHOLOGY

Histologically, paradental cyst reveals a cystic cavity lined by hyperplastic, nonkeratinized squamous epithelium.

Intense inflammatory reaction is seen in the capsule as well as in the epithelial lining.

DIFFERENTIAL DIAGNOSIS

- Lateral dentigerous cyst
- Lateral periodontal cyst
- Simple pericoronitis
- Enlarged tooth follicle
- Radicular cyst.

TREATMENT

Surgical enucleation.

NON-ODONTOGENIC CYSTS

GLOBULOMAXILLARY CYST

DEFINITION

Globulomaxillary cyst is a common type of developmental or fissural cyst that actually **arises in the bone suture, between the maxilla and premaxilla.** Clinically, the usual location of the cyst is between maxillary lateral incisor and canine teeth.

PATHOGENESIS

Earlier it was believed that the globulomaxillary cyst develops as a result of proliferation of the epithelium, entrapped along the line of fusion between the maxilla and premaxilla. But recently, this concept has been questioned by many investigators. The globulomaxillary cyst is now being considered as a variant of primordial cyst or lateral periodontal cyst.

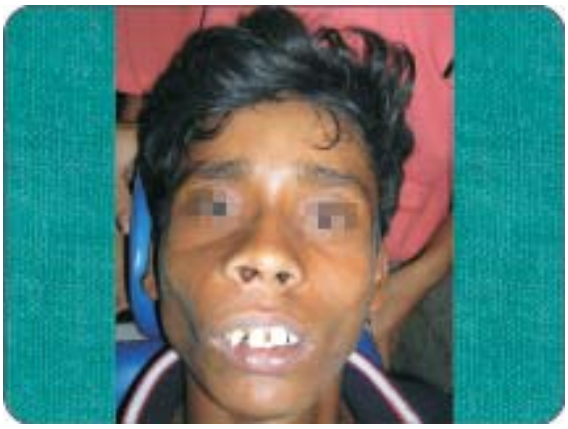

Fig. 6.32: Globulomaxillary cyst

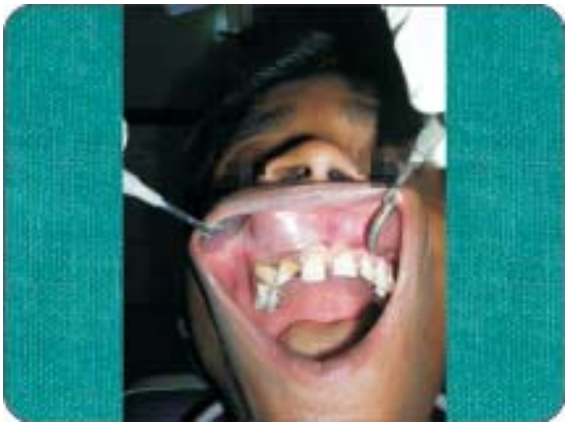

Fig. 6.33: Intraoral view of the same patient

CLINICAL FEATURES (FIGS 6.32 AND 6.33)

- This cyst is usually asymptomatic and is detected during routine radiological examinations.
- It can cause pain and discomfort, etc. only when it is secondarily infected.
- On rare occasions, there may be a small swelling in between the upper lateral incisor and canine teeth, with elevation of the lip.
- The associated teeth are always vital.

RADIOLOGICAL FEATURES

Radiograph reveals an **inverted pear-shaped**, radiolucent area between the roots of the upper lateral incisor and canine. It often causes divergence of the roots of these teeth. In many cases, the lesion is present bilaterally (Fig. 6.34).

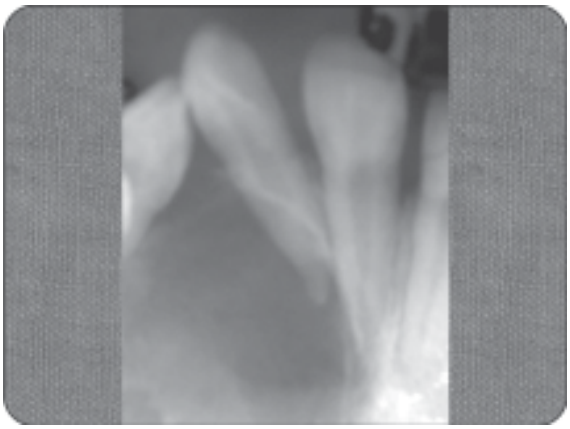

Fig. 6.34: Radiograph of globulomaxillary cyst

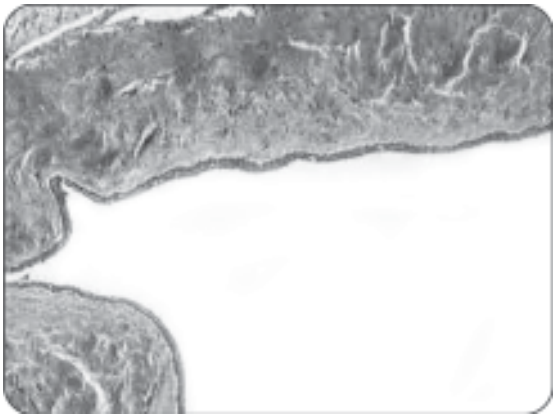

Fig. 6.35: Photomicrograph of globulomaxillary cyst

HISTOPATHOLOGY

Histologically, globulomaxillary cyst exhibits a cystic cavity, which is lined either by a stratified or pseudostratified ciliated columnar epithelium or by a thin squamous epithelium (Fig. 6.35).

The supporting connective tissue capsule often presents chronic inflammatory cell infiltration.

TREATMENT

By surgical excision, with preservation of the involved teeth.

NASOLABIAL CYST (KELSTADT'S CYST)

DEFINITION

Nasolabial cyst is a rare entirely a soft tissue cyst which arises in the upper lip deep into the nasolabial fold, just below the ala of the nose.

ORIGIN

The possible origin of this lesion is from the lower part of the embryonic nasolacrimal duct. The other theory suggests that the cyst arises from the epithelial remnants entrapped at the line of fusion of maxillary, median nasal and the lateral nasal processes during the development of face.

CLINICAL FEATURES

Age: 30 to 50 years.

Sex: The cyst is commonly seen among the females (3:1 ratio).

Site: Soft tissue of the anterior maxillary vestibule below the ala of the nose and deep in the naso-labial fold area.

PRESENTATION

- The cyst produces a small, painless, swelling in the upper lip lateral to the midline.
- The lesion often obliterates the nasolabial fold, raises the ala of the nose and distorts the nostril on one side.
- It is usually unilateral but on rare occasions it can be bilateral.
- Sometimes it can be massive in size and therefore, cause nasal obstruction and difficulty in wearing prosthesis.
- Sometimes the cyst may project into the nasal floor and deviates the nasal vestibule.
- It is generally painless, unless secondarily infected. Some cysts may rupture spontaneously.

RADIOLOGICAL FINDING

Because of its location entirely within the soft tissue, the cyst does not exhibit any radiographic change. However, sometimes it may produce focal pressure induced resorption (saucerization) of the underlying bone.

HISTOPATHOLOGY (FIG. 6.36)

- The nasolabial cysts present a small cystic lumen, which is supported by a connective tissue wall.
- It is lined on the inner aspect by a pseudo-stratified ciliated columnar epithelium with few goblet cells.

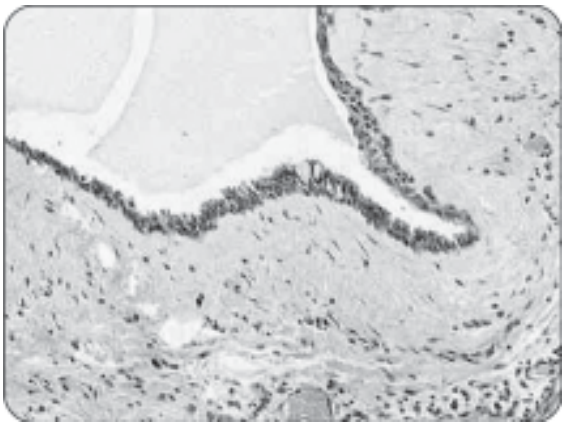

Fig. 6.36: Photomicrograph of nasolabial cyst

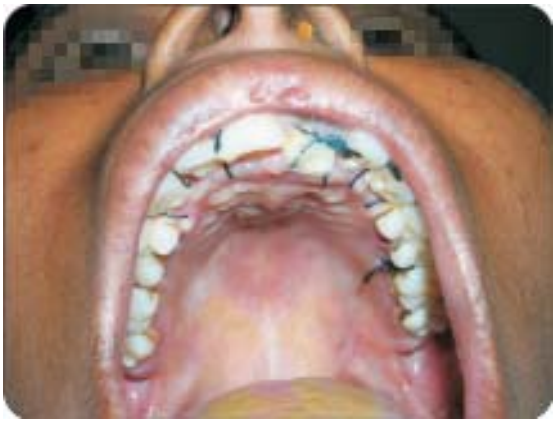

Fig. 6.37: Nasopalatine duct cyst

- Some cysts are lined by cubiodal or squamous epithelium.
- Some degrees of infoldings of the cystic lining is often seen.
- A narrow zone of dense, homogeneous fibrous tissue usually seen adjacent to the epithelial lining.
- Small mucous glands may be present in the capsule.
- Inflammatory cell infiltration is usually absent in the capsule.

TREATMENT

Surgical excision is the recommended treatment and care should be taken so that no ugly scar is formed on the lip.

NASOPALATINE DUCT CYST (INCISIVE CANAL CYST)

DEFINITION

Nasopalatine duct cyst is a relatively common, nonodontogenic intraosseous, cystic lesion, arising within the nasopalatine duct or the incisive canal. On rare cases, the cyst may develop in the soft tissue, near the opening of the incisive canal on the palate.

PATHOGENESIS

This lesion is considered as a true developmental cyst; it arises usually due to proliferation and spontaneous cystic degeneration of the epithelial remnants remaining after closure of the embryonic nasopalatine duct. The initiating factors for the development of cyst may be trauma, inflammation, mucous retention in the nearby minor salivary glands and bacterial infection, etc.

CLINICAL FEATURES

Incidence: It is a common cyst and affects about 1% of the population.

Age: Fourth, fifth and sixth decade of life.

Sex: Males are more commonly affected than females; the ratio being 4:1.

CLINICAL PRESENTATION

- The cystic lesion clinically presents a small, painful, fluctuant swelling in the midline of the anterior part of hard palate near the opening of the incisive foramen (Fig. 6.37).
- Few cysts are asymptomatic and are detected by chance during routine radiographic examination.
- The cyst often extends from palate onto the labial aspect of upper alveolar ridge.
- In case of extensive labiopalatal swelling typical through and through 'fluctuations' can be elicited during bidigital palpation.
- The lesion often causes pressure sensation on the floor of the nose and displacement of the roots of upper central incisors.
- Occasionally, there can be a purulent or salty discharge from the lesion.
- Some patients complain of episodic swelling in the soft tissue between the upper central incisors.
- The regional teeth are always vital.

RADIOLOGY

- On radiograph, nasopalatine duct cyst presents a sharply demarcated symmetrical radiolucency in the midline of the anterior maxilla (Fig. 6.38).

Key points of nasopalatine duct cyst

- Nasopalatine duct cyst is a non-odontogenic intraosseous, cyst arising within the nasopalatine duct or the incisive canal.
- The lesion is considered as a true developmental cyst and it arises from the epithelial remnants remaining after closure of the embryonic nasopalatine duct.
- It clinically presents a small, painful, fluctuant swelling in the midline of the anterior part of hard palate near the opening of the incisive foramen.
- Radiograph shows a small round or heart-shaped radiolucent area between and apical to the roots of the upper central incisors in the midline.
- Histology reveals a cystic cavity, lined by the ciliated columnar or nonkeratinized stratified squamous epithelium.
- The capsule is made up of densely collagenous fibrous connective tissue, which shows the presence of neurovascular bundles (naso-palatine as well as long sphenopalatine nerves and vessels).
- The associated teeth are vital.
- Surgical excision is the treatment.

- The most obvious presenting feature is a small **round or heart-shaped** radiolucent area between and apical to the roots of the upper central incisors in the midline.
- The typical heart shape of the cyst is found due to the radiographic superimposition of the nasal spine; the cyst often has a well-corticated border.
- Some cysts are large and destructive in nature and often cause displacement of roots of the upper central incisors.
- Root resorption is rare and the cystic cavity does not come in contact with lamina dura of the upper incisor teeth.

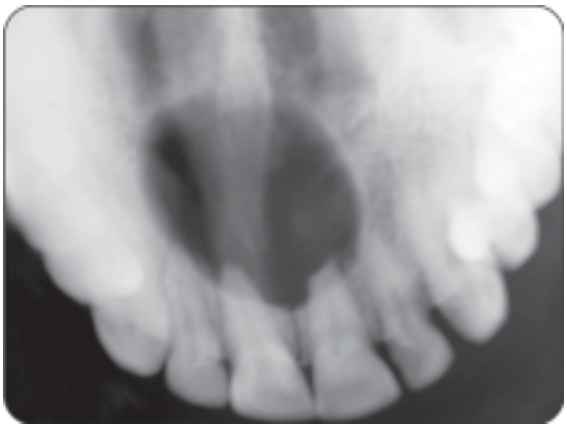

Fig. 6.38: Radiograph of nasopalatine duct cyst

- The cyst is sometimes confused with the incisive foramen and in such cases; a second radiograph should be taken at a different angle, which usually separates the incisive foramen and the nasopalatine duct cyst.
- The average size of nasopalatine duct cyst is 1 to 2.5 centimeter in diameter; whereas the average size of incisive foramen is 6 millimeter in diameter only. Therefore, when there is a suspected lesion measuring about 6 millimeter or less and there is no clinical symptom; the diagnosis should be incisive foramen and not a cyst.

HISTOPATHOLOGY (FIGS 6.39 AND 6.40)

- Histology reveals a cystic cavity, lined by the ciliated columnar or nonkeratinized stratified squamous epithelium and is backed by a connective tissue capsule.

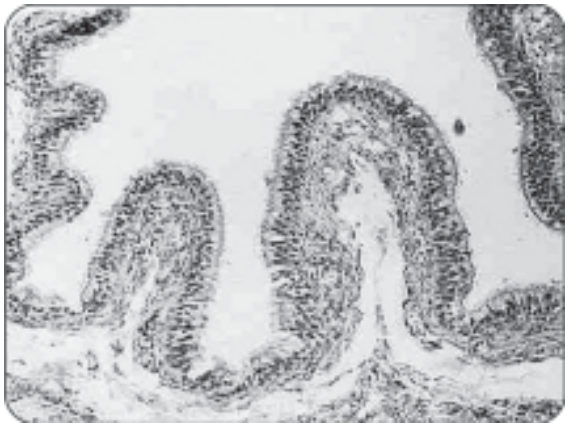

Fig. 6.39: Photomicrograph of nasopalatine duct cyst-I

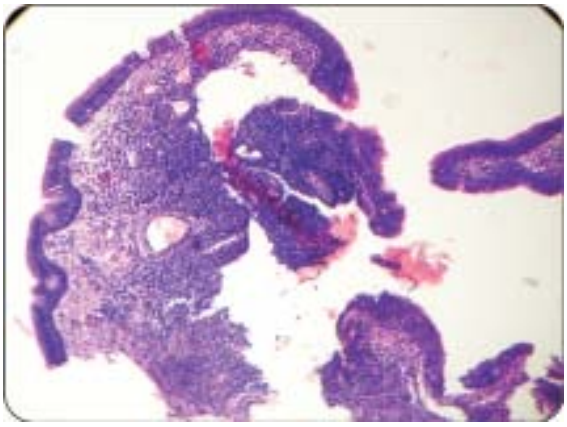

Fig. 6.40: Photomicrograph of nasopalatine duct cyst-II

- Sometimes the lining epithelium can be made up of simple columnar or cuboidal epithelial cells; however in most cases a mixed type of epithelial lining is seen in the cyst.
- Mucous secretory cells are commonly seen in the epithelial lining.
- The lining may be thick or thin and there may or may not be formation of rete-pegs in the lining.
- Sometimes there can be presence of pigments in the lining.
- The capsule is made up of densely collagenous fibrous connective tissue, which shows the presence of neurovascular bundles (naso-palatine as well as long sphenopalatine nerves and vessels).
- Presence of cartilaginous tissue and some mucous glands are often seen in the capsule.
- There may be chronic inflammatory cell infiltration in the cystic wall by lymphocytes, histiocytes and plasma cells, etc.
- Occassionally, there may be presence of few ductal tissues in the capsule.

TREATMENT

By surgical excision.

SOLITARY BONE CYST (TRAUMATIC/ HEMORRHAGIC BONE CYST)

DEFINITION

Solitary bone cyst represents a pseudocyst and it is characterized by a cavity in the bone which is lined by a fibrous tissue wall and not by an epithelium.

It arises very frequently from mandible and rarely from maxilla; however the overall incidence rate of this cyst is much higher in long bones.

CLINICAL FEATURES

Age: The cyst usually occurs among young people (between 10 to 20 years) and these are uncommon after the age of 25 years.

Sex: Females are more often affected than males (3: 2).

Site: Mandibular body, symphysis or ramus and maxillary anterior regions are the common sites. Mandible is affected more often than maxilla and sometimes bilaterally.

PRESENTATION

- In most of the cases, the cyst is asymptomatic and is detected accidentally during routine radiographic examinations.
- In other cases, it produces a painful, bony hard swelling of the jaw.
- Paresthesia of the lip, expansion of the cortical plates (mostly the buccal cortical plate of mandible) and displacement of the regional teeth are also common.
- Overlying teeth are vital.

RADIOLOGY

- Radiograph reveals an unilocular or rarely multilocular radiolucent area in the bone; with expansion and distortion of cortical plates.
- The radiographic size of the lesion is generally always bigger than the clinical size of the swelling.
- The cystic margin from the neighboring bone is well-demarcated; however in few cases it is ill-defined (in general these are less well demarcated than the odontogenic cysts).
- A prominent feature of the cyst is its tendency for scalloping in between the roots of the teeth.
- Occlusal view shows radiolucency extending along the cancellous bone of the jaw.
- Root resorption of the adjacent teeth is uncommon in this cyst.

PATHOGENESIS

The exact pathogenesis of solitary bone cyst is not clearly known, but it is believed that the condition develops due to trauma in the jawbone.

Investigators believe that following trauma to the bone and intrabony hemorrhage occurs which generally undergoes organization and repair. However, if the clot forming after hemorrhage does not organize properly or liquefaction occurs to the clot, then healing of the bony wound does not take place and as a result an intrabony cavity persists, which is later on called the solitary bone cyst.

Besides this trauma-hemorrhage theory, the other possible causes of development of solitary bone cyst include the following: local disturbance in bone growth, ischemic bone marrow defect, localized disturbed bone metabolism and failure of venous drainage, etc.

DIFFERENTIAL DIAGNOSIS

- Aneurysmal bone cyst
- Central giant cell granuloma
- Ameloblastoma
- Calcifying epithelial odontogenic cyst
- Ameloblastic fibroma
- Central ossifying fibroma.

MACROSCOPY

Once the cystic cavity is opened an empty space is found in the bone; which often contains very little blood, blood pigments and serous fluid, etc A thin fibrous tissue membrane may line the cavity.

HISTOPATHOLOGY

- Histology reveals a cystic cavity surrounded by a loose vascular connective tissue wall, but there is no epithelial lining (hence, it is called a false or pseudocyst).
- The connective tissue stroma is made up of fibrous tissue, showing areas of hemorrhage, hemosiderine pigmentation and bone resorption, etc.
- The cystic cavity often has a rough bony wall.
- Rarely there can be features of myxoid deposition in the bone and/or presence of multinucleated giant cells.

TREATMENT

The treatment is done by surgical exploration of the cyst; it helps in causing further hemorrhage in the area with subsequent healing. Some lesions may resolve spontaneously.

ANEURYSMAL BONE CYST

DEFINITION

Aneurysmal bone cyst is an uncommon cystic lesion, which involves the bone anywhere in the body including the jaws and its clinical features are similar to that of central giant cell granuloma.

CLINICAL FEATURES

Age: Usually second decade of life (10 to 19 years age group).

Sex: Females are more commonly affected.

Site: Mandibular molar-ramus area is most frequently affected, maxillary lesions also frequently involve the posterior region.

CLINICAL PRESENTATION

- Aneurysmal bone cyst clinically presents a rapidly enlarging, diffuse, firm swelling of the jaw that often causes facial asymmetry.
- The swelling is painful and the affected area of the jaw may be pulsatile in some cases.
- Occasionally severe expansion and thinning of the bone often results in "egg-shell crackling" and perforation of the cortical plates.
- Pathological fracture of the affected jawbone may occur in some patients.
- Accidental injury or perforation to the aneurysmal bone cyst may result in profuse bleeding.
- Paresthesia may be present on the affected side and regional teeth are often displaced, resulting in derangement of occlusion. The displaced teeth are always vital.
- There may be difficulty in mouth opening if the cyst causes impingement on the capsule of the temporomandibular joint.
- Maxillary lesions sometime invade into the paranasal sinuses and cause nasal bleeding, pressure sensation in the eye and nasal obstructions, etc.

RADIOLOGY

- Radiograph reveals a multilocular radiolucent area in the bone, with a typical "honey-comb" appearance.
- Border of the lesion can be either well-demarcated or diffuse.
- "Balooning" expansion of the cortical plates, displacement of teeth and resorption of the roots of the adjoining teeth are also commonly seen.
- A prominent feature of the cyst is the "**blow–out**" bulging of the lower border of mandible.

PATHOGENESIS

Pathogenesis of aneurysmal bone cyst is controversial and it is believed that the cyst arises as a result of trauma with subsequent venous occlusion inside the bone.

Key points of aneurysmal bone cyst

- Aneurysmal bone cyst is an uncommon intraosseous, cystic lesion; which often affects the young individuals.
- It is believed to develop as a result of cystic transformation of a pre-existing central giant cell granuloma.
- Clinically, the cyst presents a rapidly enlarging, diffuse, firm, painful swelling of the jaw that often causes facial asymmetry.
- Severe expansion and thinning of the bone often results in "egg-shell crackling" and perforation of the cortical plates.
- The affected area may be pulsatile and pathological fractures may occur.
- Radiograph reveals a multilocular radiolucent area in the bone, with a typical "honey-comb" appearance.
- Larger lesions cause "balooning" expansion of the cortical plate and also "blow-out" bulging of the lower border of mandible.
- Microscopically aneurysmal bone cyst presents multiple blood filled spaces of varying size, which are lined by spindle-shaped cells or flat endothelial cells.
- Multiple multinucleated giant cells, scattered osteoids, areas of hemorrhage and hemosiderine pigmentations are also seen.
- Treatment is done by surgical curettage.

It is also believed that the lesion occurs as a result of cystic transformation of a pre-existing pathology, especially the central giant cell granuloma.

DIFFERENTIAL DIAGNOSIS

- Fibrous dysplasia
- Intraosseous hemangioma
- Traumatic bone cyst
- Giant cell tumor of bone
- Osteoblastoma.

MACROSCOPY

An intact periosteum and a thin bony shell usually cover the cyst. However the cortical bone is often perforated. The bony cavity is filled with vascular soft tissue containing blood filled spaces. The intracystic tissue often looks like a blood soaked sponge.

ASPIRATION

Aspiration often reveals fresh blood.

HISTOPATHOLOGY (FIG. 6.41)

- Microscopically, aneurysmal bone cyst presents multiple blood filled spaces of varying size, which are lined by many spindle-shaped cells or flat endothelial cells.
- Epithelial lining is absent in this cyst and the blood filled intracystic spaces are separated from one another by loose connective tissue walls.
- Multiple multinucleated giant cells, scattered osteoids, areas of hemorrhage and hemosiderine pigmentations, etc. are commonly

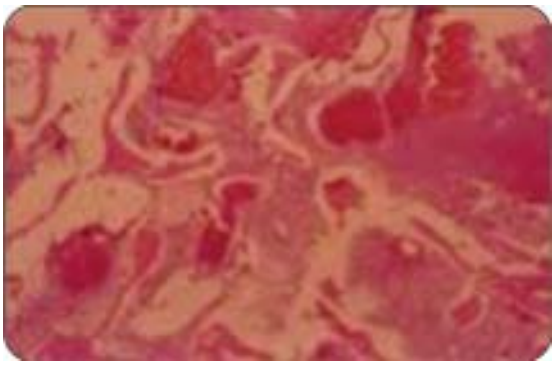

Fig. 6.41: Photomicrograph of aneurysmal bone cyst

present in the hypercellular connective tissue stroma of the cyst.
- The cyst wall occasionally exhibits a lace-like pattern of calcification.

TREATMENT

By surgical curettage.

CYST OF THE SALIVARY GLAND

Cystic lesion developing from the salivary glands are commonly known as "**mucoceles";** these lesions develop mostly in relation to the minor salivary glands and rarely, in relation to the major salivary glands.

Mucoceles basically are of two types:

A. Mucous retention cyst.

B. Mucous extravasation cyst.

ETIOLOGY AND PATHOGENESIS

The mucous retention cyst develops as a result **of obstruction to the duct of the minor or rarely major salivary glands; which leads to accumulation of saliva either within the gland or within its duct.** More and more fluid accumulations cause increased intraluminal pressure in the gland itself or in the duct; which results in swelling. The retention cysts generally develop due to obstruction to the salivary gland ducts because of the following reasons: calculus formation, scarring, obstruction from mucin plug crushing of the duct (as a result of trauma) and atresia (congenital absence of duct in the salivary gland), etc. Mucous retention cyst is a true cyst since it has a cystic epithelium made up of glandular epithelial cells of the salivary glands.

Mucous extravasation cyst on the other hand, develops as a **result of rupture of the salivary gland duct,** which leads to spillage or extravasations of saliva into the connective tissue. Local trauma is believed to be the most important etiological factor in this cyst.

CLINICAL FEATURES

- Mucoceles occur at any age; however mucous extravasation cysts are more common among children, while the mucous retention cysts are more common among adults.

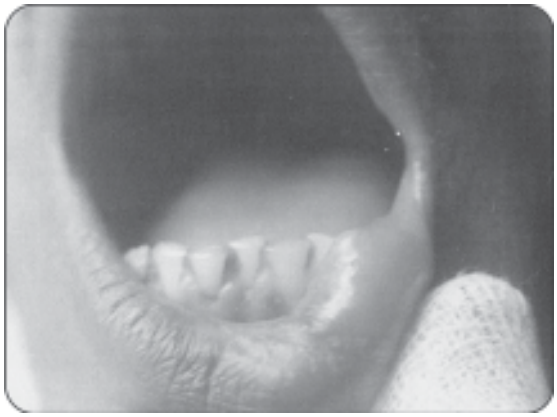

Fig. 6.42: Mucocele developing on the lower lip

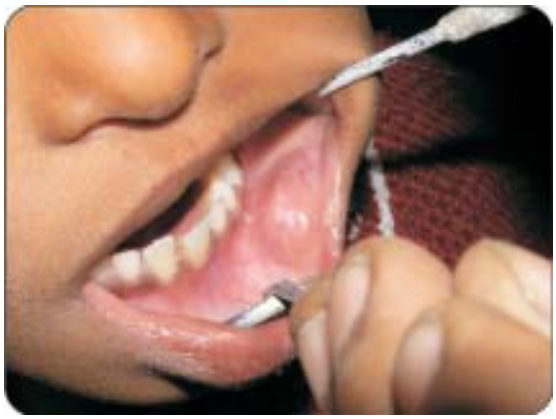

Fig. 6.42A: Mucocele

- Both sexes are almost equally affected.
- The cysts often affect minor glands but on rare occasions the major salivary salivary glands can be affected.
- Mucoceles of minor glands predominantly affect the lower lip, however the cheek, soft palate, floor of the mouth and tongue, etc. are also frequently involved (Figs 6.42 and 6.42A).
- Cysts of the major glands predominantly affect the parotid; and these lesions clinically exhibit slow enlarging, painless soft swellings in the gland.
- Some swellings develop only during mealtime and are absent during the in between periods.
- The superficial lesions appear as **small, raised, vesicle-like, fluctuant areas** measuring from few millimeters to few centimeters in diameter. The deep seated lesions produce

diffuse, relatively firm, painless swellings in the oral cavity.

- The superficial lesions often have a bluish appearance whereas the deep seated lesions do not exhibit any color change in the overlying mucosa.
- Lesions developing in the floor of the mouth near the submandibular duct area often have an amber color.
- Mucoceles rarely occur in multiple numbers; majority of the superficial lesions rupture within a short period of time and result pain, ulceration and secondary infection, etc. However few lesions can survive for several days.
- The mucoceles often recur and the recurrent cysts usually cause round or oval shaped, smooth, soft and fluctuant swellings; which tend to develop repeatedly at a particular location in the mouth.

Fig. 6.43: Photomicrograph of mucous retention cyst

HISTOPATHOLOGY

Mucous retention cyst: Mucous retention cyst histologically presents a small cystic cavity, which is filled with mucous and is lined by flattened cuboidal or columnar epithelial cells of the salivary gland duct (Fig. 6.43). Sometimes, the cyst can be lined by an atrophic stratified squamous epithelium; moreover in few cases the cystic epithelium exhibits papillary folding, which often project into the cystic lumen. The mucocele almost always have a minor salivary gland in its vicinity.

Mucous extravasation cyst: This lesion microscopically presents a cystic cavity in the connective tissue; which is filled with mucus but there is no lining epithelium present in this cyst.

Instead of a lining epithelium the cystic cavity is often surrounded by a compressed connective tissue wall or a granulation tissue. The adjacent connective stroma contains multiple macrophages, polymorphonuclear neutrophils, eosinophils and especially large number of lymphocytes. Sometimes ruptured salivary gland ducts may be seen under microscope.

DIFFERENTIAL DIAGNOSIS

- Salivary gland tumor
- Lipoma
- Fibroepithelial polyp
- Cysticercosis.

Differences between mucous retention and mucous extravasation cyst

Mucous retention cyst	Mucous extravasation cyst
• Mucous retention cyst develops as a result of obstruction to the duct of the minor salivary glands • It results due to accumulation of saliva either within the gland or within its duct • Mucous retention cysts are more common among adults • Mucous retention cyst has a cystic lining • Mucous retention cyst is a true cyst	• Extravasation cyst on the other hand, develops as a result of rupture of the salivary gland duct • It occurs due to spillage or extravasations of saliva into the connective tissue • Mucous extravasation cysts are more common among children • Mucous extravasation cyst does not have any cystic lining • Mucous extravasation cyst is a false cyst

TREATMENT

Mucoceles are treated by surgical excision of the lesion along with the involved gland.

RANULA

DEFINITION

Ranula is a form of mucocele that typically causes a large, bluish fluctuant swelling in the floor of the mouth. The lesion occurs due to spillage of saliva from the sublingual salivary glands or rarely the submandibular gland or sometimes from the minor salivary glands.

The ranulas represent the extravasation cyst of the salivary glands.

Key points of ranula

- Ranula is a form of mucocele (mucous extravasation cyst) that typically causes a large, bluish fluctuant swelling in the floor of the mouth.
- It occurs due to spillage of saliva from the sublingual salivary gland or rarely the submandibular gland.
- Obstruction, compression or perforation of the salivary gland duct is the likely causes of development of ranula.
- Clinically ranula presents a dome-shaped, soft, fluctuant, unilateral swelling in the floor of the mouth.
- The ranulas typically have a bluish translucent appearance and clinically they often look like the "distended under belly of a large frog'.
- When the ranula herniates through the mylohyoid muscle and pruduces a swelling in the neck, it is called a "plunging" type of ranula.

ETIOLOGY

- Obstruction to the duct by calculus (sialolith) formation.
- Compression of the duct by trauma or a growing tumor in the vicinity.
- Perforation of the duct due to injury.
- Absence of the duct itself (atresia).
- Scar or stricture formation to the duct, especially after surgery.

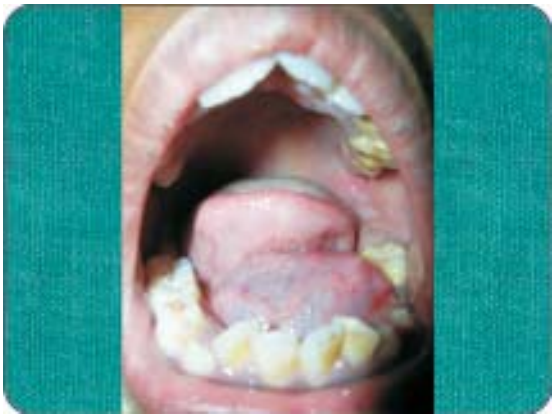

Fig. 6.44: Ranula

CLINICAL FEATURES

- Clinically "ranula" presents a **dome-shaped, soft, fluctuant, unilateral swelling** in the floor of the mouth (Fig. 6.44).
- The lesion is generally very large (several centimeters in diameter); which often fills up the floor of the mouth and causes deviation of the tongue.
- The ranulas typically have a **bluish translucent** appearance and clinically they often look like the "**distended under belly of a large frog'** (in Latin the word 'rana' means frog; for this the name 'ranula' has been given to the cyst).
- If the lesion is a deep-seated one, the bluish coloration is usually absent.
- When the ranula herniates through the mylohyoid muscle and produces a swelling in the neck, it is called a "**plunging"** type of ranula.
- Ranulas are mostly located on either side of midline in the floor of the mouth; however in many cases, they can cross the midline of the floor of mouth and can even cause air-way obstructions.
- Some ranulas rupture spontaneously and release their mucin content in the mouth.

HISTOPATHOLOGY

The extravasation type of ranula microscopically presents large mucous-filled area, which is surrounded by a connective tissue wall or

granulation tissue. Multiple foamy histiocytes are often present in the granulation tissue surrounding the cyst.

In many cases, sialoliths may be found within the duct system of the salivary gland.

DIFFERENTIAL DIAGNOSIS

- Dermoid cyst
- Benign lymphoepithelial cyst
- Salivary gland tumors
- Cystic hygroma.

TREATMENT

Treatment is done by surgical excision or marsupialization.

The etiological factor has to be removed to eliminate the possibility of further recurrence. In case of repeated recurrences, the involved gland may have to be excised.

DERMOID CYST

DEFINITION

It is a developmental cyst derived from remnants of embryonic skin.

CLINICAL FEATURES

Age: Children and young adults.

Sex: Both sexes are equally affected.

Site: Skin around the eyes, anterior upper neck and floor of the mouth on the midline.

PRESENTATION (FIG. 6.45)

- A pain less swelling, which often have a doughy or rubbery consistency.
- Dermoid cysts always develop on the midline of the floor of the mouth and thus they differ from ranulas; which develop on the lateral aspect of the midline.
- The cyst, which develops above the geniohyoid muscle, presents a sublingual swelling in the midline of floor of the mouth.
- It often causes elevation of the tongue with difficulty in eating, talking or sometimes even breathing.
- The cyst located below the geniohyoid muscle often produces a midline swelling in the submental region; which often produces a 'double chin' appearance.
- The size of the cyst varies and the maximum size could be up to 2 cm or less in diameter.

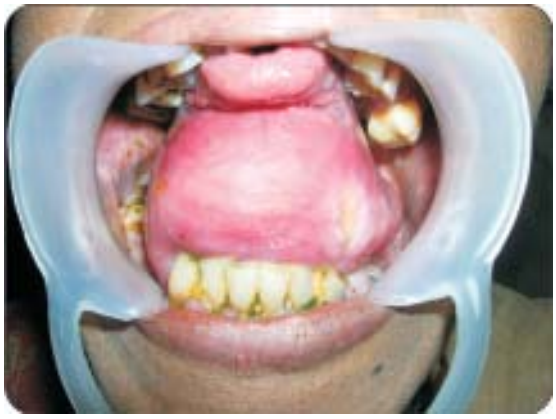

Fig. 6.45: Dermoid cyst

HISTOPATHOLOGY

- A cystic cavity lined by orthokeratinized stratified squamous epithelium, which exhibits hair follicles, sebaceous glands and erector pili muscles, etc.
- The cavity lumen is often filled with sebum, descuamated keratin and hair shafts.
- The cyst capsule is composed of a narrow zone of compressed connective tissue.

TREATMENT

Surgical enucleation.

SURGICAL CILIATED CYST OF MAXILLA

DEFINITION

It is an iatrogenic cyst, which develops as result of surgery involving .the maxillary sinus.

CLINICAL FEATURES

The cyst occurs in middle aged or older adults.

It often causes pain and tenderness in the maxilla.

All the patients have a previous history of surgery in the maxillary bone.

RADIOGRAPHIC FINDING

X–ray reveals a well-circumscribed radiolucency in close proximity of the maxillary sinus.

HISTOPATHOLOGY

- The cyst is lined by a pseudostratified ciliated columnar epithelium.
- The surrounding connective tissue is either normal or inflammed.

TREATMENT

Surgical enucleation.

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CHAPTER 7

Regressive Alterations of Teeth

Regressive alterations are the group of retrogressive changes in the teeth, which occur due to nonbacterial causes and results in wear and tear of the tooth structures with impairment of function.

Some of these regressive changes in teeth result from generalized ageing process and others occur due to chronic persistent tissue injury.

Causes of loss of enamel after tooth formation

- Dental caries
- Trauma
- Attrition
- Abrasion
- Abfraction
- Erosion
- Bruxism
- Dentinogenesis imperfecta
- Amelogenesis imperfecta
- Radiation therapy.

ATTRITION OF TEETH

DEFINITION

Attrition is a constant form of retrogressive change in teeth, characterized by wear of tooth substance or restoration as a result of tooth-to-tooth contact during occlusion, mastication or parafunction.

It is mostly an **age related physiologic process**, which occurs over a long period of time and that's why older individuals often exhibit more attrition in their teeth as compared to the young.

The rate and severity of attrition depends upon several factors such as: Diet quality, dentition, force of the masticatory muscles and chewing habits, etc.

TYPES OF ATTRITION

Although clinical distinction is difficult to make, attrition may be divided into two types:

A. Physiological attrition
B. Pathological attrition

Physiological Attrition

- The tooth loss in physiological attrition is fairly constant and is proportionate to the age of the individual.
- Physiological attrition begins with wearing of the incisal edge of incisors; it is followed by the palatal cusp of maxillary molars and buccal cusp of mandibular molars.
- Attrition also occurs in the proximal surfaces of teeth in the contact point areas.

Pathological Attrition

Pathological attrition occurs due to certain abnormalities in occlusion, chewing pattern or due to some structural defects in the teeth. It often causes extensive loss of tooth structure, which results in disturbed function and loss of esthetics.

The tooth wear in this type of attrition does not maintain a consistent pattern and the amount of tooth loss is not proportionate to the age of the individual.

CAUSES OF PATHOLOGICAL ATTRITION

- ***Abnormal occlusion:*** May be developmental, e.g. crowding of teeth or malposed teeth. In these cases, abnormal occlusal positioning of teeth many lead to traumatic contact during chewing which may lead to more tooth wear.
- ***Premature extraction of teeth:*** Extraction of some teeth from the dental arch will increase the occlusal load on the remaining teeth (overburdened teeth) as the chewing force for the individual remains constant.

- ***Abnormal chewing habits:*** Parafunctional chewing habits, e.g. bruxism (habitual grinding of teeth) and chronic persistent chewing of coarse and abrasive foods or other substance, e.g. tobacco and betel nut, etc.
- ***Structural defects in teeth:*** The structural defects, which make the tooth more vulnerable to attrition even under normal masticatory forces include—
  - Amelogenesis imperfecta
  - Dentinogenesis imperfecta

In these situations, the hardness of enamel or dentin is much more inferior as compared to the normal teeth and therefore, the rate of tooth wear is high even under normal chewing pressures.

CLINICAL FEATURES OF ATTRITION

- Attrition can occur in both deciduous as well as in the permanent teeth.
- Attrition of tooth is clinically manifested by the formation of **flat, smooth, shiny, well-polished facets** on those surfaces of teeth which come in contact with the opposing teeth (Fig. 7.1).
- Thus, attrition often occurs on the tip of the cusps, incisal edges, on the proximal contact areas, labial surface of lower anteriors and palatal surfaces of upper anteriors.
- In advanced cases, attrition may lead to severe reduction in the cuspal height with complete wearing of enamel and flattening of the entire occlusal surface.
- When the enamel is lost on the occlusal surface, the dentin becomes attrited at a faster rate and the lesion may become cap shaped, surrounded by a rim of enamel at the periphery.

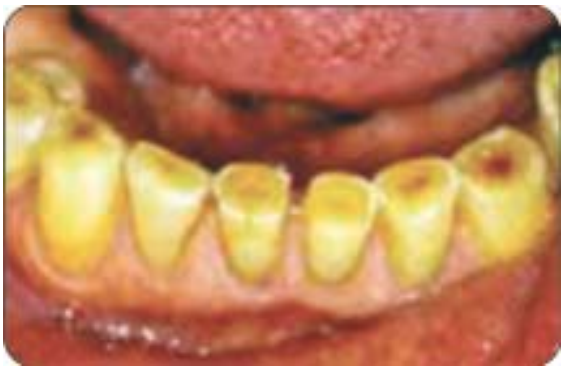


Fig. 7.1: Attrition of tooth

- When dentin becomes exposed it generally becomes discolored brown.
- Attrition in the **proximal surfaces** of teeth occurs due to vertical movements of tooth within the socket during mastication.
- Proximal surface attrition causes transformation of proximal "**contact points**" to relatively broad and flat "**contact areas**".
- This type of loss of tooth structure from the proximal surfaces may even lead to mesial migration of teeth in the dental arch.
- Normally, men often exhibit more severe attritions of teeth than women.
- Exposure of dentinal tubules in severe cases of attrition may lead to tooth hypersensitivity.
- Pulp exposure and subsequent pain are rare in case of attrition as the process is generally slow, and often allows sufficient time for formation of protective reparative dentin.
- Attrition may also occur on the restorations of teeth. A common example in this regard, is the development of shiny facets on the amalgam filled surfaces.
- Attrition may even possibly lead to fracture of the cusps of teeth or restorations.

TREATMENT

Treatment of attrition is difficult; however certain things can be done to reduce further tooth wear.

- Corrections of developmental abnormalities causing traumatic occulusion.
- Correction of parafunctional chewing habits.
- Protection of tooth by metal or metalceramic crowns where structural defects (e.g. amelogenesis or dentinogenesis imperfecta) exist.
- Construction of occlusal guard, if the habit of bruxism is persisting.

ABRASION OF TEETH (FIG. 7.1A)

DEFINITION

Abrasion is the pathological wearing of dental tissues or dental restorations by friction with foreign substances independent of occlusion.

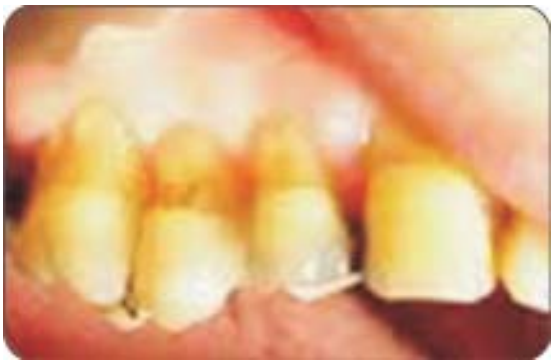


Fig. 7.1A: Abrasion of teeth

ETIOLOGY AND PATHOGENESIS

Different foreign substances produce different patterns of tooth abrasion. However, the process of tooth wear is similar in every case.

Causes of abrasion

- Toothbrush abrasion
- Habitual abrasion
- Occupational abrasions
- Abrasions by prosthetic appliances
- Ritual abrasions.

Toothbrush Abrasion

- It is the most common type of abrasion and is mostly associated with faulty tooth brushing technique.
- Abrasion mostly occurs when the tooth brushing is done in horizontal brushing strokes rather than vertical strokes.
- It also occurs if excessive force is applied on the teeth during brushing.
- The condition is made even worse when an abrasive dentifrice is used.

Habitual Abrasion

- Excessive habitual chewing of betel nut, tobacco and pan, etc. causes abrasion of teeth.
- Habitual pipe smokers may develop abrasion on the incisal edges of upper and lower anterior teeth due to continuous biting on the pipe stem.
- Chronic habitual biting of pencils, bobby pins (hair grips) and threads, etc. often cause abrasion.
- Improper and habitual use of tooth prick or dental floss, etc. can cause abrasions on the proximal surfaces of teeth.

Occupational Abrasion

Occupational abrasion develops when objects or instruments are habitually held between the teeth by professionals during work.

- Hairdressers often grip the hairpins between their teeth during work and this can cause tooth abrasions.
- Carpenters often keep small tools or nails between their teeth when they are at work and this type of practice cause abrasion of tooth resulting in notching on the tooth surface especially at the incisal edges of the anterior teeth.
- Similar occupational abrasions can also be seen among tailors and shoemakers.

Abrasion by Prosthetic Appliances

Faulty clasp design in removable partial denture prosthesis may also cause abrasion of tooth.

Ritual Abrasion

Ritual abrasions of tooth are uncommon nowadays and are mainly confined in Africa.

For example, ancient people used to believe in some pragmatic concepts and according to that they often used to mutilate their teeth with some instruments. These practices were aimed at making themselves immune from evil spirits.

CLINICAL FEATURES OF ABRASIONS

- In abrasion of tooth, the type and severity of surface wear will depend upon the duration and the type of faulty habit adopted by the person.
- Clinical manifestations differ in different types of habit, e.g. a defect in the tooth due to toothbrush abrasion will differ from that of the occupational abrasion or from the habitual abrasion.
- The abrasion produces **a 'v' shaped or wedge-shaped horizontal cervical notch** on the buccal surface of teeth. The notch will have sharp angles and highly polished dentin surface.
- Toothbrush abrasions commonly occur on the cervical areas of the labial or buccal surfaces of teeth.
- Canines and premolars being the more prominent teeth are often more severely affected by abrasion.

- Teeth on the left side of the arch are more severely involved in right-handed persons and vice versa.
- Maxillary teeth are more commonly affected than mandibular teeth.
- In cervical abrasion, lesions are more often wide than deep.
- Toothbrush abrasion may also cause gingival recession.
- In pipe smokers, abrasions develop on the insical surfaces of upper and lower anterior teeth. The lesion is characterized by a well-polished notch, whose shape typically matches with the shape of the pipe stem used by the smoker.
- Abrasion caused by habitual holding of nails or needles or other small tools by the tailors or shoe makers or carpenters, etc. often produces a small, deep, well-polished 'ditch' on the incisal edge of teeth.
- Faulty use of tooth-prick or dental floss cause loss of dentin and cementum, especially of the root surfaces on the proximal walls of teeth.
- Severe abrasion (of any type) may cause opening up of the dentinal tubules and therefore, the patient may experience sensitivity in the affected teeth due to hot and cold substances.
- Secondary or reactionary dentin usually forms on the pulpal surfaces to protect the teeth from pulp exposures.
- In untreated cases, the lesion may deepen further and it may eventually expose the dental pulp with subsequent of pulpitis and other associated manifestations.

TREATMENT

Avoidance of abnormal brushing habits prevent abrasions, however in already developed cases, restorative treatment helps to keep the tooth surface intact and also it prevents further tooth wear.

TOOTH ABFRACTION

DEFINITION

Abfraction is the pathologic loss of tooth enamel and dentin caused by biomechanical loading forces.

FORCES CAUSING ABFRACTION

- ***Static forces:*** Produced during swallowing, tongue thrusting and cleanching.
- ***Cyclic forces:*** Forces produced during chewing.

These forces cause repeated flexure and ultimate material fatigue to the affected tooth at locations away from the point of loading.

CLINICAL FEATURES

- Abfraction causes breaking down of enamel on the buccal surface of tooth.
- People with open bite or very deep class I cavity are more prone to develop abfraction of tooth.
- Sensitivity of tooth, sign of traumatic occlusion and wearing on the occlusal surface are often seen.
- Stress lines on the tooth surface and sometimes fracture of the tooth may occur.
- Repeated failure of restorations on the cervical area due to damaging lateral forces.

EROSION OF TEETH

DEFINITION

Erosion can be defined as progressive irreversible loss of hard dental tissues by some chemical process that does not involve bacterial action (Fig. 7.1B).

In erosion, dissolution of the mineralized tooth structure occurs upon contact with acids, which are introduced into the oral cavity either from intrinsic sources or from extrinsic sources. However, it is important to note that erosion may render the teeth more susceptible to other retrogressive changes like attrition and abrasion, etc.

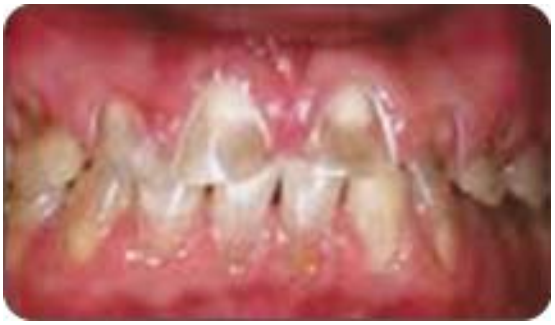


Fig. 7.1B: Erosion of tooth

ETIOLOGIC FACTORS FOR EROSION

(A) EXTRINSIC FACTORS

Acidic Foods and Beverages

Acids from extrinsic sources (source is outside the body), which can cause erosion of tooth usually, come from acidic beverages, foods, and medications, etc. or from the environment itself.

- Most of the fruits and fruits juices have a low pH and these can cause erosion of tooth if consumed regularly.
- Carbonated soft drinks and sports drinks are also very acidic in nature and frequent consumption of these drinks may result in erosion of tooth.
- Rate of erosion of tooth is proportional to the amount and frequency of consumption of acidic beverages/foods.

The erosive potential of acidic foods/beverages can be reduced if:

- They contain large amount of calcium, phosphate and fluoride, etc. which help in tooth remineralization.
- If tooth brushing is done after every intake of beverage.
- If drinks are taken by a straw rather than from a glass (it minimizes contact time with tooth).

Medications

Some medicines can be highly acidic in nature (e.g. vitamin C and hydrochloric acid preparations, etc.) and they can cause erosion of teeth when chewed or kept in the mouth for a long time prior to swallowing.

Occupational erosions

- Occupational erosions are seen among workers who often come in contact with acids at their place of work. Commonly vapors of different acids, e.g. chromic acid, hydrochloric acid, sulphuric acid and nitric acids, etc. are released into the work environment during industrial electrolyte process. These vapors can cause erosion of teeth, on those surfaces, which are normally exposed to the atmosphere (incisal third of incisors).

The systemic diseases associated with erosion of teeth

- Gastroesophageal reflux disease (GERD)
- Chronic alcoholism
- Pregnancy
- Esophagitis
- Gastritis
- Peptic ulcer
- Hyperparathyroidism
- Bulimia
- Nervous system disorder.

- Commonly the workers involved in manufacturing of lead acid batteries or sanitary cleansers or soft drinks, etc. or those who are working in galvanizing or plating factories often develop occupational erosions of teeth.
- Occupational wine tasters often have erosion in their teeth.
- Swimmers who practice regularly in the pools can have erosion of their teeth if the pool water contains higher concentrations of acids.

(B) INTRINSIC FACTORS

The intrinsic pathology of erosion means the acids are produced within the body and cause erosion of tooth. This type of erosion occurs in cases of certain systemic diseases, which cause increased vomiting and regurgitations of bowel contents into the mouth. When the gastric acids (having pH as low as below 1) come in contact with the teeth extensive erosions occur.

CLINICAL FEATURES OF EROSION

- Acids from extrinsic source cause erosion on the labial or buccal surfaces of teeth and acids from intrinsic source cause erosion on the lingual or palatal surfaces of teeth.
- The commonest site of dental erosion is the gingival third of the labial surfaces of maxillary incisors.
- In chronic severe cases of erosion, the disease can involve even the proximal surfaces of teeth besides involving the labial and lingual surfaces.
- Clinically the condition is manifested by shallow, broad, 'scooped-out' concavities on the enamel with highly polished surfaces.

- The shape and size of the lesion may vary considerably and it usually involves multiple teeth.
- There will be cupping of occlusal surfaces of molar teeth or grooving of the incisal edges of anterior teeth with exposure of dentin.
- Increased incisal translucency of teeth also occurs.
- In severe erosion there may be loss of entire buccal cusp of the molar teeth which results in a 'ski slope' like depression of the tooth that extends from lingual cusp up to the buccal cervical area.
- Erosion causes raised amalgam restorations above the level of the tooth surface. The remaining part of the tooth looks clear, polished and unstained.
- Erosion causes loss of tooth structure from the palatal surfaces of upper anteriors, which results in increased concavity.
- Amalgam restorations often have a clean, non-tarnished appearance due to action of acids on the metal surface.
- Preservation of enamel "cuff" on the gingival crevice is common.
- Loss of enamel often causes hypersensitivity in the teeth and it may also trigger secondary dentin formation; however the tooth sensitivity occurs only in cases of rapid erosions. Sensitivity of tooth does not occur in slowly progressing erosions; as there is enough time for formation of reactionary dentin in the tooth, which protects the pulp.
- Severe cases of erosion however can cause exposure of pulp in deciduous teeth.
- Microradiography shows a gradual demineralization of surface enamel to a depth of about 100 µm.

TREATMENT

Preventive treatment: Identification of etiology is important in the management of erosion. Proper counseling is needed in case the patient is consuming excessive amount of carbonated beverages.

Patients with chronic vomiting or GERD are to be referred to concerned specialists for initiation of proper therapy.

Restorative treatment: Depending upon the degree of tooth wear, restorative treatments can be undertaken to maintain the structural integrity of the eroded teeth.

ROLE OF SALIVARY FUNCTION IN THE PREVENTION OF DENTAL EROSION

Salivary function is an important factor in the prevention of erosion since **buffering action** of saliva can neutralize the intrinsic and extrinsic acids in the oral cavity and this in turn prevents erosion of teeth. Moreover, mineral ions in saliva can cause **remineralization** of the enamel damaged by the acids.

However, there is a relationship between the **salivary flow rate** and its buffering capacity (i.e. buffering capacity of saliva increases as the flow rate increases).

Therefore, if the salivary flow rate is decreased either due to some medications or disease, etc. there will be more and more erosion of teeth.

It has also been found that if there is an increase in the **citric acid and mucin** content in the saliva, these agents prevent the precipitation of mineral ions from saliva and hampers the remineralization process.

RESORPTION OF TEETH

DEFINITION

Resorption of teeth can be defined as a chronic progressive damage or loss of tooth structures (mostly roots of the teeth or sometimes crowns) due to the action of some specialized cells called odontoclasts. Resorptions sometimes occur as a physiological phenomenon as in case of root resorption of deciduous teeth. However, resorptions can also occur in a number of conditions as a pathological entity in relation to the permanent dentition.

Resorption is generally associated with some attempt at repair by the apposition of cementum or bone and the involved tooth may occasionally become ankylosed to the surrounding bone.

Resorption of teeth

Physiological	Pathological	
Resorption of roots of the deciduous teeth	**External resorption**	**Internal resorption**
	• Secondary to periapical or other pathology • Idiopathic (burrowing)	• Secondary to pulpitis • Idiopathic

PHYSIOLOGICAL RESORPTION

Physiological resorption occurs in the root portion of the deciduous teeth, which helps in their natural shedding before eruption of the permanent successors.

Physiological resorption occurs by the following mechanism:

- Reduced enamel epithelial cells present as a protective covering on the erupting permanent tooth crown release some chemical substances, which cause resorption of the roots of deciduous teeth.
- According to some people, deciduous root resorption occurs as an inherent developmental process.
- According to other investigators the pressure exerted by the permanent successor teeth on the deciduous teeth and alveolar bone during their eruption may cause resorption of the later.

EXTERNAL RESORPTION OF TOOTH

DEFINITION

Pathological resoption that begins peripherally on the surface of the tooth root and moves towards the pulp is called the external resorption. Sometimes the process can affect the crowns of the unerupted teeth.

Role of Individual Factors

- *Periapical inflammation:* An inflammatory process in the periodontium (which has occurred as an extension of the gingival inflammation or which has extended via periapical foramen from the inflamed pulp) often leads to the formation of granulation tissue around the root. The highly vascular granulation tissue triggers the process of bone or tooth resorption mainly by stimulating the osteoclast and dentinoclast cells. The later cells, which can be either mononucleated or multinucleated; cause damage to the alveolar bone, cementum and dentin, etc. and leads to resorption of tooth surface.
- *Trauma in the tooth:* May initiate an inflammatory response in the periapical region of tooth; which triggers the odontoclast cells to resorb the roots.
- *Reimplanted teeth:* As the reimplanted or transplanted teeth are almost always nonvital and their roots have no surrounding viable periodontal ligaments, these are often resorbed externally and replaced by bone.
- *Cysts:* Cystic lesions developing in and around the root of the permanent teeth may cause external resorption in the following mechanisms:
  - Cysts exert pressure on the roots of the adjacent teeth and cause their resorption.

Causes of external resorption

- Periapical or periradicular inflammation
- Trauma in the tooth
- Cysts in the jaw (especially dentigerous cyst)
- Excessive mechanical forces on the tooth
- Excessive occlusal forces
- Tumors in the jaw (especially ameloblastoma)
- Reimplanted tooth
- Periodontal surgery
- Pressure from impacted tooth
- Paget's disease of bone
- Alveolar bone grafting
- Hormonal imbalance
- Herpes zoster
- Pulpless tooth
- Idiopathic

  - Epithelial cells of the lining epithelium of cyst can release some chemical mediators, which cause root resorption.
  - The dentigenous cyst, which develops from the reduced enamel epithelial cells, (these cells are responsible for deciduous root resorptions in normal conditions) often has a tendency for root resorption of the surrounding permanent teeth.
- *Tumors:* Benign and malignant tumors in the jawbone cause resorption of the roots of the surrounding teeth. In such conditions, resorption takes place either due to pressure effect from the growing tumor or due to the action of the chemical mediators released by the tumor cells.
  Ameloblastoma is very much known for its ability to resorb the roots of the surrounding teeth.
- *Excessive mechanical or occlusal forces:* Trauma from malocclusion or excessive orthodontic forces can cause injury or necrosis of the periodontal ligaments, which may initiate resorption of the tooth roots.
- *Periodontal surgery:* As an after effect of periodontal surgery granulation tissue forms on the external surface of the root, which stimulates the odontoclast cells; as a result external resorption often occurs.
- *Impacted tooth:*
  - When an impacted tooth exerts pressure on the root of the adjoining erupted tooth, it can cause resorption.
  - An impacted tooth itself may undergo resorption in its crown portion and it probably happens due to partial loss of the protective covering of reduced enamel epithelium around the crown.
- *Idiopathic external resorption (Burrowing resorption):*
  - A burrowing type of external resorption is commonly seen in relation to a single or multiple erupted teeth.
  - Initially a localized area of the root surface near the cervical region (below the gingival epithelial attachment) is resorbed.
  - Following this, the resorption process borrows deeply into and ramifies throughout the dentin producing a 'labyrinthine network' of lacunae and channels.
  - The resorbed tooth structures are replaced by granulation tissue and ankylosis sometimes develops.
  - The circumpulpal dentin and predentin are generally spared and they remain as narrow shell as the resorption encircles the pulp.
  - Radiographically burrowing type of resorption resembles the dental caries.
  - There is another pattern of external resorption of tooth, which starts at the root apex and progresses slowly in the occlusal direction.
  - Idiopathic external resorptions can affect almost all the teeth simultaneously.

RADIOGRAPHIC APPEARANCES OF EXTERNAL RESORPTION

- Radiographically external resorption often shows loss of continuity in the peripheral or external outlines of teeth; however the radiographic image of root canals remains intact.
- External resorption sometimes appears as carious lesions.
- Lesions in the initial stages produce raggedness or blunting of the root apex. Larger lesions may even produce a 'moth-eaten' appearance due to irregular or uneven destruction patterns of tooth.
- External resorption in the apical regions of endodontically treated teeth radiographically exhibits as if the root canal filling materials are projecting beyond the apex.
- Often there is obliteration of the periodontal ligament space with development of ankylosis.
- When external resorption involves the crown of an impacted tooth, it may look like dental caries.

CONSEQUENCES OF EXTERNAL RESORPTION

External resorptions in severe cases may extend up to the pulp leading to loss of vitality of the affected tooth. Restorative treatments coupled with endodontic therapy can be effective in some

cases. However, there is always the danger of fracture of the tooth.

INTERNAL RESORPTION OF TOOTH

DEFINITION

Internal resorption of tooth refers to an uncommon condition in which the resorption process starts internally within the tooth itself and the dentin is gradually resorbed from the pulpal side towards the periphery.

ETIOPATHOGENESIS

- The disease can occur as part of an inflammatory response to pulpal injury, however, in many instances even no such initiating factors could be identified.
- The inflammatory reaction in the pulp causes activation of osteoclast or dentinoclast cells in the internal surfaces of the root or crown, which result in the resorption of dentin.
- Gradually small resorption lacunas develop, which enlarge and coalesce together; and the entire dentin is eventually resorbed.
- Hyperplastic pulpal tissues gradually occupy the spaces created due to the dentinal resorption.

CLINICAL FEATURES

- Internal resorption may involve either the crown portion of the tooth or the root portion
- Any tooth may be involved (both anterior and posterior teeth) and usually only a single tooth is affected.
- As the disease initiates from the central portion of the tooth, there is no early symptom of the disease as long as the external outline of the tooth remains intact.
- In advanced stages when the coronal dentin is resorbed, the tooth often appears **pink in color**; because the hyperplastic and highly vascular pulp tissue fills up the resorbed spaces in dentin and is visible through the transparent enamel. This typical appearance is known as **'pink tooth of mummery'** (Fig. 7.2).
- The pink appearance of the tooth may also occur in cases of severe external resorptions (especially in burrowing type), when the gingival tissue projects into the resorbed spaces of dentin.
- When internal resorption affects the root of the tooth no color change is usually evident.
- The affected tooth remains vital unless there is pulp necrosis due to fracture of the tooth or due to its perforation.
- Untreated cases of internal resorption generally lead to perforations and eventual fractures of teeth.
- On rare occasions the resorption process may stop spontaneously without any apparent reason.

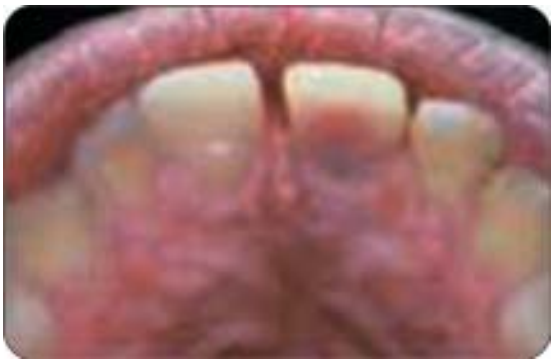


Fig. 7.2: Pink tooth of internal resorption

RADIOLOGICAL FEATURES

- Radiographically, internal resorption presents a well-defined, spherical shaped, radiolucent area in the dentin, which is usually continuous with the pulp chamber or root canal.
- The radiographic image of the external outline of the tooth remains intact.
- When internal resorption leads to perforation of tooth, radiograph shows a communication between the pulp chamber or root canal and the periodontal ligament space.
- Sometimes there can be balloon type expansion of the root canal of the affected tooth.

TYPES OF INTERNAL RESORPTIONS

Internal resorptions are of two types:

A. Internal inflammatory resorption
B. Internal replacement resorption

Internal Inflammatory Resorption

- The condition occurs probably due to an intense inflammatory reaction within the pulp tissue.
- Microscopy reveals a chronically inflammed pulp tissue containing numerous inflammatory

cells along with few multinucleated dentin resorbing cells (dentinoclasts).
- Radiograph exhibits an uniform, spherical, enlargement of the root canal.

Internal Replacement Resorption
- This resorption occurs in the absence of any inflammatory reaction within the pulp.
- Microscopy shows a fibrous granulation tissue in the pulp containing ectopic, bone-like calcified masses.
- Radiographically, an irregular 'moth-eaten' type of radiolucency is formed in the dentin.

HISTOPATHOLOGY
- Multiple irregular or smooth areas of resorptions in the pulpal surface of the dentin.
- A hyperplastic, highly vascular, pulp tissue is projecting into the spaces in dentin, which are created by resorption.
- Multiple multinucleated dentinoclasts (reabsorbing cells) are found near the resorbing front of dentin.
- Occasionally, partial repair of the defect by an atypical dentin may occur and few reversal lines mark these areas.

TREATMENT
- Extirpation of pulp tissue and conventional endodontic therapy.
- When the tooth is perforated, extraction is the only treatment possible.

PULP CALCIFICATION

DEFINITION
Deposition of calcified mass(s) within the dental pulp for no apparent reason is called pulp calcification.

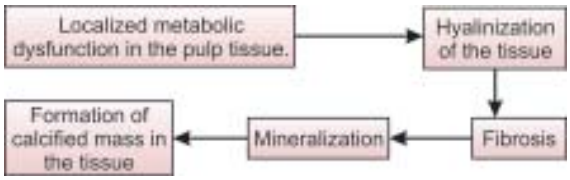
Pulp calcification may be an age related process and occurs more often with increasing age; however it can also occur as a local pathologic change in the dental pulp especially in those teeth, which are subjected to trauma or chronic caries. The calcification process probably initiates in relation to the damaged pulp tissue.

Causes of pulp calcification
- Idiopathic formation of pulp stones
- Formation of secondary dentin in response to caries
- Calcific metamorphosis-Pulp obliteration due to aging or trauma
- Dentinogenesis imperfecta-excessive secondary dentin formation causing pulp obliteration
- Dentin dysplasia Type-I-chevron shaped pulp chambers
- Dentin dysplasia Type- II- pulp obliteration in deciduous teeth and pulp stone formation in permanent teeth
- Ehlers-Danlos syndrome
- Regional odontodysplasia

PATHOGENESIS OF PULP CALCIFICATION
The etiology of pulp calcification is unknown and it appears to be not related to inflammation, trauma or any systemic disease.

The possible pathogenesis is as follows (Flow chart 7.1):

Flow chart 7.1: Pathogenesis of pulp Calcification



Types of pulp calcification

Nodular/discrete (pulp stone)			Diffuse calcification		
Pulp stones (Types)					
False			True		
Attached	Free	Interstitial	Attached	Free	Interstitial

TYPES

Calcification in the pulp may be either diffuse (linear) or nodular (pulp stones).

- *Denticles:* These are small masses of tubular dentin formed within the pulp near the furcation area of tooth.
- *Pulp stones:* Pulp stones are nodular calcified bodies having an organic matrix and they occur frequently in relation to the coronal pulp. Pulp stones develop around a central nidus of pulp tissue (consisting of collagen fibrils, ground substance and necrotic cell debri).
- *Diffuse linear calcifications of pulp:* These are amorphous, unorganized, fine fibrilar strands of calcified masses and are typically formed within the radicular and coronal pulp.

TYPES OF PULP STONES

Pulp stones can be of two types: **true and false.**

A. True pulp stones are composed predominantly of dentin and have dentinal tubules. They may have an outer layer of predentin and are often located adjacent to the odontoblast cells.

B. False pulp stones are composed of concentric layers of calcified material with no tubular dentinal tubules.

According to their location in the dental pulp, stones can be described as **free, attached and interstitial types.**

- **Free pulp stones** are surrounded on all sides by pulpal tissue and are not attached to the dentinal wall.
- **Attached pulp stones** are those, which are attached to the dentinal wall of the pulp chamber.
- **Interstitial pulp stones** are those where the pulp stones have become surrounded by reactionary or secondary dentin they are called interstitial pulp stones.

CLINICAL SYMPTOMS

Pulp stones do not cause any clinical symptoms and the affected tooth is vital, however mild, neurologic pain has sometimes been reported in the tooth because of their presence.

DIAGNOSIS

Pulp calcifications can be detected by the following methods:

- Large pulp stones are often detected by radiographs.
- Ground section preparation of the affected tooth.
- Microscopic examination helps in differentiating between the true and false pulp stones (on the basis of presence or absence of dentinal tubules).
- Serial sectioning of tooth or multiple radiographs taken at different angles may help to detect whether the pulp stone is free or attached to the dentinal wall.

CLINICAL SIGNIFICANCE OF PULP CALCIFICATIONS

Both pulp stones and dystrophic pulp calcifications may cause difficulties during endodontic treatment of the affected tooth.

HYPERCEMENTOSIS

DEFINITION

Increase in the thickness of cementum (specially cellular cementum) on the root surfaces of tooth due to excessive cementogenesis is called hypercementosis and the condition results from some local or systematic disorders.

ETIOLOGY OF HYPERCEMENTOSIS

Periapical inflammation: Low grade sustained periapical inflammation often causes stimulation of the apical cemetoblasts cells. This produces either a broad area of thickening of cementum or a localized 'knob-like' cemental overgrowth on the root surface.

Mechanical stimulation: Mechanical stimulation (e.g. orthodontic force) in to a tooth below a certain threshold level may induce apposition of cementum, which in the long run results in hypercementosis.

Functionless or unerupted tooth: In such cases, cemental apposition overpowers cemental resorption due to the lack of adequate occlusal stress. More and more cementum deposition eventually leads to hypercementosis.

Paget's disease of bone: Hypercementosis of tooth is often associated with Paget's disease of bone.

Etiology of hypercementosis	
Local factors	**Systemic factors**
• Periapical or periradicular inflammation • Occlusal trauma • Mechanical stress • Functionless tooth • Unerupted tooth • Tooth repair.	• Aging • Paget's disease of bone • Cementoblastoma • Acromegaly • Pituitary gigantism • Arthritis • Calcinosis • Rheumatic fever • Thyroid goiter • Vitamin A deficiency • Idiopathic.

The cemental tissue in this disease produces a mosaic pattern similar to that of bone.

Tooth repair: Excessive cementogenesis may occur during the repair process of a tooth root especially in the apical third region.

Idiopathic: In most of the cases the exact cause of the disease is not known.

CLINICAL FEATURES

Clinically the involved teeth are completely asymptomatic and the condition is often discovered during routine radiographic examination. The condition is mostly seen in adults and either single or multiple teeth can be involved.

RADIOGRAPHIC FEATURES

Radiograph shows excessive cemental thickening with a typical bulbous appearance of the roots. The thickened or blunted root is separated from the surrounding alveolar bone by a well-defined periodontal ligament space.

MICROSCOPY

Microscopically hypercementosis reveals excessive disposition of normal cellular or acellular cementum on the root surfaces of tooth in concentric layers.

CLINICAL SIGNIFICANCE

- Hypercementosis sometimes causes obliteration of the periodontal ligament space resulting in ankylosis of tooth, especially when the cementum develops in continuity with the alveolar bone.
- It may result in concrescence of teeth.
- Because of ankylosis and bulbous nature of the root, the tooth is difficult to extract.

AGE CHANGES IN TEETH

Age changes in teeth include the changes in structure and composition of the dental tissues as well as the changes in morphology associated with tooth wear.

CHANGES IN ENAMEL

- Enamel becomes more brittle with age.
- Less permeable for the ionic exchanges as the intercrystalline pores become smaller and smaller with age.
- More and more darkening due to absorption of organic materials.
- Enamel is progressively worn away with age, in the regions of masticatory attrition.
- Decrease in the amount of water content in enamel tissue.
- Progressive increase in the fluoride content of surface enamel due to ionic exchanges with the oral fluid, which causes conversion of hydroxyapatite crystals of enamel into fluroapatite crystals.
- Progressive decrease in the incidence of caries.

CHANGES IN DENTIN

- Continuous formation of secondary dentin causing reduction in size and even obliteration of the pulp chamber.

- Dentinal sclerosis due to continued production of peritubular dentin.
- Roots of the teeth become more brittle due to dentinal sclerosis.
- Sclerosis of dentin also causes increasing translucency of the roots.
- Root translucency of tooth starts at the apex and extends coronally with age; therefore this phenomenon can be used as a guideline in forensic odontology as a method of age determination of person.

CHANGES IN CEMENTUM

- Cementum continues to form in the apical third of the root throughout life.
- Increase in the thickness of cementum at the root-end helps to compensate for the occlusal and interproximal attrition of tooth.
- The amount of secondary cementum apposition increases with age and it can be an important factor in age determination in forensic dentistry.
- Besides cementum appositions, there can be areas of cemental resorptions with increasing age.

CHANGES IN PULP

Following changes always occur in the pulp tissue with age:

- Decreased cellularity
- Reduced vascularity.
- Increased fibrosis due to continued formation of collagen fibers.
- Pulpal response to tissue injury can be impaired, which may cause reduced healing potential.
- Pulp volume gradually decreases with continued production of secondary dentin.
- Incidence of pulp calcification will be higher with age.

CEMENTICLES

Cementicles are small calcified bodies lying free in the periodontal ligament and are formed as a result of dystrophic calcifications.

PATHOGENESIS

Cementicles may develop in the following manner:

- Calcification of the epithelial cell rest of Malassez in the periodontal ligament tissue.
- Calcification of the soft tissue between the Sharpey's fiber bundles.
- Fragmentation and detachment of small piece of cementum from the root surface due to excessive force on the tooth.
- Calcification of thrombosed blood capillaries within the periodontal ligament.

Cementicles are not necessarily the mass of true cementum, any calcified tissue including alveolar bone are collectively referred to as cementicles. Their size can increase due to further disposition of calcium.

Cementicles are not usually visible in the radiograph and they do not have any clinical significance.

DENTINAL SCLEROSIS

Dentinal sclerosis is the condition characterized by calcification of the dentinal tubules of the tooth.

It is usually caused by several factors:

- Injury to dentin by caries.
- Aging process.
- Abrasion or erosion of tooth.

Dentinal sclerosis presents a translucent zone in the dentin, which can be seen when the tooth is viewed by transmitted light.

Sclerosis often decreases the conductivity of the dentinal tubules.

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CHAPTER 8

Bacterial, Viral and Fungal Infections

SPECIFIC BACTERIAL INFECTIONS

TUBERCULOSIS

Tuberculosis is a very contagious, chronic bacterial infectious disease of worldwide prevalence. Tuberculosis predominantly affects the lung and the condition is called 'pulmonary tuberculosis'; however sometimes the disease can also affect other organs, e.g. oral cavity, intestine and bone, etc. and these lesions are called 'extra-pulmonary tuberculosis'.

It is a granulomatous infection and is caused by ***Mycobacterium tuberculosis*** or rarely by ***Mycobacterium bovis***. The incidence of tuberculosis has declined greatly all over the world due to the improvement in living standards, nutritional status and particularly due to the more and more availability of antitubercular drugs. However, the recent observations indicate that the disease is making an alarming and widespread comeback throughout the world in association with HIV infections or AIDS.

The other factors backing the comeback of the disease include increased poverty, poor living conditions and development of multi-drug resistant tuberculous microorganisms, etc.

PATHOGENESIS

Tuberculosis is mostly caused by ***Mycobacterium tuberculosis*****,** which is an aerobic, slender, non-motile, non-spore forming, rod shaped organism. Both human and bovine types of tuberculous organisms can cause the disease. Each year about 8 million people are infected with tuberculosis; out of which about 3 million people die and 2 million people develop the latent form of the disease. Upon exposure to the bacteria, 90 percent people remain clinically asymptomatic, 5 percent develop the disease in the first year and the remaining 5 percent people develop the disease later in their life.

- Most of the people make the first contact with the bacteria in childhood through **airborne (droplet)** infections. Less frequently the disease can be caused by ingesting unpasteurized cow's milk infected with ***M. bovis*** **or other atypical mycobacterias**. The initial exposure causes tissue hypersensitivity to the bacilli and it results in the development of host–response to the subsequent infections.
- The primary infection usually occurs in lung tissue where a transient inflammatory reaction takes place upon introduction of the micro-organism, this is usually followed by exudation and accumulation of PMN (polymorphonuclear neutrophils) and macrophages. Later on the PMN get destroyed but the macrophages cause phagocytosis of the organism .
- After phagocytosis, tuberculous bacilli start to multiply within the macrophage itself and this results in a change in the shape of the macrophage cell, which appear as an epithelial-like cell, with ill-defined borders and hence are called **"epitheloid cells".**
- The epitheliod cells fuse together and form **Langhan's type of giant cells** with horse-shoe pattern of arrangement of nuclei.
- Lymphocytes and fibroblasts also accumulate in the area as **caseation necrosis** begins in the center of the infected tissue which results from hypersensitivity to tuberculoprotein (the bacillary antigen).
- Most of the lesions heal by fibrosis and calcification, the further progression of the disease is prevented by the development of a cellular immune response in the body against the bacteria.
- A person infected with tuberculous micro-organisms may remain asymptomatic for a long time and the condition is called **'latent tuberculosis'**. The disease may turn into active

form again between two weeks to several years time due to reactivation of the micro-organisms; whenever the patient's body resistance is suppressed.

- In some cases, depressed host immunity may result in a widespread disseminated infection in the lungs as well as in the extra pulmonary organs and this type of infection is known as **"miliary tuberculosis"**.

CLINICAL FEATURES

- The disease commonly occurs in adult males but children also do suffer from this disease very often .
- "Pulmonary tuberculosis" is the most common form of this infection and it has a male predilection (5:1).
- The tuberculosis patients commonly complain of **gradual weight loss, evening rise of temperature, loss of energy, anorexia, persistent productive or unproductive cough, chest pain, malaise, night sweats and easy fatiguability, etc**.
  However, many patients can be fully asymptomatic.
- Hemoptysis (coughing of blood), abundant sputum and pleuritic pain are very common.
- The untreated disease in people with low immunity spreads widely in the pulmonary and extra-pulmonary organs of the body like bone, kidney, liver, etc. and at this stage, the disease is known as "**miliary tuberculosis**".
- Involvement of central nervous system may result in the development of tuberculous meningitis.
- Tuberculosis infection in the lymph node is called "**scrofula**" and usually a group of lymph nodes are involved in the disease (Fig. 8.1).
- The infected lymph nodes are often **enlarged**; they have a **rubbery consistency** and become **matted** in appearance.
- In untreated cases there may be **abscess formation** in these lymph nodes (**cold abscess**) with pain, swelling and development of pus discharging sinus, etc.
- Sometimes calcification occurs in the infected nodes, which indicates a past healed disease rather than an active current infection.

Key points of tuberculosis

- Tuberculosis is a contagious, chronic bacterial infectious disease of worldwide prevalence; it also occurs frequently in association with HIV/AIDS.
- The disease is caused by *Mycobacterium tuberculosis;* which is an aerobic, slender, non-motile, non-spore forming, rod shaped acid fast bacillus.
- Tuberculosis predominantly affects the lung and the condition is called 'pulmonary tuberculosis'; however other organs of the body like oral cavity, bone, kidney, liver, etc. are also sometimes affected.
- The general symptoms of tuberculosis include gradual weight loss, evening rise of temperature, loss of energy, anorexia, persistent productive or unproductive cough, chest pain, malaise, night sweats and easy fatiguability, etc.
- Oral lesions of tuberculosis frequently occur in relation to the tongue, palate, lips, tonsillar area, salivary gland, jawbone and lymph nodes, etc
- In the oral cavity, various tuberculous lesions may develop, which include- tuberculous ulcer and patches, tuberculous gingivitis tuberculous osteomyelitis, tuberculous lymphadenopathy and tonsillitis, etc
- Tuberculous ulcers are the most common oral manifestations of the disease; which is well-defined, painful, firm and yellowish-grey in colour with a granulating floor and minimum indurations.
- Tuberculosis of the lymph node is called "**scrofula**" and the infected lymph nodes are often **enlarged**, matted and have a **rubbery consistency.**
- Tuberculous lesion microscopically presents a granulomatous tissue with central areas of caseous necrosis, surrounded by lymphocytes, epithelioid cells and occasional multi-nucleated Langhans type of giant cells.
- Common investigations in tuberculosis are Ziehl-Nellsen staining of the sputum, chest radiograph, bacterial culture in Lowenstein-Jensen media, animal inoculation, Tuberculin test, ELISA test and PCR, etc.
- Treatment is done by antitubercular drugs, e.g. rifampicin, isoniazid, streptomycin, ethambutol, etc.

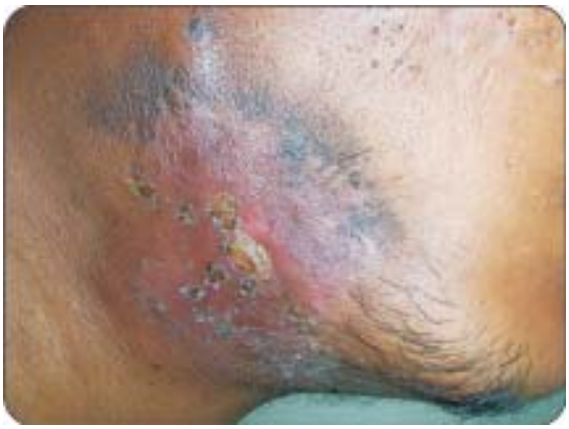


Fig. 8.1: Scrofula

- Primary tuberculosis of the skin is called "**lupus vulgaris**", involvement of bone by this disease may often lead to "**tuberculous osteomyelitis**".
- Sometimes renal tuberculosis may occur due to involvement of the kidney or the urinary bladder and this condition often produces hematuria or pyuria, etc.
- Severe cases of pulmonary infection may cause intestinal tuberculosis (resulting from swallowing of the sputum) which is characterized by ulceration of the intestinal mucosa with hypertrophy or adhesion of the walls.

Oral Manifestations of tuberculosis

- Tuberculous ulcers
- Tuberculous patches
- Tuberculous gingivitis
- Tuberculous nodules
- Tuberculous osteomyelitis or simple bone radiolucency
- Tuberculosis of the salivary glands
- Tuberculosis of the lymph nodes
- Tuberculous tonsillitis

Normally, the intact oral mucosa does not permit tuberculous bacilli to enter into the tissue; however preexisting oral lesions may facilitate the entry of these organisms into various oral structures.

IMPORTANT ORAL LESIONS OF TUBERCULOSIS

- Tuberculous lesions of the oral cavity are mostly secondary to the pulmonary infections and are usually caused by the implantation of microorganisms in the oral mucosa during constant coughing. However, primary oral tuberculosis may occur in some cases. The overall incidence of oral tuberculosis is about 0.75 to 1.44 percent.
- Moreover tuberculous infections in the oral cavity may also produce ulcers, nodules, vesicles, fissures, plaques, granulomas or verrucal-papillary lesions.
- **Chronic ulcers** are the most common oral lesions of tuberculosis. These ulcers are superficially located with irregular edges and minimal indurations. The base is either granular or it may be covered with a pseudomembrane.
- There may be presence of a single or multiple nodules of varying size, these nodules are semitransparent lesions of pin-head size and are grey in color.
- Oral mucosal lesions may occur in any intraoral site; however tongue is the most common location, besides this, palate, gingiva, lips, buccal mucosa, alveolar ridge and vestibules may also be affected.
- ***Tongue lesions:*** Tuberculous lesions of tongue mostly develop on the lateral borders and they appear either as single or multiple ulcers which are well-defined, painful, firm and yellowish-grey in color. These ulcers have a granulating floor with minimum induration, moreover the surrounding mucosa appears inflamed and edematous.
- ***Palatal lesions:*** Palatal lesions of tuberculosis are mostly seen over the hard palate and these lesions often appear as small ulcers or granulomas.
- ***Lip lesions:*** Labial tuberculous lesions often produce small, nontendered, granulating ulcers at the mucocutaneous junctions and sometimes they can also produce small nodular growths (Fig. 8.2).
- ***Gingival lesions:*** Gingival lesions of tuberculosis usually produce small granulating ulcers or erosive lesions with concomitant gingival hyperplasia. Sometimes there can be presence of diffuse, hyperemic, nodular or papillary projections from the margin of the gingival tissue.
- ***Tuberculous lesions of salivary gland:*** The tuberculous infection may involve either the

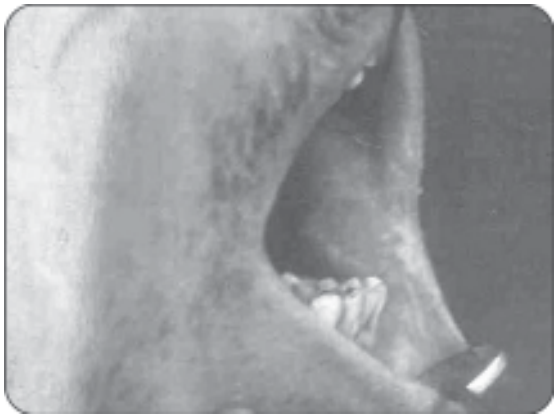


Fig. 8.2: Tuberculous ulcer of the lip

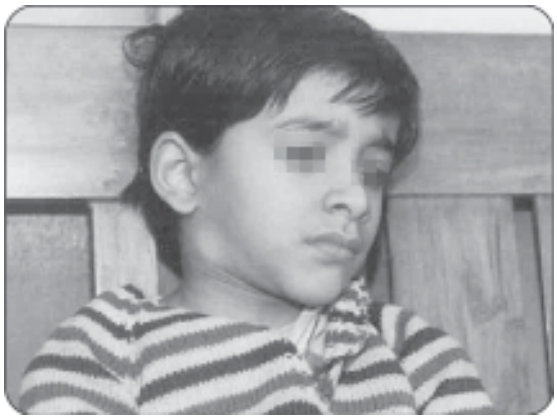


Fig. 8.3: Tuberculous lymphadenitis

salivary gland tissue itself or it may affect the intra or peri-glandular lymph nodes (Figs 8.3 and 8.4). There can be generalized glandular swelling or abscess formation along with pain, facial nerve palsy and fistulas tract formations, etc.

- ***Tuberculous lesions of jaw bone:*** Chronic osteomyelitis of the maxilla and mandible may occur in case of tuberculosis, and the infection reaches the bone via the blood stream or root canals of tooth or via the extraction sockets. The bone infection may also result from extensive gingival or periapical lesions. Tuberculous osteomyelitis of the jaw bones clinically produces pain, swelling, sinus or fistula formation, trismus, paresthesia and lymphadenopathy.

DIFFERENTIAL DIAGNOSIS OF ORAL TUBERCULOUS LESIONS

- Squamous cell carcinoma
- Sarcoidosis

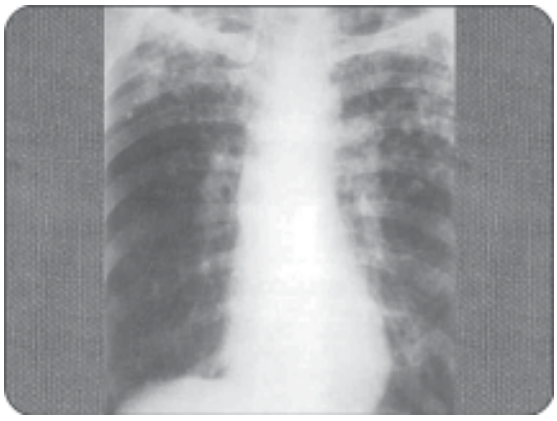


Fig. 8.4: X-ray shows prominent hyalar lymph nodes in a tuberculosis patient

- Syphilis
- Aphthous ulcer
- Deep mycotic infections
- Traumatic ulcer
- Wegner's granulomatosis
- Tularemia
- Foreign body reaction

HISTOPATHOLOGY OF TUBERCULOUS LESIONS (FIG. 8.5)

- The tuberculous lesions microscopically reveal granulomatous tissue with central areas of caseous necrosis, surrounded by lymphocytes, epithelioid cells and occasional multi-nucleated Langerhans type of giant cells.

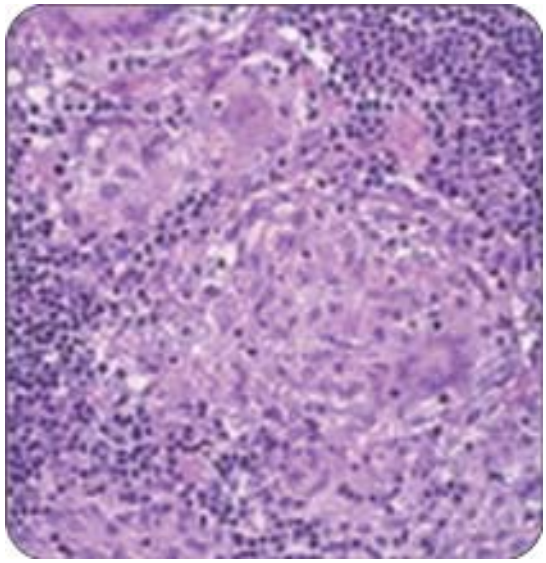


Fig: 8.5: Photomicrograph of tuberculous granuloma

- The epitheloid cells are morphologically altered macrophages which phagocytose the tuberculous bacilli and they look like epithelial cells.
- The area of caseous necrosis appears eosinophilic with hematoxylin and eosin staining.
- The granuloma is usually surrounded by fibrous tissue and lymphocytes. In some cases there may be areas of dystrophic calcifications.
- In some cases, tuberculous bacilli may be detected within the tissue in histologic sections.

Investigations in tuberculosis

- Staining of the smear prepared from sputum by **Ziehl-Neilsen stain** (it helps staining of tuberculous bacilli in a smear as well as in the tissue, e.g. granuloma)
- Chest radiograph
- Bacterial culture in Lowenstein-Jensen media (materials used for culture may be sputum, laryngeal swab, gastric lavage, urine, cerebrospinal fluid and pus, etc.)
- Animal inoculation
- Histopathology
- Tuberculin test
- Enzyme-linked immunosorbent assay (ELISA) test
- PCR (polymerase chain reaction)

TREATMENT

By antitubercular drugs, e.g. rifampicin, isoniazid, streptomycin, ethambutol, etc. in different standard regimens.

SYPHILIS

Syphilis is a sexually transmitted disease (STD) caused by infection with a spirochete named *Treponema pallidum*. The disease is generally classified into two types:

A. Acquired syphilis

B. **Congenital syphilis.**

ACQUIRED SYPHILIS

It is mostly contracted by venereal means, e.g. sexual intercourse with an infected partner, but in many cases, the disease may be acquired innocently by professionals like dental surgeons, nurses or other individuals while carelessly handling the infected patients.

The acquired syphilis manifests in three stages:

A. Primary syphilis

B. Secondary syphilis

C. Tertiary (late) syphilis.

Primary Syphilis

General Features

- The incubation period average about 21 days.
- The clinical symptoms appear at the site of inoculation, i.e. male and female genitalia and extragenital site like-fingers, perianal region and nipples, etc. (at these sites the spirochetes undergo rapid replication and enter into the lymphatics or blood stream).
- The characteristic primary lesion of syphilis is called **"chancre "**and it is a solitary, painless, indurated, non-tendered, non-hemorrhagic, ulcerated or eroded lesion (Fig. 8.5A).
- The primary lesion appears between 3 to 90 days after the initial exposure.
- Initially the chancre starts as a dull red macule or papule, which later on becomes eroded or ulcerated.
- Regional lymph nodes are enlarged, painless and are rubbery in consistency.
- Both the chancre and the lymphadenopathy resolve within 6 to 8 weeks.

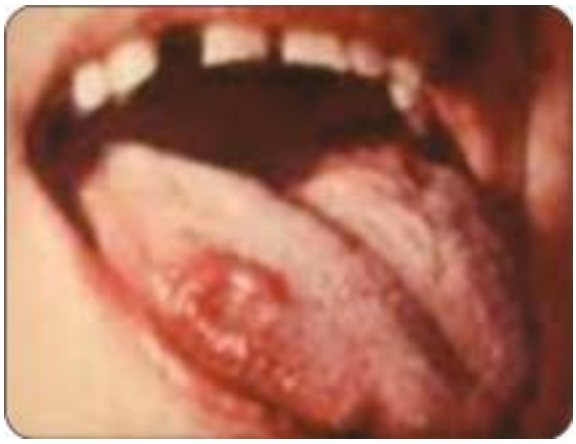


Fig. 8.5A: Oral syphilitic chanre

Oral manifestations of primary syphilis

- Oral lesion of primary syphilis is called **"chancre"** which generally occurs 3 weeks after the contact with the organism.
- Most of the oral lesions occur on the lip; the other sites include tongue, palate, gingiva, uvula and tonsils, etc.
- The oral lesions of primary syphilis start as a painless nodule of about 1 centimeter in diameter, which gradually exhibits breakdown of the surface with development of an ulcer.
- Most of the male patients tend to develop lesions on the upper lip while most of the female patients develop chancres on the lower lip.
- The fully developed oral lesions of primary syphilis are called **chancres.** These are painless, rounded, ulcers with indurated margins and are often covered by a grayish-white membrane. The chancres are often mistaken for oral squamous cell carcinomas.
- Some oral lesions are vascular and proliferative in nature and hence resemble the pyogenic granulomas.
- Tongue lesions may be commonly seen on the lateral surface of the anterior two-third area or on the dorsal surface and often there is enlargement of the folate papilla.
- The uvula appears red and swollen. Moreover, the tonsils show edema, redness and surface erosions or ulcerations.
- Chancres may be painful due to secondary infection and are highly contagious in nature.
- Lymphnodes are enlarged bilaterally. These are painless and rubbery in consistency.
- Oral chancres usually heal by scarring within 3-6 weeks time

Secondary Syphilis

General features

- Secondary syphilis usually appears in about 6 to 8 weeks after the appearance of the primary chancre.
- This stage occurs due to the generalized hematogenous dissemination of the infection in the body.
- Secondary syphilis is generally characterized by skin lesions, mucosal lesions and few constitutional symptoms along with generalized lymphadenopathy.
- The skin lesions appear as diffuse painless macular, papular, follicular, lenticular or papulo-squamous patches or rashes.
- Skin lesion may also occur in the form of nodular, flat or papillary condition; which often resembles the viral papilloma, called **condyloma lata**.
- Circinate (coin-like) lesions on the face are characteristic of secondary syphilis.
- Moreover there can be development of moist flat, papulonodular lesions at the mucocutaneous junctions and over the mucosal surfaces of genitalia.
- Areas of hyperpigmentations or hypopigmentations may be seen on the palms and soles.
- **Constitutional symptoms** associated with secondary syphilis include—malaise, headache, sore throat, anorexia, weight loss, fever, joint and muscle pain, laryngitis and pharyngitis, etc.
- Generalized lymphadenopathy is a common feature and the lymph nodes are painless, discrete and not fixed to the surrounding tissues.
- With or without treatment secondary lesions usually heal within 2to 4 weeks time.
- Sometimes immuno-compromised patients may exhibit a widespread and explosive form of secondary syphilis called **" lues maligna"**; characterized by large atypical necrotic ulcers of the face, scalp and oral mucosa, etc.

Oral manifestations of secondary syphilis

- The secondary lesions are mucocutaneous in nature and they usually occur 6 to 8 weeks after the primary infection.
- The oral lesions in this stage are called "**mucous patches**", and these are commonly seen over the tongue, lips, buccal mucosa, gingiva, tonsils, larynx, pharynx and palate, etc
- These patches are characterized by multiple, flat, irregular or circular, slightly raised, painless, white round erosions.
- Mucous patches are covered by a thin yellowish-gray (glistening) slough and are surrounded by a painful erythematous halo.
- Multiple "mucous patches" in the oral cavity sometimes coalesce together and form irregularly linear "snail track" like ulcers. This stage is also contagious since both the discharge

from the ulcer as well as the patient's saliva contains many ***Treponema pallidum*** organisms.
- Some moist papules are often seen at the angle of the mouth and they have a typical "split pea" like appearance.
- Sometimes the mucous patches can undergo superficial epithelial necrosis; which can lead to sloughing and exposure of the underlying connective tissue.
- In secondary syphilis the tongue is often fissured.

Tertiary (Late) Syphilis

General features

- Tertiary syphilis (third stage of the disease) usually occurs about 5 to 10 years after the primary infections; it affects nearly every organ of the body and this stage is associated with the most severe forms of systemic complications.
- It mainly affects skin, mucous membrane, central nervous system (CNS) and cardiovascular systems. Besides this, muscles, bones and joints are also frequently affected.
- Typical lesion of tertiary syphilis is called "**gumma**", which is a localized, indurated, chronic granulomatous lesion; having either nodular or ulcerated surfaces. Moreover this lesion is also associated with extensive tissue destruction in the affected organs.
- Granulomatous ulcerative lesion often appears as a **"punched-out"** ulcer, having vertical walls and a dull red granulomatous base with an irregular outline.
- Skin lesions heal very slowly and often they leave **"tissue paper"** like scars.
- Tertiary syphilis occuring in pregnancy often results in congenital syphilis of the newborn.
- This disease also frequently occurs in association with AIDS.
- The most serious complication of tertiary syphilis is the destruction of the walls of large blood vessels, aneurysm of the arch of aorta, left ventricular hypertrophy and congestive cardiac failure, etc.
- Involvement of central nervous system (neurosyphilis) results in generalized paresis, dementia and strokes.
- Bone lesions cause osteomyelitis and destructions of the joints.

Oral manifestations of tertiary syphilis

- Intraoral lesions of tertiary syphilis are called "**gumma**" and are commonly seen on the hard and soft palate, tonsils, lips and tongue, etc.
- These lesions begin as firm, small, pale, nodular masses in the midline of the palate.
- They frequently ulcerate by central necrosis and produce painless, deep, rounded ulcers; which have punched-out edges and a wash-leathery floor.
- The ulcers can be either single or multiple and their size varies from one to several inches in diameter.
- In tertiary syphilis, progressive necrosis and sloughing often leads to perforation of the palate with development of oro-nasal communication. This is a very characteristic finding in tertiary syphilis and it often results in breathing and swallowing difficulties.
- Destruction of the soft palate and uvula may result in obstruction of the nasopharyngeal airway in few cases.
- In the tongue, often there is presence of superficial glossitis called "**syphilitic glossitis"**; since these lesions appear as diffuse, large leukoplakic patches, the condition is often known as "**syphilitic leukoplakia**" as well. This stage of the disease is not contagious.
- Loss of filliform and fungiform papilla in tertiary syphilis results in a bald tongue. Moreover as the so called 'gumma' lesions heal up, they cause considerable distortion of tongue and the soft palate.
- Moreover an ulcerative gummatous lesion of the tongue may closely resemble squamous cell carcinoma.
- In tertiary syphilis, destruction of the nasal septum and collapse of the nasal cartilage results in "**saddle-nose**".

CONGENITAL SYPHILIS

Definition

Congenital syphilis is a rare entity that occurs in children born of an infected mother. The condition occurs due to transplacental infection with *Treponema pallidum* during fetal development.

Congenital syphilis presents the following features:

- Mulberry molars with constricted and atrophic cusps.

Key points of syphilis

Syphilis is a sexually transmitted disease caused by ***Treponema pallidum*** and it occurs in two basic forms Acquired syphilis and Congenital syphilis.

Acquired syphilis	Congenital syphilis
Acquired syphilis is contracted by veneral means and it has three types—Primary syphilis, secondary syphilis and tertiary syphilis. • **Primary syphilis**—The primary lesion of syphilis is called "**chancre**", which develops at the site of contact (genitalia) and clinically presents as a solitary, painless, indurated, non-tendered, ulcerated or eroded lesion. Oral lesions of primary syphilis (chancres) occur on the lip, tongue, palate, gingiva, uvula and tonsils, etc. • **Secondary syphilis**—Secondary syphilis is generally characterized by skin lesions, mucosal lesions and few constitutional symptoms along with generalized lymphadenopathy. Oral lesions of secondary syphilis are called "**mucous patches"**; these are flat, irregular, slightly raised, painless, white round erosions covered with a yellow-gray slough. Multiple mucous patches may coalesce together to form snail tract- like ulcer. • **Tertiary syphilis**—It affects skin, mucous membrane, bone, central nervous system (CNS) and cardiovascular systems. Typical lesion of tertiary syphilis is called "**gumma**", which is a localized, indurated, chronic granulomatous lesion with nodular or ulcerated surface. **Intra-oral lesions of tertiary syphilis (gumma)** are commonly seen on the hard and soft palate, tonsils, lips and tongue, etc. Moreover, syphilitic leukoplakia is also seen.	Congenital syphilis occurs in children born of an infected mother through transplacental infection. The most characteristic feature of congenital syphilis is the: • **Hutchinson's triad**—Which consists of hypoplasia of the incisor and molar teeth (Hutchinson's teeth) • Eighth nerve deafness and • Interstitial keratitis of the eye. Besides these the other symptoms like frontal bossing, hypoplasia of maxillary bone, saddle-nose and rhagades, etc. are frequently seen.

- Screwdriver-shaped incisors, these teeth are narrower at the incisal edge.
- Rhagades (fissuring and scarring of the corner of the mouth).
- Frontal bossae and saddle-nose or bull dog nose (occurs due to destruction of the nasal spine).
- Short maxilla and high palatal arch and saber (pointed) shins.
- Relative mandibular prognathism and increased interdental spaces.
- Hutchinson's (notched) incisors and peg laterals.
- Delayed eruptions of teeth.
- Hypodontia and enamel hypoplasia.
- Deciduous teeth are less frequently affected as compared to the permanent teeth.
- Pathognomonic of the disease is the occurrence of **Hutchinson's triad**, which consists of:
  A. Hypoplasia of the incisor and molar teeth (Hutchinson's teeth)
  B. Eighth nerve deafness;
  C. Interstitial keratitis of the eye.
- The **mulberry molars** (also known as **Moon's molars**) and **screwdriver-shaped incisors** are important characteristic features of congenital syphilis; the screwdriver-shaped incisors typically exhibit wide middle-third of the crown with tapered incisal edges.

- The mulberry molars look dirty yellow in color which occurs as a result of hypocalcification of these affected teeth.
- The changes in the shape of teeth occur in congenital syphilis due to involvement of the developing tooth germs by *T. pallidum* organisms during the stage of morphodifferentiation. These organisms cause inflammation in and around the tooth germs which results in hyperplasia of the epithelium of the enamel organ.

Histopathology of Acquired Syphilitic Lesions

Primary Syphilis

The chancre histologically presents the following features:

- A proliferative granulation tissue is present at the margin of the ulcer.
- Dense infiltrates of plasma cells, lymphocytes and macrophages.
- Obliterative endarteritis with perivascular infiltration of chronic inflammatory cells .
- *T. pallidum* may be seen when immunofluorescent studies or silver staining are done.

Secondary Syphilis

- The macular lesion shows inflammatory cell infiltration and obliterative endarteritis .
- The papular lesion exhibits endothelial proliferation, swelling and perivascular chronic inflammatory cells infiltration.
- Condyloma lata reveals hyperplastic epithelium with hyperkeratosis and acanthosis.
- Obliterative endarteritis may also be seen and there may be occasional presence of epitheloid cells.

Tertiary Syphilis

- The gumma microscopically presents a peripheral rim made up of fibroblasts, which surrounds a central zone of coagulative necrosis.
- Fibroblasts are plump and they often resemble epitheloid cells.
- Occasional presence of giant cells and regular presence of chronic inflammatory cells like plasma cells, lymphocytes and histiocytes, etc.

Diagnosis

- Detection of bacteria in smear by dark ground illumination microscopy.
- Bacterial culture in artifical media.
- Serological tests like Washerman reaction, Khan test, venereal disease research laboratory (VDRL) test, fluorescent treponemal antibody test (FTA), rapid plasma reagin (RPR) test, microhemagglutination assay-*T. pallidum* (MHA-TP) test.
- ELISA.
- Histopathology.

Treatment

High doses of penicillin.

GONORRHEA

DEFINITION

Gonorrhea is a sexually transmitted disease (STD) caused by *Neisseria gonorrhoeae* bacteria; the disease is often called "the clap". The microorganisms are often present in the moist part of the body, e.g. vagina, penis, eyes, throat and rectum, etc. The disease affects both males and females; and it can be spread through all forms of sexual activity including oral, vaginal and rectal sex.

CLINICAL FEATURES

Age: People of any age group can be affected, however it is more prevalent in the age group of 15 to 30 years.

Sex: Both sexes can be affected; however a man having sex with an infected woman has 30 to 50 percent chance of becoming infected, whereas a woman having sex with an infected partner has a higher (60 to 90) percent risk of getting infected.

Moreover as the women do not develop many clinical symptoms of the disease like men, the disease often remains undetected and it can have a devastating effect on the reproductive system in these women. The symptoms occur 2 to 10 days after the initial contact with the bacteria via the infected partner.

CLINICAL PRESENTATION OF GONORRHEA

Symptoms in men

- Yellow, white or green pus-like discharge from tip of the penis.
- Fever and vomiting.
- Redness of the glans penis.
- Swelling of the testicles.
- Stinging during urination.
- Presence of blood in urine and frequent urination.
- Swelling of the lymph nodes in the groin region.

Symptoms in women

The initial infection occurs in the uterine cervix, however in severe cases it spreads to the deeper structures, e.g. uterus and ovarian tube.

- Bleeding during intercourse and pain.
- Fever and vomiting.
- Abnormal intermenstrual bleeding.
- Vaginal discharge.
- Pain in the abdomen.
- Burning or itching sensation during urination.
- Complications develop due to diffuse spread of infection in the form of pelvic inflammatory disease, tubal infertility, ectopic pregnancy and chronic pelvic pain, etc.

ORAL MANIFESTATIONS OF GONORRHEA (FIG. 8.5B)

- Oral lesions mostly occur due to fellatio and these mostly develop in the oropharynx, tonsils and uvula, etc.
- Diffuse erythema in the oropharynx with sore throat.

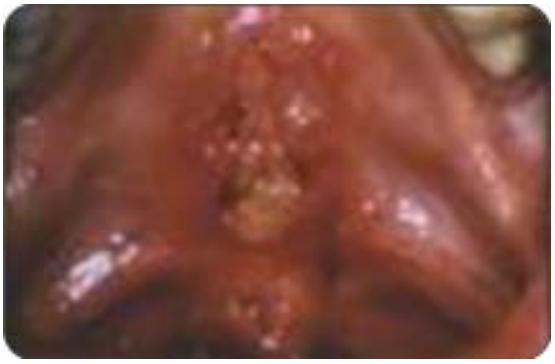


Fig. 8.5B: Oral lesion of gonorrhea

- Erythema, edema and discharge of pus from one or both tonsils.
- Cervical lymphadenopathy.
- Vomiting tendency due to irritation and soreness in the throat.
- Difficulty in swallowing.

DIAGNOSIS OF GONORRHEA

- *Neisseria gonorrhoeae* can be demonstrated by gram staining and it appears as a gram negative diplococcus under microscope.
- Bacterial culture of the samples obtained from the purulent discharge.
- Sugar fermentation test.
- Identification of bacterial DNA from the urine samples of the patient.

TREATMENT

High doses of antibiotics.

ACTINOMYCOSIS

Actinomycosis is a chronic granulomatous, suppurative and fibrosing infection; it was very common in the past but now-a-days has become rare. The disease is caused by filamentous, gram positive, anaerobic actinomycotic group of organisms, namely *Actinomyces israelii. A naeslundii, A. bovis, A. odontolyticus* and *A viscosus, etc.*

TYPES

Actinomycosis predominantly occurs in three forms:

A. **Cervicofacial**
B. **Abdominal** and
C. **Pulmonary actinomycosis.**

The cervicofacial actinomycosis is the most common form (occurs almost in 50% cases) of the disease.

PATHOGENESIS

The disease is more common among cultivators. Normally *A. israelii* and other members of the family are present as normal inhabitants of the oral cavity and the tonsillar crypts; besides these areas they can be present within carious teeth, infected dental pulp and calculus deposits, etc.

Infection often develops as the microorganisms take entry into the deeper tissues following tooth extraction, root canal treatment, trauma and jaw fracture, etc. The infection may also occur in presence of certain oral diseases like—periapical granuloma and pericoronitis, etc. Moreover, the actinomycotic group of organisms can also cause infection in combination with *Staphylococcus and Streptococcus*, etc.

CLINICAL FEATURES

Age: The disease occurs mostly in the fourth and fifth decade of life.

Sex: More prevalent among males.

Site: The disease commonly involves the jaw bones, upper neck and salivary glands, etc.

PRESENTATION

- Initially, the disease starts as a soft tissue swelling over the upper part of the neck or below the ear, or near the angle of mandible with intense pain.
- The overlying skin appears dusky-red or bluish-red; which is firm and slightly tendered on palpation.
- The skin lesion is often classically described as "**wooden indurated area of fibrosis**".
- Later on, the swelling becomes fluctuant at the center and some areas of the skin gradually break down to produce multiple pus discharging sinuses. Similar sinuses can also be seen intraorally.
- The pus contains clinically visible, small, yellowish-green granules which are known as '**sulphur granules**' and each of them represents a colony of organisms.
- The pus discharging sinuses heal-up with fibrosis but later on, some new sinuses appear in the region and the process continues for years. This leads to the formation of many disfiguring scars in the area with development of trismus.

ORAL MANIFESTATIONS

- The tonsillar tissue is most frequently affected along with buccal mucosa, submandibular and submental areas.
- Tonsillar lesions often cause tonsillar hyperplasia.
- There can be painful swelling of the salivary glands (mostly parotid and submandibular glands) followed by abscess formation.
- Trismus is a constant feature of this disease which develops before the pus formation begins.
- The abscess also can form in the submandibular and submasseteric spaces; which can further intensify the trismus.
- Involvement of the jaw bones by this disease often results in chronic osteomyelitis.
- Periapical abscess and granulomas frequently develop which cause pain, swelling in the jaw with formation of draining sinuses.
- The periapical lesions in actinomycosis frequently affect the maxillary anterior teeth and the mandibular molars.
- Actinomycosis infections do not spread to the lymph nodes; however the lymphadenopathy associated with the disease may be due to secondary infections caused by some other organisms.

HISTOPATHOLOGY (FIG. 8.6)

- The cervicofacial actinomycosis microscopically exhibits chronic suppurative inflammation in the affected tissue with formation of numerous abscesses; whose centers are typically occupied by the bacterial colonies.
- The abscess eventually drains through discharging sinuses over the skin and the pus often contains the so called '**sulphur granules**' which are nothing but colonies of actinomyces.

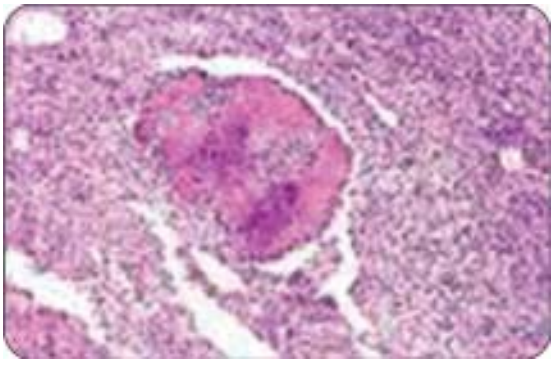


Fig. 8.6: Photomicrograph of actinomycosis

- Bone tissue often exhibits extensive necrosis with multiple areas of granuloma formations.
- The bacterial colonies consist of dense, eosinophilic masses of gram-positive filaments.
- The periphery of each colony shows club-shaped swellings; which produces a typical "**ray fungus**" like appearance.
- The colonies are gradually surrounded by neutrophils (PMN) followed by mononuclear cells (lymphocydes and plusma cells) and multinucleated giant cells.
- The colonies are surrounded by a fibrous tissue wall at the outer margin.

TREATMENT

By high doses of any of these drugs like—penicillin, cephalosporin, clindamycin and lincomycin, etc.

SCARLET FEVER

Scarlet fever is a rare specific bacterial disease caused by *Streptococcus B-hemolyticus* and it commonly occurs in children. The disease develops only when the organisms are systemically disseminated.

CLINICAL FEATURES

- The disease affects children between the ages of 3 to 12 years.
- Fever, headache, vomiting, tonsillitis, pharyngitis and generalized lymphadenopathy, etc.
- The tonsils, soft palate and pharynx become erythematous and these areas often exhibit a yellowish exudation.
- A diffuse, bright red skin rash appears on the second or third day of the disease that starts on the chest and gradually spreads to the other body surfaces. The rash occurs as a result of damage of the small superficial blood vessels by erythrogenic toxins liberated by the bacteria.
- The lips, nose and chin, etc. are generally not involved.
- Skin rashes last for about one week following which the affected area undergoes desquamation.

Key points of scarlet fever

- Scarlet fever is a rare bacterial disease of children caused by *Streptococcus B-hemolyticus.*
- Fever, headache, vomiting, tonsillitis, pharyngitis and generalized lymphadenopathy, etc. are the common symptoms of the disease.
- A diffuse, bright red skin rash often appears over the skin.
- On the facial skin the rash typically appears as **"sunburn with goose pimples".**
- The tongue exhibits the characteristic appearances of "**strawberry tongue**" and "**raspberry tongue**".
- These complications include rhinitis, sinusitis, otitis media, arthritis, pneumonia, meningitis, rheumatic fever, etc.

ORAL MANIFESTATIONS

- The skin rash is particularly more noticeable over the face and it is often referred to as **"sunburn with goose pimples".**
- The face is flushed, except for a zone of circumoral palor.
- The oral cavity exhibits generalized edema, elongation of uvula and diffuse petechiae especially over the soft palate.
- The palate appears congested and inflamed, and the hard palate exhibits punctiform redness.
- There is generalized congestion of the oral mucosa with presence of halitosis.
- During the first 2 days of the disease the tongue becomes covered with a white coat; through which only the enlarged and reddened fungiform papillae project like small, red knobs. This phenomenon is called "**strawberry tongue**".
- By the 4th or 5th day of the disease the white coating over the dorsum of the tongue is lost by desquamation; the tongue appears beefy red in color with many hyperplastic fungiform papillae and the condition is called "**raspberry tongue**".

Oral complications of scarlet fever: Several oral complications develop as the consequences of scarlet fever and these include cancrum oris, ulceration with perforation of the palate, osteomyelitis, peritonsillar abscess, mastoiditis and temporomandibular joint disturbances, etc.

Systemic complications of scarlet fever: The disease usually subsides within a week or 10 days, but complications may occur in few cases due to the bacterial metastasis or hypersensitivity reactions.

These complications include rhinitis, sinusitis, otitis media, arthritis, pneumonia, meningitis, rheumatic fever, acute glomerulonephritis and septicemia, etc.

Rheumatic fever causes permanent damage to the heart valves and patients in future may become susceptible to subacute bacterial endocarditis.

TREATMENT

Administration of penicillin or erythromycin.

DIPHTHERIA

Diphtheria is an acute contagious infection caused by *Corynebacterium diphtheriae,* and it commonly involves the children. Humans are sole reservoir of the microorganisms and the infection can be acquired through contact with an infected person.

CLINICAL FEATURES

- The clinical manifestations begin to appear about 1 to 5 days after the initial contact with the infective organism.
- The disease starts with low grade fever, malaise, vomiting, anorexia, headache and lymphadenopathy, etc.
- There is extreme difficulty in taking food or drink due to severe sore-throat.
- Widespread involvement of the mucosal surfaces causes exudation from the nasal, tonsillar, laryngeal, tracheal and pharyngeal areas.
- Initially exudation in the tonsillar area produces a thin, patchy yellowish film; which gradually thickens.
- Later on there is formation of a thick, fibrinous, gray colored, "**pseudomembrane**" (**diphtheric patch**) over the tonsil, larynx, pharynx and uvula, etc (Fig. 8.6A).
- The pseudomembrane or the patch is the most important characteristic of diphtheria. Whenever the patch is stripped away it leaves a bleeding surface.

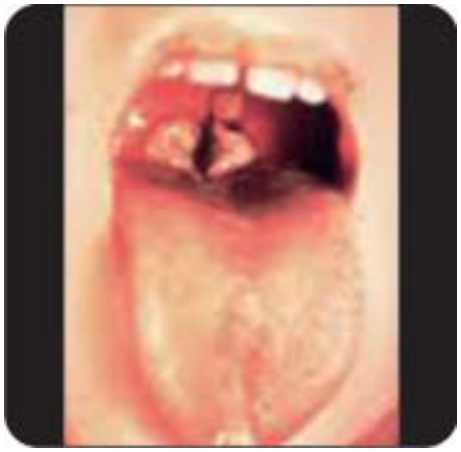


Fig. 8.6A: Diptheria patch

- Paralysis of the soft palate, nasal intonation of voice and nasal regurgitations, etc. may be seen in the later phases of the disease.
- There may be severe cervical lymphadenopathy and edematous swelling of the neck and the later condition is known as "**bull neck**".
- In untreated cases the patch may cover the entire soft palate, uvula, larynx and trachea; which may cause **respiratory obstruction** and even death due to blockade of the airway.
- In diphtheria, complications may arise in the heart, nervous system and kidney, etc. during or after the disease.

TREATMENT

Diphtheria antitoxin injection, in combination with antibiotics.

SARCOIDOSIS

Sarcoidosis is a multi-system chronic granulomatous disease of unknown etiology; which resembles another disease, the tuberculosis in many respects.

CLINICAL FEATURES

- The disease commonly affects the young adults between the ages of 20 to 40 years; it affects females more than the males.
- The body organs which are often involved in sarcoidosis include the lymph nodes, salivary glands, skin and bone, etc.

- Fever, malaise, dry cough, weight loss, chest pain and dyspnea etc. are the usual symptoms of the disease.
- There may be multiple, slow growing, red patches occurring on the skin, which tend to ulcerate.
- In sarcoidosis, granulomatous lesions may also arise in relation to other organs such as kidney, GI tract, heart, liver, spleen and nervous system, etc.

ORAL MANIFESTATIONS

- Involvement of the lacrimal glands may produce a typical 'keratoconjunctivitis' like symptoms.
- In the oral region, parotid gland is often (unilaterally or bilaterally) enlarged with concomitant facial nerve paralysis.
- There may be involvement of the minor salivary glands; which results in swelling and xerostomia.
- Occasionally small nodular submucosal growths over the soft palate, gingiva, floor of the mouth or cheek may be seen.
- Multiple erythematous nodules may develop over the cheek, labial mucosa and hard palate.
- In rare cases, central lesions in the maxilla, mandible or nasal bones may occur in sarcoidosis.

HISTOPATHOLOGY

In the orofacial region, biopsy samples are usually obtained from the minor salivary glands.

- The microscopic picture of sarcoidosis reveals multiple, circumscribed, non-caseating granulomas within the affected organ.
- The granulomas are often consisting of clustered epithelioid cells, lymphocytes and multiple multinucleated giant cells.
- The giant cells are either Langhan's type or foreign body type.
- The granulomas often contain star-shaped "**asteroid bodies**" or basophilic calcified "**Schaumann bodies**" (these are various inclusion bodies).

DIAGNOSIS

- Elevated serum angiotensin converting enzyme (ACE).
- In most of the cases, diagnosis of sarcoidosis is established by positive Kveim-siltzbach skin test.
- Chest X-rays reveal bilateral hilar lymphadenopathy.
- Jaw X-rays reveal ill-defined radiolucent lesions with erosion of the cortical bone.

TREATMENT

Treatment of sarcoidosis is often difficult, however, many lesions respond well to the antitubercular drugs.

LEPROSY

Leprosy is a chronic granulomatous infection caused by *Mycobacterium leprae* which primarily affects the skin and peripheral nerves.

This slightly contagious disease is broadly divided into four types-***tuberculoid leprosy, lepromatous leprosy, borderline leprosy and intermediate leprosy***. The disease progresses through the stages of–invasion, proliferation, ulceration and resolution through fibrosis.

CLINICAL FEATURES

- Multiple macules, papules or nodules develop over the facial skin.
- Enlargement of these facial lesions cause considerable distortion in the facial appearance (**leonine facies**).
- Dry, wrinkled and burn-out skin of the body with absence of sweating.
- Nose is very frequently damaged by the disease and it results in epistaxis, loss of nasal hard tissue with **collapse of the nasal bridge** and loss of sensation of smell.
- Facial and Trigeminal paralysis are common; which results in loss of light touch, temperature and pressure sensations.
- Loss of hair including those of the eyebrows and eye lashes.
- Difficulty in closing the eyes resulting in corneal ulceration, keratitis and occasional blindness.

Oral manifestations of leprosy

- In the oral cavity, the disease produces tumor-like lesions called "**lepromas**", which are found on the lips, gingiva, tongue, buccal mucosa, hard and soft palate, etc.
- Oral lesions appear as yellowish, soft or hard, sessile papules, which have a tendency to breakdown and ulcerate over time.
- Repeated ulcerations in the mouth and attempted healing every time thereafter lead to ugly scarring and loss of tissue.
- Ulcerations, necrosis and perforation of the palate are common.
- Fixation of the soft palate with loss of uvula is also seen in some cases.
- Difficulty in swallowing and regurgitation are commonly seen.
- Erosive lesions develop over the tongue followed by formation of large lobules; which gives a typical '**cobble-stone**' appearance of the tongue with loss of taste sensation.
- Lip lesions cause severe disfigurement with development of macrochelia.
- Chronic gingivitis and periodontitis frequently seen.
- Increased tendency for the development of candidiasis.
- Enamel hypoplasia of teeth with pinkish-red discoloration and pulpitis.
- Tapering of teeth, increased destruction of alveolar bone with loss of anterior teeth and premature loss of teeth (especially upper teeth).

HISTOPATHOLOGY

- Microscopically the lesion shows granulomatous nodules consisting of epithelioid cells, lymphocytes, Langhan's type giant cells and vacuolated macrophages called **"lepra cells"**.
- Nerves are infiltrated and destroyed.
- Acid fast bacilli may be seen within the nerves or within the macrophages.

DIAGNOSIS

By determination of acid fast bacilli (*M. leprae*) in the smear or in the tissue.

TREATMENT

Treatment is done by long-term chemotherapy.

TETANUS

Tetanus is a serious type of bacterial disease caused by the bacteria named *Clostridium tetani.* The microorganism releases exotoxins that affect motor neurons and results in severe muscle spasms.

PATHOGENESIS

- ***Clostridium tetani*** is a gram-positive, non-encapsulated, motile organism having terminally located spore, with a typical drumstick like appearance.
- Hot and damp climates with fertile soil rich in organic matter are favorable environment for the growth of these microorganisms.
- After introduction of the bacilli at the site of injury, tetanus can develop within few days to 2 months.
- In traumatized tissue the spores get converted into vegetative forms and during autolysis the vegetative form of the organism releases exotoxinsm, namely **tetanospasmin** and **tetanolysin.**
- The tetanospasmin affects brain, sympathetic nervous system, the skeletal muscle motor end plates and the spinal cord, etc.
- Initially tetanospasmin is bound to the peripheral nerves at the site of inoculation and then it is carried in a retrograde direction along the axons to the central nervous system.

CLINICAL FEATURES

- Clinical manifestations usually appear 2 weeks after the infection and are characterized by severe pain and stiffness of the facial and neck muscles, resulting in **trismus**.
- Masseter muscle spasms can be so strong that it can cause severe tongue bite or even fracture of the anterior teeth or jaw bones.
- Rigidity of the facial muscles may also produce a typical grinning expression called "**risus sardonicus**".
- In few cases, spasm of the entire body muscles produce "**opisthotonus**" and board-like regidity of the abdomen.
- Laryngospasm occurs when the patient tries to swallow saliva.

- Body temperature is increased due to increased metabolic rate.
- Spasm of the muscles of deglutition results in **dysphagia**.
- Airway obstruction often occurs due to spasm of the pharyngeal, intercostal and diaphragmatic muscles.
- Patients often exhibit restlessness and irritability.
- Acute, paroxysmal, incoordinated spasm of the muscles is an indicator of the moderate to severe form of the disease.
- Patients with tetanus **may die of anoxia** or due to pulmonary complications like—broncho-pneumonia and pulmonary embolism, etc.

Key points of tetanus

- Tetanus is a serious bacterial disease caused by *Clostridium tetani;* which releases exotoxins **tetanospasmin** and **tetanolysin.**
- These enzymes attack the motor neurons and results in severe muscle spasms in various vital organs.
- Clinically the disease causes severe pain and stiffness of the facial and neck muscles, resulting in **trismus**.
- Rigidity of the facial muscles may also produce a typical grinning expression called "**risus sardonicus**.
- Patients if left untreated often die of anoxia, broncho-pneumonia and pulmonary embolism, etc.

TREATMENT

By injection of tetanus antitoxin, along with antibiotics, anticonvulsants and surgical wound care.

MIDLINE LETHAL GRANULOMA

Midline lethal granuloma is a serious disease that involves the nasal cavity, maxilla, palate and nasopharynx, etc.

ETIOLOGY

Etiology of the disease is unknown, according to different investigators, midline lethal granuloma can be of infective origin or it may develop as an immunopathologic collagen disorder.

CLINICAL FEATURES

Age: Mainly adults.

PRESENTATION

- Midline lethal granuloma begins with **pain, stiffness in the nose and nonspecific ulceration over the palate or upper respiratory tract.**
- The condition does not respond to any treatment.
- The disease **progressively destroys the soft and hard palate and nose** by causing extensive necrosis with concomitant purulent exudation.
- **Perforation of the palate** is a very common feature of this disease.
- Erythematous, granular, tumor-like lesions may be seen on the gingiva and other parts of the oral mucosa.
- With time the **entire midface may be destroyed** with involvement of the orbit.
- The disease is often associated with granulomatous lesions of the kidney and lung.
- The patients often die due to exhaustion, hemorrhage, malnutrition and cachexia, etc.
- Clinically midline lethel granuloma often resembles a carcinoma but microscopically it appears as an innocuous, nonneoplastic lesion.

HISTOPATHOLOGY

Destruction of the normal osseous and soft tissues of the face with replacement by an inflamed granulation tissue. Infiltration by mononuclear cells and scattered eosinophils are often evident.

TREATMENT

High dose of radiation therapy is the treatment of choice along with antibiotics and immunosuppressant drugs.

WEGENER'S GRANULOMATOSIS

Wegener's granulomatosis is a rare disease with poorly understood pathogenesis (probably having some immunological basis). It is characterized by necrotizing vasculitis of the larynx, trachea, salivary glands, palate, etc. and is often associated with a fatal outcome.

CLINICAL FEATURES

- This potentially lethal disease often starts with rhinitis, sinusitis and nasal crusting, etc. with gradual destruction of the nasal septum.
- It often results in a "**saddle nose**" deformity.
- Persistent cough with hemoptysis and uremia is common.
- The oral lesions include generalized severe proliferative or hyperplastic gingivitis and ulceration of the other mucosal surfaces.
- The gingival lesions produce swelling with a granular surface; the color of the gingiva is either dusky red or bright red (strawberry gingiva).
- These gingival lesions can be either localized or diffuse; and they often resemble the pregnancy gingivitis.
- Failure of healing of the extraction wounds is an important characteristic of this disease.
- Wegener's granulomatosis frequently involves the internal organs, specifically the kidneys and the lungs.
- Death usually results from renal failure.

HISTOPATHOLOGY

Microscopically the disease shows necrosis and granulomatous inflammation of the tissue; with scattered giant cells, vasculitis and destruction of the small arteries.

TREATMENT

The disease is responsive to steroid and cytotoxic drug therapy.

NOMA (CANCRUM ORIS)

Noma is a rapidly spreading and extremely severe gangrenous infection of the orofacial tissues; which is characterized by perforation and destruction of large areas of the face. The disease is often fatal if not properly treated or left untreated.

ETIOLOGY

The disease probably develops as a result of infection caused by fusospirochetal organisms, in immunocompromised patients. The microorganisms include—*Fusobacterium necrophorum*, *F. nucleatum* and *Prevotella intermedia*, etc. However, other organisms which often complicate the disease process include *Saureus* and *Borrelia vincentii*, etc .

Predisposing factor in noma

- Protein-energy malnutrition due to extreme poverty
- Exanthematous diseases like-typhoid fever, leukemia, etc.
- Stress
- Vitamin deficiency
- Poor oral and general hygiene
- Depressed immunity including AIDS
- Chemotherapy

CLINICAL FEATURES

- The disease is more prevalent in children between the ages of 1 to 10 years; it was very common among starving prisoners (particularly children) in the Nazi concentration camps during the Second World War
- In the initial stage of the disease there is formation of a painful, red, indurated papule over the gingiva, at this stage it looks like typical ANUG with extreme edema.
- It is soon followed by the formation of an ulcer over the gingiva, which spreads rapidly on both facial and lingual directions and exposes the underlying bone.
- The ulcer rapidly extends to the mucosal surfaces of the lips and cheek; and this condition is known as '**necrotizing ulcerative mucositis'**.
- Within a few days a small, dark, reddish-purple area appears on the skin over the cheek, which rapidly undergoes gangrenous necrosis.
- As the tissue becomes ischemic, the overlying facial skin appears blue-black.
- Later on, **a large hole of few inches size develops on the cheek** due to sloughing of the tissue; which exposes the interior of the mouth (teeth and bone) with severe disfigurement.
- Severe sore mouth, increased salivation and diffuse edema of the face occur; along with extreme foul smell.
- Lesions may be unilateral or bilateral and it involves both the jaws.
- Spread of infection into the jawbone results in osteomyelitis; which results in sequestration of bone with exfoliations of teeth.

- Noma eventually creates a large gaping facial defect in the mouth and death may occur due to aspiration pneumonia, severe diarrhea or dehydration, etc.

TREATMENT

Treatment is done by antibiotic therapy along with nutritional supplements.

PYOGENIC GRANULOMA

Pyogenic granuloma represents an over-exuberant tissue reaction to some known stimuli or injuries. The term pyogenic granuloma is somewhat a misnomer since the condition is not associated with pus formation.

CLINICAL FEATURES

Age: The disease occurs at an early age.

Sex: It is seen more frequently among females.

Site: Pyogenic granuloma mostly occurs in relation to the gingiva, however on rare occasions other mucosal sites may be involved.

PRESENTATION

- The lesion appears as a small, pedunculated or sessile, painless, soft, lobulated growth on the gingiva (Figs 8.8 and 8.9).
- Labial surface of the gingiva is more frequently affected than the lingual surface.
- The lesion is often ulcerated and bleeds profusely, either upon provocation or spontaneously.

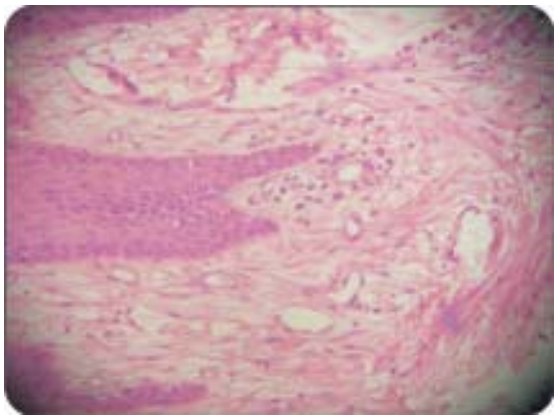


Fig. 8.7: Photomicrograph of pyogenic granuloma

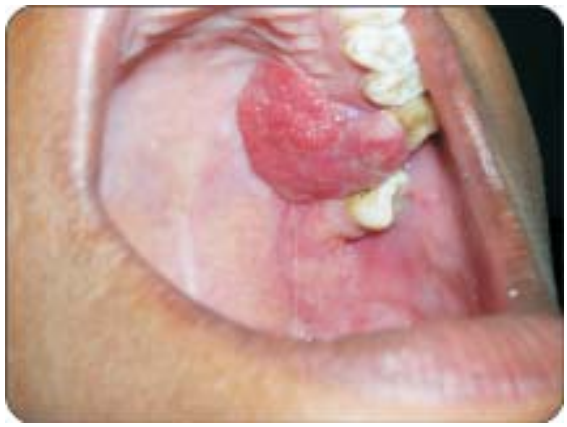


Fig. 8.8: Pyogenic granuloma

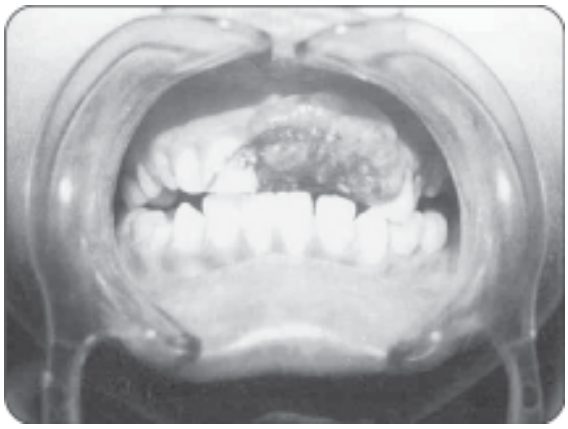


Fig. 8.9: Pyogenic granuloma developing from maxillary gingiva

- The ulcreated area of the lesion is often covered by a yellow fibrinous membrane.
- The rate of growth of the lesion is very rapid and its maximum size could be upto 1 cm in diameter (Fig. 8.10).
- If pyogenic granuloma is left untreated, the lesion undergoes fibrosis due to decreased vascularity and in such cases it appears small, firm with little tendency to bleed. This lesion is called "fibro-epithelial polyp" (Figs 8.11 to 8.12).
- Sometimes a lesion similar to the pyogenic granuloma appears on the gingival tissue of pregnant women, which is known as "pregnancy tumor".

HISTOPATHOLOGY (FIGS 8.7, 8.13A AND B)

- Histologically, the lesion is composed of lobular masses of hyperplastic granulation

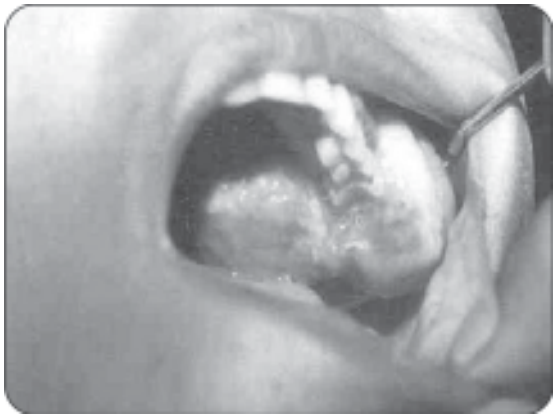


Fig. 8.10: Pyogenic granuloma of a very large size

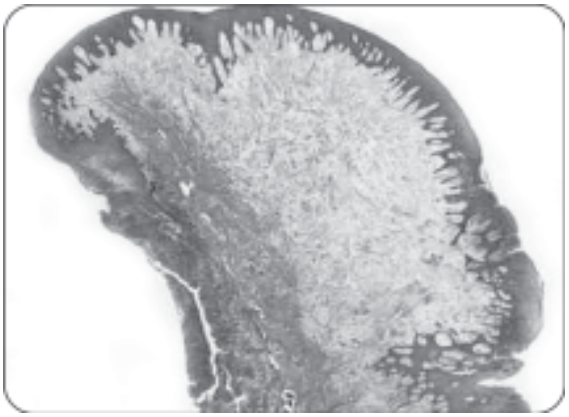


Fig. 8.13A: Photomicrograph of fibroepithelial polyp

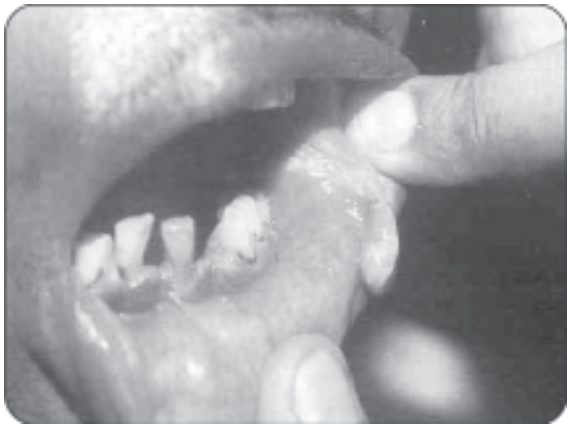


Fig. 8.11: Fibroepithelial polyp of the lip

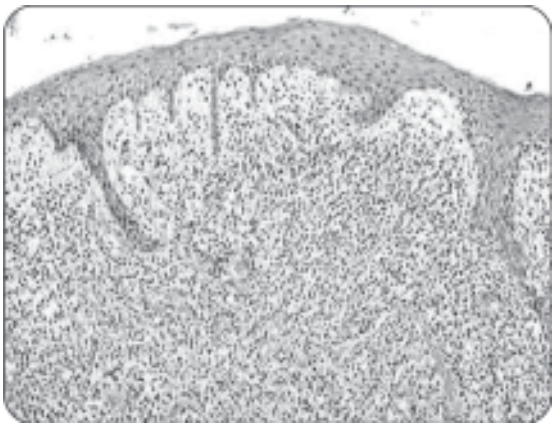


Fig. 8.13B: Photomicrograph of pyogenic granuloma

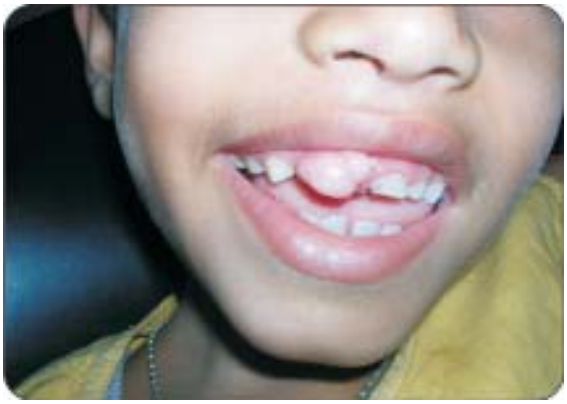


Fig. 8.12: Fibroepithelial polyp

Fig. 8.14: X-ray shows peripheral bone destruction in pyogenic granuloma

tissue, containing multiple proliferating fibroblasts, many blood capillaries and variable number of chronic inflammatory cells.

- The lesion is a vascular one and it occurs due to proliferation of the endothelial cells.
- The overlying epithelium is thin and ulcerated, and in most of the cases the underlying connective tissue shows **intercellular edema**.
- Areas of hemorrhage and hemosiderine pigmentation is often seen within the connective tissue stroma.

TREATMENT

Pyogenic granuloma is treated by surgical excision.

VIRAL INFECTIONS

A virus is an **obligatory intracellular parasite**, which codes the host cell by contributing its own nucleic acids to produce a new generation of virions.

The virus consists of a central core of either DNA or RNA, which is surrounded by a shell or capsid that is made up of protein. In some cases, there is another outer envelope composed of glycoproteins and lipids.

When a virus comes in contact with a susceptible cell, it adsorbs on to the cell surface at a "specific receptor site" which determines the susceptibility of the host cell to the particular virus. Subsequently, the virus penetrates the cell wall by a process of pinocytosis, during which the lipid envelope and the protein capsid is stripped off, to release the viral nucleic acid. The latter is than passed into the nucleus of the host cell and is coded for producing viral products.

Within the host cell, the virus may produce the following functions:

- It may influence the host cell to produce more and more virions, which come out of the cell by rupturing it and then they go on to attack the new cells.
- It can influence the host cell's own mitotic activity and cause increased host cell multiplication, eventually leading to the development of a neoplasm.
- In some instances, the viral infections may induce immunological changes either by causing direct infections to the cells of the immune system or by stimulating the production of antibodies, which may potentiate autoimmune reactions.

The methods of controlling the viral infection by killing these organisms is very difficult, because these organisms are always living intracellularly and one cannot kill them without killing the host cell itself. Another problem is difficulty in their identification inside the host cells, as the viruses are always changing their protein code, so that they can hide easily without being noticed by the body's own immuno surveillance network.

ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

AIDS is a predominantly lethal type of viral infection, caused by human immunodeficiency virus (HIV) and is characterized by severe depletion of T4 lymphocytes in the body, with associated opportunistic infection of several varieties.

ETIOLOGY AND PATHOGENESIS

- The etiologic agent for AIDS is the HIV virus (type-I and type-II), which are nononcogenic "lentiviruses" of the human "retrovirus" family.
- When the HIV virus enters into the body, it primarily infects the CD4+T lymphocytes (the helper or inducer cells of the cell-medited immune system) by binding on to the specific CD4+receptor site on these cell surfaces.
- Following this, the HIV genomic RNA is uncoated and is internalized inside the CD4+T lymphocyte. Once the virus is within the host cell, it causes replication of its single stranded viral RNA into double stranded DNA by the process of "reverse transcription" which is helped by the enzyme called"reverse transcriptase".
- The newly formed viral DNA enters into the host cell nucleus and becomes spliced into the genome of the host cell. Periodically this proviral DNA is transcribed to RNA, where it directs the metabolic activity of the host cell to synthesize more HIV RNA genome, the retroviral structural proteins like— nef, tat and rev, etc.
- Ultimately the involved cells die and more and more attack to the newer cells leads to quantitative and qualitative deficiency of CD4+ lymphocytes in the blood. CD4+T cell count is the vital marker to express the level of body immunity of the infected individual.
- The normal count of CD4+ T cells is 500 to 1500/cubic mm of blood; if the count falls below 350/cubic mm, the situation should be considered serious.

- The process eventually results in the depletion of CD4+T cells even below a critical level (less than 200 cells/cubic mm), which causes severe lack of protection of the body from infections (depressed cell mediated immunity).
- Viral load (VL) is also an important parameter that indicates the disease progression; when the viral load is 5,50,000 copies per ml of blood, it is the time to start the treatment.
- The normal ratio of CD4 helper lymphocytes and the CD8 suppressor lymphocytes is 2:1 but it is severely depleted in AIDS. Depletion of CD4 cells results in loss of production of noncellular components of the defense system of the body, e.g. interleukin-2, interferon, macrophage activating factor and factor that stimulates the production of natural killer cells, etc.
- Moreover, these infected CD4 T-cells also exhibit variable types of dysfunctions like—abnormal antigen recognition, aberrant cell triggering and loss of function of the memory cells, etc.
- As the disease progresses, the HIV specific cytotoxic CD8 T-cells also loose their functional capacity. Besides T-cells, the B-lymphocytes also exhibit the features of dysfunctions and they produce compensatory hypergamma-globulinemia that may lead to several auto-immune reactions.
- Thus the HIV infection destroys the entire immune system of the body (both cell-mediated and humoral), which results in a variety of opportunistic infections as well as the development of many other pathologies, e.g. malignancies, etc. and the patient often fails to survive.

MODE OF TRANSMISSION OF HIV

Sexual transmission: It is the major mode of transmission of the virus and the infection can occur in both homosexuals and heterosexuals if one of the partners is suffering from the disease. The risk of infection by this route increases if the patient is already having a pre-existing sexually transmitted disease like syphilis, gonorrhea, etc.

Blood or blood products: A person may be infected with HIV if he/she receives blood or blood products from an infected donor or if the transfusion kit used, is somehow contaminated by the virus.

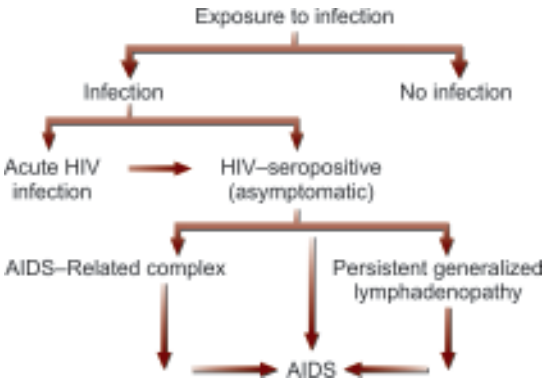
Injection drug users: Risk of HIV infection is more among the injection drug users because of sharing the contaminated needles by many people in the group.

Occupational transmission: HIV transmission following skin puncture by needle or sharp instrument that was contaminated earlier by the virus, is a common risk for the doctors and other related professionals.

Maternal-fetal/infant transmission: HIV can be transmitted from an infected mother to the fetus during pregnancy or to the infant during delivery.

Other body fluids: The risk of transmission of the virus via the saliva, milk or tears, etc. from the infected person is reported, however, insects do not transmit the virus from one person to other.

CONSEQUENCES OF HIV INFECTION



CLINICAL SPECTRUM OF AIDS

Clinical manifestations of AIDS may be classified as follows—

Group-I: Acute Infections

Infectious mononucleosis.
Hepatitis.
Meningitis.
Meningoencephalitis.

Group-II: Chronic Asymptomatic Infections

It is the potentially most dangerous group and seropositive individuals who are apparently

Key points of oral manifestations of AIDS	
Oral candidiasis	• Erythematous, hyperplastic and pseudomembranous (the last one is most common among children). • Esophageal candidiasis • Angular cheilitis
Viral infections of oral mucosa	• Herpes simplex and herpes zoster-causing atypical and chronic ulcers. • Epstein-barr virus—Causing hairy leukoplakia • Papilloma virus—Causing proliferative lesions, e.g. verruca vulgaris, condyloma acuminatum and focal dermal hyperplasia. • Cytomegalovirus infection
Bacterial infections	• Tuberculous ulcers • Osteomyelitis of the jaw • Submandibular cellulitis
Deep fungal infections (ulcers and proliferative lesions)	• Coccidioidomycosis • Histoplasmosis • Toxoplasmosis
Hairy leukoplakia	
Gingivitis and periodontitis	• HIV- gingivitis • HIV- rapidly progressive destructive periodontitis • Necrotizing ulcerative gingivitis • Exacerbation of atypical periodontitis • Halitosis
Persistent generalized lymphadenopathy	
Tumors	• Kaposi's sarcoma—flat or nodular purplish lesion (mostly on the palate • Non-Hodgkin's lymphoma • Burkitt's lymphoma • Squamous cell carcinoma
Stomatitis	• Progressive necrotizing ucerations of the oral mucosa • Recurrent major aphthous ulcers • Atypical oropharyngeal ulcers • Acute nonspecific ulcers of oral mucosa
Salivary gland disease	• Parotitis and enlarged parotids • Sjogren's syndrome • Xerostomia • Unilateral or bilateral swelling of other salivary glands • Cystic benign lymphoepithelial lesions
Neurological disorders	• Facial palsy • Trigeminal neuropathy • Paresthesia and hyperesthesia
Autoimmune disease	• Thrombocytopenic purpura • Systemic lupus erythematosus
Miscellaneous diseases	• Sinusitis • Vesiculobullous lesions • Bacillary angiomatosis • Adissonian pigmentations • Delayed wound healing

healthy but capable of infecting others. Patient may have enlarged axillary glands as well as hematological and immunological abnormalities.

Group-III: Persistent Generalized Lymphadenopathy (PGL)

Unexplained lymphadenopathy in 2 or more extrainguinal sites persisting for more than 3 months in the absence of any concurrent illness or causative drugs.

Group-IV

A. ***Constitutional diseases (AIDS-related complex):*** It is characterized by prolonged unexplained pyrexia, chronic persistent diarrhea, weight loss more than 10% of the previous normal body weight.

B. ***Neurologic diseases:***
- Progressive dementia.
- Meningoencephalitis.

C. ***Opportunistic infections:***

a. ***Pneumonia or sinusitis:***
- Pneumocystis carinii pneumonia
- Cryptococcosis
- Mucormycosis
- Toxoplasmosis
- *Pseudomonas aeruginosa*
- Tuberculosis
- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*

b. ***Gastrointestinal infections (diarrhea):***
- Cryptosporidiosis
- Isosporiasis
- *Giardia*

c. ***Mucocutaneous infections*:**
- Herpes simplex
- Herpes zoster
- Candidiasis
- *Staphylococcus aureus*
- Histoplasmosis.

d. ***Meningitis and encephalitis:***
- JC-virus (Jamestown Canyon virus)
- Toxoplasmosis.

e. ***Disseminated infections:***
- Atypical mycobacteriasis
- Cryptococcosis
- Histoplasmosis

D. ***Specified Secondary Neoplasms***
- Kaposi's Sarcoma
- Lymphoma (Immunoblastic)
- Burkitt's lymphoma
- Squamous cell carcinoma of mouth, anus or rectum
- Leukemia.

E. ***Others:***
- Encephalopathy
- Purpura
- Lupus erythematosus
- Adisson's disease
- Seborrheic dermatitis
- Thrombocytopenia.

ORAL MANIFESTATIONS OF AIDS (DETAILED)

The oral manifestations of AIDS are many and the important among those are as follows:
- Candidiasis—Erythematous, hyperplastic and pseudomembranous (the last one is most common among children).
- Esophageal candidiasis
- Herpes simplex and herpes zoster
- Halitosis
- Hairly leuloplakia—Soft painless plaque on the lateral border of tongue with a vertically corrugated surface (Fig. 8.14A).
- Persistent cervical lymphadenopathy
- Kaposi's sarcoma—One or more, bluish swelling with or without ulceration on the gingiva and palate (Figs 8.15A and B).

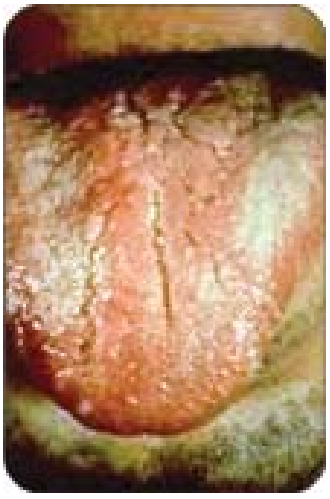


Fig. 8.14A: Oral hairy leukoplakia in aids

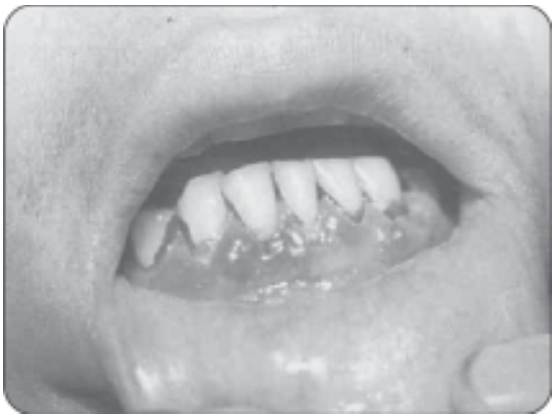


Fig. 8.15A: Kaposi's sarcoma of the gingiva

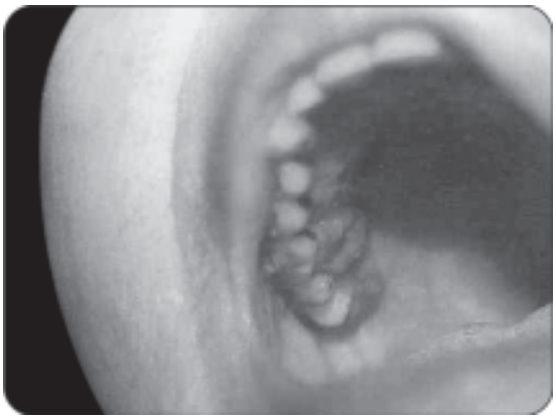


Fig. 8.15B: Kaposi's sarcoma of the palate

- Angular cheilitis—Linear ulcers or fissures at the angle of mouth
- HIV-gingivitis: **Linear gingival erythema**; which is a fiery red band along the gingival margin and attached gingiva with profuse bleeding; sometimes resembles desquamative gingivitis.
- Necrotizing ulcerative gingivitis—Destruction of interdental papilla
- Rapidly progressing HIV–Periodontitis—advanced necrotic destruction of the periodontium, rapid bone loss, loss of periodontal ligament and sequestration.
- Necrotizing stomatitis—Oral ulcerations over the gingiva, hard palate and the edges of the lips.
- Major aphthous ulcers—Single or multiple, recurrent ulcers with whitish pseudomembrane and surrounding erythematous halo. Mostly seen over the cheek, soft palate, tongue and tonsillar areas.
- Vasiculobullous lesions
- Parotitis and enlarged parotids (unilateral or bilateral diffuse swelling)
- Unilateral or bilateral swelling of the salivary glands
- Atypical oropharyngeal ulcerations
- Coccidioidomycosis
- Molluscum contagiosum infection
- Toxoplasmosis and histoplasmosis
- Purpura
- Osteomyelitis of the jaw
- Tuberculous or histoplasmal ulcers
- Acute nonspecific ulcers
- Bacillary angiomatosis
- Condyloma acuminatum
- Addisonian hyperpigmentations of the oral mucosa
- Cytomegalovirus infection
- Human papilloma virus infection—Development of oral squamous papilloma
- Verruca vulgaris
- Herpes zoster virus infection
- Epstein-Barr virus infection
- Squamous cell carcinoma
- Lymphoma (Non-Hodgkin's lymphoma)
- Xerostomia
- Cystic benign lymphoepithelial lesions in salivary gland
- Neurological abnormality (facial palsy and trigeminal neuropathy)
- Submandibular cellulitis
- Delayed wound healing.

DIAGNOSIS OF AIDS

- Clinical—According to WHO recommendations, existence of at least 2 major signs, e.g. chronic persistent diarrhea (more than one month), generalized pruritic dermatitis, recurrent herpes zoster, esophageal candidiasis, chronic progressive and disseminated HSV infection, Kaposi's sarcoma or cryptococcal meningitis suggests the diagnosis of AIDS.
- Western blot analysis
- Enzyme-linked immunosorbent assay (ELISA)
- Polymerase chain reaction (PCR)
- Detection of antibody to the virus in serum
- Detection of virus from the peripheral blood
- Lymphopenia

- Reversal of normal ratio of T helper to T suppressor lymphocytes
- Hypergammaglobulinemia
- Viral culture
- P24 antigen detection
- Immunological tests—CD4+ T cell count, CD4+T cell% and CD4/CD8 ratio tests.
- Salivary tests to capture the HIV IgG antibody.

TREATMENT OF AIDS

HIV Anti-Retroviral Treatment (HAART) is the most standard and accepted mode of treatment in AIDS; in which 3 to 4 anti-retroviral drugs are used at a time. The common anti-retroviral drugs used in India are as follows:

- **Nucleoside Reverse Transcriptase Inhibitor (NRTI)**—Consisting of Zidovudine(AZT/ZDV), Stavudine(d4T), Lamivudine(3TC), Emtricitabine(FTC), Didanosine (DDI), Zalcitabane(ddC), Abacavir (ABC) and Tenofovir (TDF).
- **Non Nucleoside Reverse Transcriptase Inhibitor (NNRTI)**—A group consisting of Nevirapine (NVP), Efavirenz (EFV)
- **Protease Inhibitor (PI)**—Consists of Saquinavir (SQV), Nelfinavir (NFV), Indinavir (IDV), Lopinavir (LPV), Ritonavir (RTV), Atazanavir.

Recommended combination regimens
2 NRTIs + 1 NNRTI or 2 NRTIs + 1 PI or 2 NRTIs + 2 PIs

Administration of multiple drugs significantly prevents the development of resistant strains. Basically the disease is incurable so far and stress is given mostly to prevent or cure the secondary infections. Zidovudine may prolong and improve the quality of life in those with active AIDS. **Cotrimoxazole** is given for *Pneumocystis carinii* pneumonia and **fluconazole** is given for candidiasis.

HERPES VIRUS INFECTIONS

The term herpes is derived from the Greek word *herpein* which means to "creep or crawl" and it was used to describe the spreading nature of the skin lesions caused by this group of viruses.

Herpes virus family comprises of about 50 different DNA viruses and man is the host and exclusive reservoir of four important members of this group namely:

- Herpes simplex virus (HSV)—type I and type II
- Varicella-zoster virus
- Human cytomegalovirus
- Epstein-Barr virus

HERPES SIMPLEX VIRUS TYPE-I DISEASES

It is responsible for a number of conditions such as:

- Acute herpetic gingivostomatitis
- Herpetic eczema
- Keratoconjunctivitis
- Meningoencephalitis
- Herpes labialis
- Genital herpes (occasional).

HERPES SIMPLEX VIRUS TYPE-II DISEASES

This virus is responsible for the following diseases:

- Genital herpes (very common)
- Neonatal herpes
- Uterocervical cancer
- Oral herpes (rare).

VARICELLA-ZOSTER VIRUS DISEASES

This virus causes usually two diseases namely:

- Chickenpox
- Herpes zoster or shingles.

HUMAN CYTOMEGALOVIRUS DISEASES

It produces the following diseases:

- Salivary gland disease
- Kaposi's sarcoma.

EPSTEIN-BARR VIRUS DISEASES

This virus is responsible for a variety of conditions like:

- Infectious mononucleosis
- Burkitt's lymphoma
- Nasopharyngeal carcinoma
- Hairy leukoplakia.

HERPES SIMPLEX VIRUS TYPE–I INFECTIONS

PRIMARY ACUTE HERPETIC GINGIVOSTOMATITIS

This acute infection of the oral cavity is caused by the HSV type I and the disease usually occurs during childhood, between 3 to 5 years of age. The disease is not seen in children below 12 months of age (due to passive immunity coming through the maternal antibodies). The disease is transmitted by close contact with an infected individual.

Clinical Features

- The disease is usually preceded by some other disease conditions, e.g. upper respiratory tract infection and fever.
- The initial generalized signs and symptoms of the disease include: headache, nausea, anorexia, lack of tactile or sensory perceptions of the affected area, etc.
- These are followed by features like—**sore mouth, irritability, drooling, refusal of food, bilateral painful cervical lymphadenopathy and fever (103 to 105 degree F), etc.**
- The oral symptoms include reddening of the oral mucosa followed by **numerous small vesicle** formations. The vesicles are **dome-shaped or pin-head type** and measure about 2 to 3 millimeters in diameter.
- Both movable and attached mucosa can be affected and the common sites include the gingiva, hard palate, dorsum of the tongue, lips, vermillion border, perioral skin and nasopharynx, etc. (Figs 8.16 to 8.19).
- The vesicles usually contain clear fluid and they rupture to leave multiple, small, circular, punctate, shallow painful ulcers. Ulcers are sharply defined with red margins and have yellowish or grayish floor.
- Adjacent tiny ulcers coalesce to form diffuse, large, whitish ulcers which are surrounded by a red ring of inflammation **(halo).** These ulcers often cause pain and difficulty in taking food.
- The gingival margins are particularly red, swollen and painful; occasionally there may be presence of punched-out erosions on the free gingival margin (mostly on the facial aspect).
- In case of HIV infection, these herpetic ulcers will be larger, deeper, more painful and more persistent in nature.
- The ulcers may become secondarily infected and it is often covered by a purulent membrane.

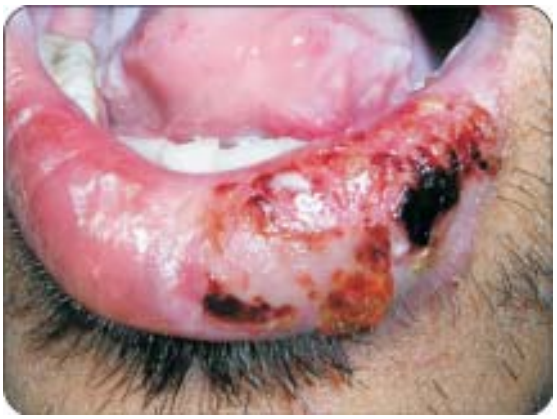


Fig. 8.16: Herpetic simplex stomatitis-I

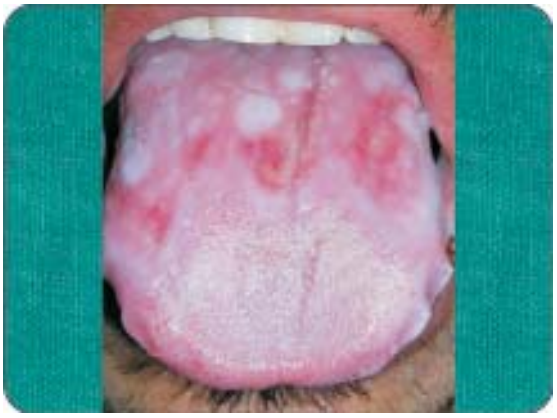


Fig. 8.17: Herpetic simplex stomatitis-II

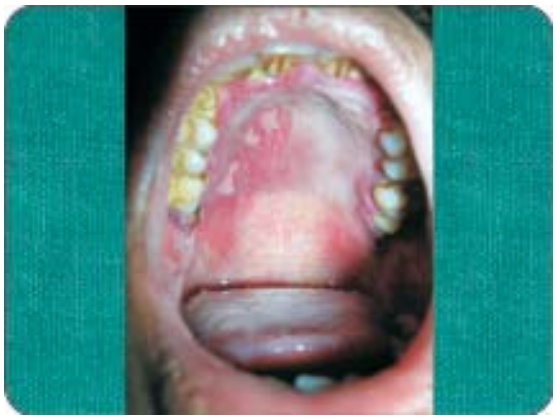


Fig. 8.18: Herpetic stomatitis

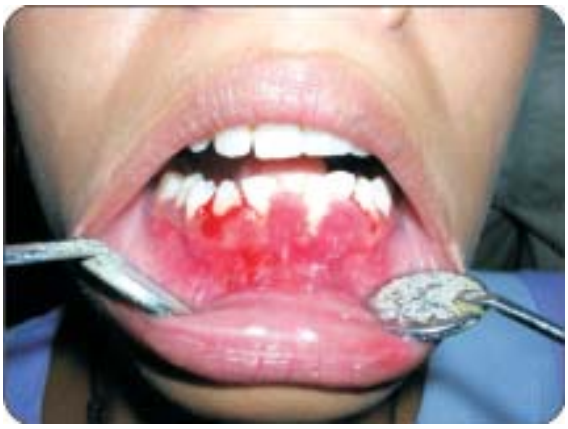


Fig. 8.19: Herpetic periodontitis

- Healing starts in about 3 days and the lesion is completely healed up within 7 to 14 days without any scar formation.
- Patient also suffers from myalgia or muscle soreness, difficulty in mastication and difficulty in swallowing.
- Primary HSV infections in adults produce pharyngotonsillitis characterized by numerous vesicles on the tonsillar area and posterior pharynx with subsequent ulcerations.

Histopathology

Acute herpetic gingivostomatitis histologically produces the following features:

- Formation of sharply defined vesicles in the superficial part of the keratinized epithelium.
- Ballooning degeneration of the prickle cells, with intranuclear inclusion body and marginated chromatin.
- Multiple multinucleated syncytial giant cells are occasionally present in the lesion (these are formed by fusion of adjacent degenerated prickle cells).

Differential Diagnosis

- Erythema multiforme
- Pemphigus
- Pemphigoid
- Chickenpox
- Allergic dermatitis

Key points of primary acute herpetic gingivostomatitis

- This is one of the commonest viral infections caused by Herpes simplex virus Type I and it predominantly affects the children.
- The disease starts with headache, nausea, anorexia, lack of tactile or sensory perceptions of the affected area, etc.
- The initial symptoms are followed by features like — sore mouth, irritability, refusal of food, painful cervical lymphadenopathy and fever (103 to 105° F), etc.
- Oral symptoms of acute herpetic gingiviostomatitis include reddening of oral mucosa with formation of numerous small, dome-shaped vesicles.
- These vesicles develop over the movable as well as attached mucosa on the gingiva, hard palate, dorsum of the tongue, lips, vermillion border, perioral skin and nasopharynx, etc
- The vesicles usually contain clear fluid and they rupture soon to leave multiple, sharply defined, small, circular, shallow painful ulcers.
- Several ulcers may coalesce to form diffuse, large, whitish ulcers which are surrounded by a red ring of inflammation **(halo).**
- Histologically, the disease shows ballooning degeneration of the prickle cells, with intranuclear inclusion body and marginated chromatin.
- It is a self limiting disease and the lesions healed up completely within 7 to 14 days without any scar formation.

Diagnosis

Cytologic smear: Cytologic examination of vesicular fluid reveals the presence of inclusion bodies and ballooning degeneration of infected cells.

Biopsy: See the histopathological features.

Culture: Aspiration of vesicle contents and subsequent tissue culture produces change in the culture cells in 24 hours.

Fluorescent antibody test: HSV specific antibodies are labeled with fluorescent dye and seen microscopically.

Serology: Examination of blood (serum) for detection of HSV specific antibodies.

TREATMENT

In acute herpetic gingivostomatitis, only the palliative treatment is done (e.g. antibiotics are given to prevent secondary infections and antipyretics are given to control fever). Acyclovir shortens the recovery period of primary herpetic gingivostomatitis.

RECURRENT HERPETIC INFECTIONS

After the primary infection is over, the herpes virus retreats to the trigeminal ganglion where it lies dormant in a latent form. Later on, under some appropriate stimulations the virus becomes reactivated once again and it proceeds from the ganglion and moves centrifugally down the axon of the sensory nerve to the epithelium. The virus then produces secondary herpetic lesions over the lips, palate and gingiva, etc.

Factors causing stimulation or reactivation of the virus:

- Emotional stress
- Trauma
- Gastric upset
- Common cold
- Fever
- Menstrual cycle
- Immunosuppression
- Exposure to sunlight
- Radiations.

Clinical Features

- Recurrent infection by HSV 1 most frequently affects the vermillion border of the lips or skin adjacent to the lips; these lesions are commonly known as 'herpes labialis' or "cold sores".
- The lesion starts with pain, paresthesia and burning or itching sensation over the lips; with reddening of the mucosa.
- Sometimes the disease spreads to the palate and gingiva as well.
- Within 24 to 40 hours, clusters of fluid filled vesicles appear in these areas, which rupture soon and form multiple ulcers.
- The lesions begin to dry and heal up finally within 7 to 10 days without any scar formation.

HERPETIC ECZEMA

Herpetic eczema is an uncommon infection caused by HSV type-I virus and the disease consists of an epidermal form of lesion superimposed upon a preexisting disease like eczema, seborrheic dermatitis, impetigo or scabies, etc. The lesion is characterized by diffuse, vesicular eruptions in a typical umbilicated pattern and it commonly involves the children. The disease is often associated with high fever and other systemic manifestations.

KERATOCONJUNCTIVITIS

This eye lesion caused by HSV type-I virus presents severe swelling and congestion of the palpebral conjunctiva with or without corneal ulceration and keratitis. The initial lesion heals up rapidly, but recurrent attacks may cause serious corneal scarring which may ultimately lead to blindness.

MENINGOENCEPHALITIS

Meningoencephalitis is a serious form of HSV type-I infection of the brain and it is characterized by fever, headache, convulsions, paralysis of different muscle groups and even death.

HERPES SIMPLEX VIRUS TYPE-II INFECTIONS

GENITAL HERPES

The HSV type-II viruses are commonly found in the genitalia, and they often produce vesicular lesions in the genital mucosa of both sexes along with fever, and inguinal lymphadenopathy. Genital herpes is a somewhat more virulent infection than the oral herpes and is more significantly associated with the development of uterocervical cancer in females. However due to the altered sexual practices in recent times, the HSV-II virus may sometimes be transported in the oral cavity where these viruses may produce oral herpes as well.

NEONATAL HERPES

The neonatal herpes is an uncommon disease in which, the newborn infant acquires the HSV

type-II infection during the passage through the birth canal of the mother suffering from herpetic vulvovaginitis. The disease usually manifests in the fourth to seventh day of life, and it exhibits widespread signs and symptoms which eventually cause death of the infant in most cases or cause severe neurologic abnormalities in those who survive.

VARICELLA-ZOSTER VIRUS INFECTIONS

CHICKENPOX

Chickenpox is the primary infection caused by varicella-zoster virus and it is characterized by a minor self-limiting disease, which usually affects children and on rare occasions, nonimmune adults.

Clinical Features

- The disease begins with fever, headache, anorexia, nausea, vomiting, myalgia, sore throat, malaise, lung congestion and headache, etc.
- These are followed by a papular rash first appearing over the trunk and then rapidly spreading to face and limbs.
- After 3 to 4 days, unusual sequences of macules, vesicles, ulcerations and scabbing of the skin and oral mucosa are seen.
- The individual vesicle appears as **'dew drop' on rose petals** and is often surrounded by a zone of erythema at the periphery.
- The oral lesions often precede the skin lesions and produce vesicles and ulcerations which are similar to those of the skin. The oral lesions mostly develop over the palate, buccal mucosa and gingiva, etc.
- Following rupture of the oral vesicles, there is often formation of aphthous–like ulcers in the oral mucosa which are not painful.
- The infection subsides within a few days, but it may sometime produce complications like meningitis and pneumonia, etc. in children and in immunosuppressed adults.
- Occasionally, skin lesions become secondarily infected and these lesions heal with formation of a depressed scar (pock).

Diagnosis

The diagnosis is made on the basis of clinical findings and by the detection of virus specific antibodies in the serum.

Treatment

Only palliative treatment is given, which includes antibiotics, antipyretics and vitamins, etc.

HERPES-ZOSTER (SHINGLES)

Definition

Herpes Zoster is a recurrent regional infection caused by the Herpes Zoster virus and is characterized by vesicular eruptions over the skin and mucous membrane in a distinctively unilateral pattern.

Pathogenesis

After producing chickenpox, the V-Z virus **remains dormant in the trigeminal ganglion** for decades. The virus may become reactivated following stress, trauma, malnutrition and immunosuppression, etc. Moreover these lesions also frequently develop among patients with organ transplant, HIV infection and Hodgkin's, etc. Following their reactivation the virus travel along the first, second and third branch of the trigeminal nerve and produce the disease called herpes-zoster or shingles in the sensory dermatome.

Exactly a similar mode of action is seen in case of infections caused by the poliomyelitis virus; however, the basic difference between the herpes-zoster and the poliomyelitis virus infection is that the later affects the motor neurons whereas the V-Z virus affects the sensory neurons.

Clinical Features (Figs 8.20 to 8.22)

- The herpes zoster occurs in the fifth, sixth and seventh decade of life; the disease occasionally attacks even children.
- The disease begins with fever, malaise, headache and painful lymphadenopathy, etc.
- Severe pain, irritation or burning sensation develops in the dermatome along the course of the involved sensory nerve.

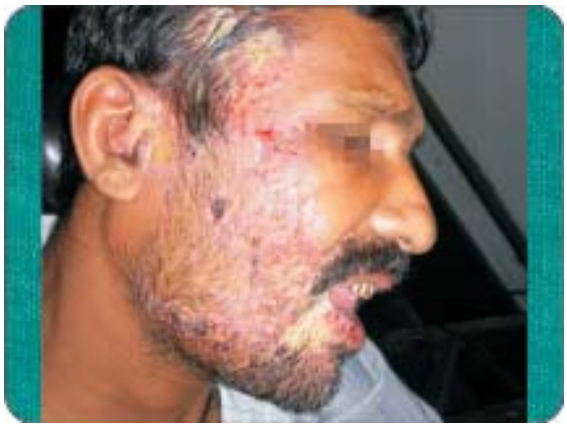


Fig. 8.20: Herpes zoster

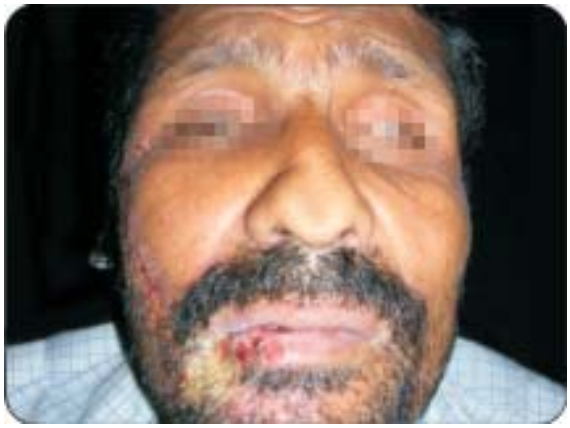


Fig. 8.21: Herpes zoster

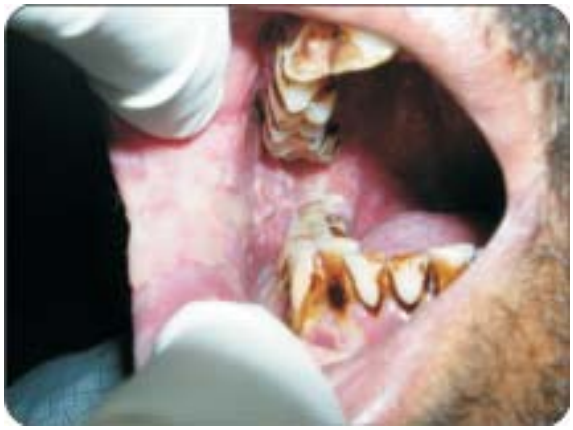


Fig. 8.22: Herpes zoster

- The first branch of the trigeminal nerve is most commonly affected and the disease beside affecting the first branch, may also involve the following other branches like:
  - Nasociliary nerve—Causing herpetic keratitis.
  - Ciliary nerve—Causing Argyll Robertson pupil.
  - Facial nerve—Causing Ramsay Hunt syndrome.
- After the prodromal phase of **intense pain**, the disease produces **clusters of vesicles over the skin and oral mucosa; which characteristically develop on one side of the face up to the midline.**
- The lesion usually develops and spreads along the distribution of the sensory nerve unilaterally on one side of the face, while the other side of the face remains completely free of symptoms.
- Within the oral cavity the vesicles also develop unilaterally over the buccal mucosa, soft palate and tongue, etc. and cause stinging pain, paresthesia and severe stomatitis.
- In due course of time the fragile vesicular lesions of the skin and the oral mucosa rupture and they leave painful, '**crateriform**' ulcers.
- The ulcers eventually heal up in a few days time without scar formation.

Key points of herpes-zoster

- Herpes-zoster is a recurrent viral infection caused by the Herpes zoster virus.
- It causes severe pain and burning sensations in the dermatome along the course of sensory nerve; (fifth cranial nerve is more frequently affected).
- The disease begins with fever, malaise, headache and painful lymphadenopathy, etc.
- These are followed by intense pain with development of clusters of vesicles over the skin and oral mucosa.
- The painful vesicles characteristically develop unilaterally on one side of the face up to the midline; the other side of the face remains completely free of symptoms.
- The vesicles also develop unilaterally inside the oral cavity, which cause stinging pain, paresthesia and severe stomatitis, etc.
- Herpes-zoster histologically presents swelling of the infected epithelial cell due to intracellular edema (ballooning degeneration) and margination of the nuclear chromatin.
- Treatment is done by antiviral drugs and antibiotics to prevent secondary infections.

- In herpes zoster, the neuralgic pain in the oral cavity often simulates "toothache". Paralysis of the facial nerve is also sometimes reported in association with Herpes zoster.
- The pain may persist long after the lesions have healed up and this condition is often known as post-herpetic neuralgia.
- In immunocompromised patients, herpes-zoster besides producing deeper and widespread lesions, becomes a chronic condition with persistent pain and occasional CNS involvement causing death.

Histopathology

- Herpes-zoster is histologically characterized by swelling of the infected epithelial cell cytoplasms due to intracellular edema **(ballooning degeneration).**
- Margination of the nuclear chromatin and formation of intranuclear inclusion bodies.
- Reticular degeneration of the epithelial cells along with presence of multiple multinucleated giant cells and polymorphonuclear neutrophilic infiltration in the connective tissue.

Diagnosis of Herpes-Zoster

Clinical: The disease is nearly always diagnosed on the basis of its very characteristic clinical findings, e.g.

- Unilateral distribution of the lesion.
- Early severe pain and paresthesia.
- Facial rash accompanying the stomatitis.

Histopathology: See histopathological features.

Serology: The disease is diagnosed by the detection of virus-specific antibodies in the serum.

Cytologic smear: Cytologic smears prepared from the vesicular fluid reveal inclusion bodies and ballooning degeneration of the infected cell.

Culture: Tissue culture using vesicular contents produces change in the culture cells which could be correlated with the clinical findings found in the primary infection.

Immunofluorescence: HZV specific antibodies are labeled with fluorescent dye and seen microscopically.

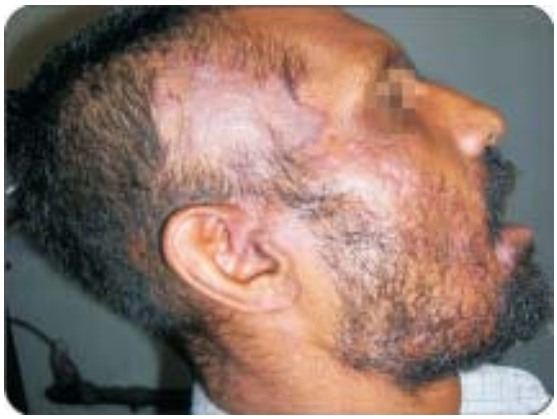


Fig. 8.23: Herpes zoster after anti viral treatment

***Molecular techniques*:** Dot blot hybridization and PCR.

Treatment

Antiviral drugs such as acyclovir is given along with antibiotics to prevent secondary infections (Fig. 8.23).

CYTOMEGALOVIRUS INFECTION

In case of cytomegalovirus infection, the infected cells often contain large intranuclear or paranuclear inclusion bodies, which make the cells dramatically swollen.

The disease primarily affects the salivary gland tissue during early childhood. It is mostly transmitted via the saliva, blood, milk, semen and urine, etc. It can also be transmitted through blood to blood contact, during intimate physical contact, organ transplant or due to maternal-fetal transmission during intrauterine life.

During periods of latency, the virus resides or replicates in the epithelial cells of the kidney or oropharynx.

CLINICAL FEATURES

- Cytomegalovirus infections are mostly subclinical in nature and during the initial period it produces fever, malaise, pharyngitis, myalgia and lymphadenopathy, etc.
- If the infection is contracted during fetal life from an infected mother, stillbirth is a very common possible outcome.
- Aphthous-like ulcers may develop in the mouth, in which cytomegalovirus can be demonstrated.

- In severe cases the disease may produce hepatosplenomegaly, jaundice, pneumonia, purpura, microcephally, cerebral calcification and dental or neurological abnormalities, etc.
- On rare occasions this virus may produce Kaposi's sarcoma in AIDS patients.
- Painful swelling of the parotid and submandibular glands often occurs.
- Besides this, CNS infection by cytomegalovirus in AIDS patients is always fatal.
- In immunocompromised patients the disease cause widespread involvement of the major and minor salivary glands; which results in painful sialadenitis and xerostomia.

HISTOPATHOLOGY

- Vascular endothelial cells and odontogenic epithelial cells are frequently affected.
- Infected cells contain large intranuclear inclusion bodies.
- Often there is presence of paranuclear bodies, which indents the nuclei.
- Individual cells are dramatically swollen (cytomegaly) and these cells often have a typical 'owl-eye' type of appearance.

TREATMENT

Only palliative treatment with analgesics, antipyretics and antibiotics are given. No standard antiviral agent is available against this virus.

EPSTEIN-BARR VIRUS INFECTIONS

Epstein-Barr virus is a member of the herpes virus group and it exhibits tropism for the human B-lymphocytes. The virus produces several diseases, namely (i) infectious mononucleosis, (ii) burkitt's lymphoma and (iii) nasopharyngeal carcinoma, etc.

Epstein-Barr virus can also be found in B-cell lymphomas and in Hairy leukoplakias of the tongue.

The virus gains access into the epithelial cells of the oropharynx and nasopharynx by means of B lymphocytes.

Infectious Mononucleosis

Infectious mononucleosis or glandular fever is a self-limiting disease which commonly involves the children and young adults. The virus is mainly transmitted via saliva, during intimate kissing and the incubation period is about 7 weeks.

Clinical Features

- Initially the disease manifests only in the oral cavity by producing features like gingivostomatitis, gingival bleeding and **multiple pinpoint petechiae at the junction of the hard and soft palate.**
- About 3 to 5 days after the appearance of the oral symptoms, other features of the disease appear which include vague illness with fever, malaise, fatigue, pharyngitis and severe sore throat, etc.
- The fully developed disease exhibits pharyngitis, severe cough, pharyngeal edema, generalized as well as cervical lymphadenopathy, hyperplastic tonsilar glands with tonsillar exudation, thrombocytopenia and hepatosplenomegaly, etc.
- Acute necrotizing ulcerative gingivitis (ANUG) type of lesion commonly develops in the oral cavity.
- The disease terminates spontaneously within about one month time, however, the lymphadenopathy, fatigue and malaise, etc. may persist for several months.

Histopathology

- Tissue from enlarged tonsils or lymph nodes histologically exhibits germinal hyperplasia and large, abnormal, nonneoplastic lymphocytes.
- The aberrant lymphocytes are basophilic with vacuolated cytoplasms and large kidney shaped nuclei.

Diagnosis

Infectious mononucleosis is diagnosed by a heterophil antibody test called "Paul-Bunnell test".

Treatment

Only palliative treatment is done, complete bed rest is essential.

HUMAN PAPILLOMAVIRUS INFECTION

Human papillomavirus (HPV) belongs to the family of papovirus; these are DNA virus having spherical virion measuring 50 nm in diameter.

They enter the body by direct or indirect contact and finally reach the basal or suprabasal parts of the skin and epithelium.

The virus replicates in the stratum spinusum, while the mature viral capsids are found in the stratum granulosum or stratum corceum or even in the superficial part of the nonkeratinized epithelium. Human papilloma virus usually produces diseases like-squamous papilloma, verruca vulgaris and occasionally condyloma acuminatum, etc.

CLINICAL FEATURES

In the oral cavity the virus produces **wart-like, self-regressing, multiple tumors** in the oral mucosa (Fig. 8.24).

The virus sometimes can even induce carcinogenic changes in the oral mucosa, in presence of cofactors like smoking and drinking, etc.

Treatment is done by surgical excision or by physical or chemical destruction of the lesion.

PARAMYXOVIRUS INFECTION

MEASLES (RUBEOLA)

Measles is a catarrhal inflammation of the dermal, respiratory and oral epithelium which is characterized by focal degeneration and exfoliation of the affected cells.

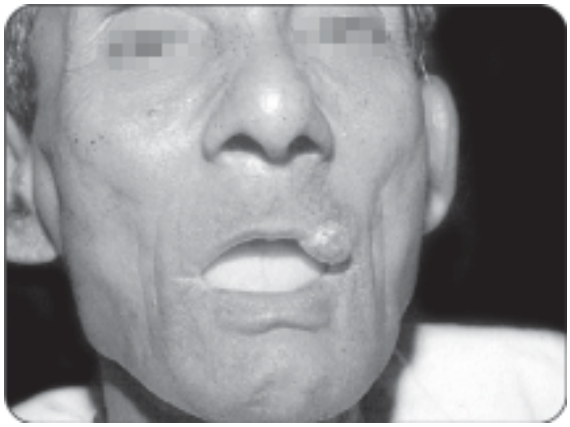


Fig. 8.24: Viral wart on the upper lip

ETIOLOGY AND PATHOGENESIS

The disease is caused by **paramyxovirus,** these are a group of large RNA viruses responsible for causing measles and mumps. Both viruses are transmitted through saliva and easily contracts young individuals. Measles is one of the most common viral diseases affecting humans, the virus enters the body through the respiratory system, undergoes replication within the respiratory epithelium and then it spreads to the regional lymph nodes and eventually throughout the body via blood.

CLINICAL FEATURES

- Measles is a **highly contagious** disease which often occurs among children and sometimes, in immunocompromised adults.
- Initially the disease produces severe headache, skin rash, high fever, malaise, photophobia and cough, etc.
- One of the most important features of the disease is the presence of **"Koplik's spots"** in the oral mucosa, which consist of a **cluster of white or white-yellow pinpoint papules** on an inflamed, red background of the buccal mucosa, labial mucosa and soft palate, etc
- Besides Koplik's spots, few red macular lesions may also be present in the oral cavity.
- Following the development of Koplik's spots in the oral cavity, **diffuse erythematous maculopapular skin rashes** begin to appear over the facial skin followed by skin of the trunk and extremities.
- There may be presence of **palatal petechiae** and inflamed gingival or oral mucosa. The oral lesions resemble necrotizing stomatitis, while the gingival lesions resemble the ANUG.
- Severe measles during early childhood can disturb the normal tooth development; and the affected teeth often exhibit 'pitted enamel hypoplasia' in the permanent dentition.
- It is important to note that all the oral lesions appear about 2 to 4 days before the appearance of the general symptoms of the disease, which include typical maculopapular skin rashes.
- Complication often develops in the form of pneumonia, bronchitis, diarrhea, encephalitis and keratoconjunctivitis, etc.

- The maculopapular skin rashes clear within few days and these rashes leave behind few brownish pigmented areas on the skin.

TREATMENT

Only palliative treatment is done and antibiotic therapy is necessary to combat secondary infections.

MUMPS

Mumps in an acute contagious, localized viral infection, caused by the paramyxovirus; which primarily affects the salivary glands. The disease is characterized by unilateral or bilateral, non-suppurative enlargement of the parotid glands and sometimes other major salivary glands.

PATHOGENESIS

Mumps virus spreads through saliva and nasal droplets. Initially it infects and replicates in the respiratory mucosa and becomes disseminated into the salivary gland, CNS, testes, ovaries, pancreas, eye and middle ear, etc.

CLINICAL FEATURES

- The disease occurs more commonly among children and young adults and the incubation period is about 2 to 3 weeks.
- The initial features of the disease include low grade fever, myalgia, headache, malaise, loss of test sensation and loss of appetite, etc.
- Pain in the parotid region with subsequent **unilateral or bilateral parotid swelling** is the most common clinical manifestations of the disease. However in some cases submandibular and sublingual salivary glands are also involved.
- In case of parotid enlargement, elevation of the ear-lobe on one or both sides can be seen when it is clinically viewed from behind the patient. The swelling can extend below up to the posterior inferior border of the mandible.
- The enlarged glands are very painful during meals (especially those containing citrus foods) and during chewing.
- Intraorally the parotid papilla over the opening of the Stensen's duct is enlarged.
- Painful swelling of the testicles occurs frequently.
- Involvement of pancreas, breast and other salivary glands are also seen in adult patients.

HISTOPATHOLOGY

Microscopic section of the diseased tissue reveals the presence of degenerative changes in the ductal epithelium of the salivary gland. Interstitial infiltration of lymphocytes and mononuclear cells in the glandular lobules, and few areas of acinar atrophy also observed.

COMPLICATIONS

Pancreatitis, meningitis, oophoritis, etc. occur commonly but the most important complication is the occurrence of "**orchitis**" in adult males which may sometimes lead to sterility.

DIAGNOSIS

- Detection of virus specific antibodies in the serum.
- Detection of mumps virus in the urine.

TREATMENT

Only symptomatic treatment is done.

COXSACKIE VIRUS INFECTIONS

HERPANGINA

Herpangina is a viral disease caused by **coxsackie virus type A** and the disease occurs more commonly among children.

The disease spreads via saliva or by inhalation of air-borne droplets.

CLINICAL FEATURES

- The disease usually occurs in localized fashion, which involves the soft palate and nasopharynx.
- Initially it produces headache, nausea, vomiting, fever, malaise, sore throat, dysphagia, myalgia and lymphadenopathy, etc.
- Oral lesions start as erythematous macules on the soft palate near uvula and anterior pharynx (lesions are never seen anterior to these locations).

- Later on there is formation of multiple, small, fragile vesicles in the locations mentioned above.
- Soon the fragile vesicles rupture and leave shallow, pinpoint ulcers.
- The ulcers often resemble herpetic infections and each ulcer is surrounded by a zone of intense erythema (halo).
- The ulcers heal spontaneously within a few days.

TREATMENT

Only palliative treatment is done.

HAND, FOOT AND MOUTH DISEASE

Hand foot and mouth disease is caused by **coxsackie virus (A-16 and A-9)** type and it also commonly occurs among children.

CLINICAL FEATURES

- It is a **highly contagious systemic infection** in which **vesicular eruptions occur on the palm of the hand, sole of the foot and mucosa of the anterior part of mouth.**
- The disease starts with the features like fever, sore throat, dysphagia and malaise, etc.
- The other associated features of the disease include cough, rhinorrhea, diarrhea, nausea, vomiting, anorexia and lymphadenopathy, etc.
- The skin lesions are common in this disease and the lesions begin as erythematous macules over the feet and hands.
- The initial lesions are followed by development of multiple vesicles, papules or ulcers on the skin.
- In the oral cavity there is often formation of vesicles and ulcerations on the hard palate, tongue, labial mucosa and buccal mucosa.
- Unlike herpangina, these lesions are uncommon in the oropharyngeal area.
- Vesicular skin rash is more particularly seen around the base of the fingers or toes; however any other part of the extremities can be affected by the disease.
- Hand, foot and mouth disease can spread as minor epidemic among the schoolchildren and teachers; Moreover, parents are also sometimes affected by the disease.

TREATMENT

Only symptomatic treatment is advised in this disease.

APHTHOUS ULCERS

Aphthous ulcer is the most common type of nontraumatic, ulcerative condition of the oral mucosa. Highly placed professionals and people of the higher socioeconomic status tend to suffer from this disease more often than others.

ETIOLOGY

The exact etiology is not known and only few probable factors have been identified which are as follows:

- ***Genetic predisposition:*** The disease often affects several members of the same family and moreover identical twins are more frequently affected.
- ***Exaggerated response to trauma:*** The ulcer develops in those mucosal sites which are subjected to trauma in the past (e.g. tooth prick injury).
- ***Immunological factors:*** The disease may occur due to some autoimmune reactions, or in patients with immunosuppression (e.g. AIDS). Some investigators believe it is an immune complex mediated Type III or cell mediated Type IV reaction.
- ***Microbiologic factors:*** The disease may be caused by herpes simplex virus Type-I or *Streptococcus sanguis* or L forms organisms.
- ***Nutritional factors:*** Deficiency of vitamin B12, folate and iron, etc. often reported in patients with aphthous ulcer; moreover supplementation of these elements may cause rapid recovery.
- ***Systemic conditions:*** Behcet's syndrome, Crohn's disease and Celise disease are often associated with increased incidences of the aphthous ulcer.
- ***Hormonal imbalance:*** Hormonal change during menstrual cycle may be associated with higher incidence of aphthous ulcer.
- ***Non-smoking:*** The disease almost exclusively occurs in non smokers or the people those who have given up smoking recently.

- ***Allergy and chronic asthma:*** Allergic manifestations to any medicines or foods (e.g. nuts and chocolates, etc.) may lead to the development of aphthous ulcer.
- ***Miscellaneous factors:*** Stress and anxiety.

List of etiological factors in aphthous ulcer

- Genetic predisposition
- Exaggerated response to trauma
- Immunological factors
- Microbiologic factors
- Nutritional factors
- Systemic conditions
- Hormonal imbalance
- Non-smoking
- Allergy and chronic asthma
- Miscellaneous factors.

CLINICAL FEATURES

- Aphthous ulcers usually **develop over the movable, non keratinized oral mucosa** like the tongue (lateral borders), vestibule, lips, buccal mucosa, soft palate and floor of the mouth, etc (Fig. 8.25).
- Most patients are **clerical, semiprofessional or professional workers**; and are mostly nonsmokers.
- **Highest incidence** of the disease is reported **during early adult life**.
- Before the appearance of the ulcer, the involved area produces a burning or tingling sensation, but the ulcers are never preceded by vesiculations.
- These ulcers recur in an interval of about 3 to 4 weeks.

TYPES

Clinically aphthous ulcers present three recognizable forms, namely:
A. Minor aphthous ulcers;
B. Major aphthous ulcers;
C. Herpetiform ulcers.

Minor Aphthous Ulcer

- It is the most common type of aphthous ulcer of the oral cavity and it appears episodically either as single lesion or in clusters of 1 to 5 lesions.
- The ulcers are very painful, shallow, round or elliptical in shape and they measure about 0.5 cm in diameter with a crateriform margin.
- The lesion is usually surrounded by an erythematous "halo" and is covered by a yellowish, fibrinous membrane.
- Minor aphthous ulcers mostly develop over the non-keratinized mucosa, e.g. lips, soft palate, anterior fauces, floor of the mouth and ventral surface of the tongue (gland bearing mucosa), etc (Fig. 8.26).
- The ulcer lasts for about 7 to 10 days and then heals up without scarring but recurrence is common.
- New lesions may continue to appear during an attack for about 3-4 weeks period.
- Few lesions may be present in the mouth almost continuously.

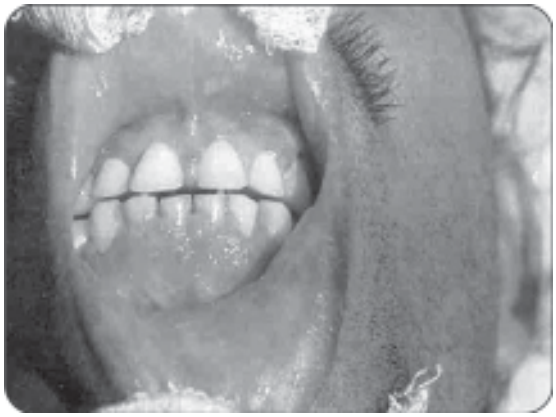


Fig. 8.25: Minor aphthous ulcer of the upper lip

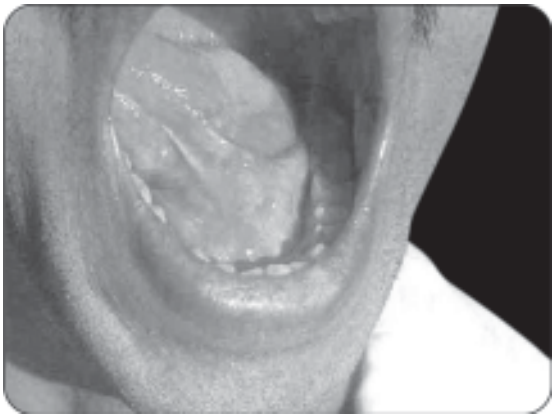


Fig. 8.26: Minor aphthous ulcer of the under surface of tongue

- The disease mostly causes difficulty in taking food, mastication and speech, etc.

Major Aphthous Ulcers

- Major aphthous ulcers are less common than the minor form of the disease.
- These are larger, 0.5 cm in diameter and can be as big as several centimeters in diameter.
- Major aphthous ulcers are more painful lesions than the minor variety; and they persist in the mouth for longer durations as they take more time to heal.
- These lesions are considered to be the most severe among all types of aphthae and they often make the patients ill (due to the psychologic stress and difficulty in food intake).
- Only one or two lesions develop at a time and are mostly seen over the lips, soft palate and fauces, etc. Besides involving the non-keratinized mucosa, major aphthous ulcers can involve the masticatory mucosa as well, such as the dorsum of the tongue and gingiva, etc.
- The ulcer appears crateriform (owing to its increased depth) and it heals with scar formation in about 6 weeks time.
- Few lesions may look like malignant ulcers, moreover sometimes these lesions occur in association with HIV infections.
- Major aphthous ulcers often become secondarily infected and in such cases the healing process is further delayed.

Herpetiform Ulcer

- Herpetiform type of aphthous ulcers produce recurrent crops of extremely painful, small ulcers in the oral mucosa, which resemble herpetic ulcers. However, these ulcers do not develop following vesiculations and exhibit no virus infected cells.
- Their numbers vary from few dozens to several hundreds and each ulcer is surrounded by a wide zone of erythema.
- Size of these ulcers ranges between 1 to 2 mm in diameter only. However on few occasions small ulcers coalesce together to form large irregular ulcers.
- The ulcers last for several weeks or months (duration is much longer then the other two types).
- Children in their late teens often suffer from this disease and the lesions occur in both gland-bearing mucosa as well as over the keratinized mucosa.
- The lesions usually heal up within 1 to 2 weeks time.

Histopathology of Aphthous Ulcers

The histopathologic findings are non-specific and are not pathognomonic for aphthous ulcers.

- Aphthous ulcer microscopically shows the presence of an overlying degenerated and ulcerated epithelium being covered by a fibrinopurulent exudate.
- Vacuolization and necrosis of the individual epithelial cells occur.
- In the underlying connective tissue, dense infiltration of neutrophils are found in the superficial layer.
- In the deeper layers of connective tissue lymphocytes, macrophages, plasma cells and mast cells, etc. often predominate.
- Mononuclear cells are often seen to surround the small blood vessels (perivascular cuffing).

CYTOLOGY

Cytologic smears prepared from the materials obtained from around the recurrent aphthous ulcer reveals the presence of **"Anitschkow's cells".** These cells are characterized by the presence of elongated nuclei containing a linear bar of chromatin, with few radiating processes extending towards the nuclear membrane.

DIFFERENTIAL DIAGNOSIS

- Herpetic ulcers
- Traumatic ulcers
- Pemphigus vulgaris
- Cicatricial pemphigoid
- Ulcers due to neutropenia
- Crohn's disease.

TREATMENT

Treatment of aphthous ulcers is unsatisfactory and empirical. Topical and systemic administration of steriods is useful for the containment of the disease and in few cases immunomodulator

drugs produce some beneficial effects. Recurrence is very common.

BEHÇET'S SYNDROME

Behçet's syndrome is a multisystem disease that predominantly affects young males and is characterized by multiple superficial, painful "aphthous-like ulcers" in the oral cavity. However to fulfill the criteria of being Behçet's syndrome, clinically there should be presence of aphthous-like ulcer in the oral cavity along with at least two of the following lesions e.g. skin lesion, eye lesion or genital lesion, etc.

ETIOLOGY

Etiology of Behçet's syndrome is unknown; however the disease is believed to be caused by some immunologic abnormality.

CLINICAL FEATURES

Oral lesions: Aphthous-like ulceration in the oral cavity.

Skin lesions: Erythematous macular, papular, vesicular or pustular lesions in the skin; thrombophlebitis may also sometimes develop.

Eye lesions: Ocular lesions in Behçet's syndrome include uveitis, conjunctivitis, photophobia and retinitis, etc.

Genital lesions: Ulceration in the genitalia, which looks similar to those of the oral cavity.

Other lesions: Behçet's syndrome sometimes presents some additional features like neural, vascular, articular, renal or gastrointestinal lesions of various kinds.

HISTOPATHOLOGY

Microscopically the lesions produce similar feature to what is found in minor aphthous ulcer. However there can be some additional features like severe vasculitis and vascular damage, etc.

TREATMENT

Behçet's syndrome is treated by systemic steroid therapy.

REITER'S SYNDROME

Reiter's syndrome is a disease commonly found among white adult males, which produces the classic triad comprising of non-gonococcal urethritis, arthritis and conjunctivitis.

ETIOLOGY

Mostly unknown, however it is believed to be an immunologically mediated disorder; which is often triggered by some infections.

CLINICAL FEATURES

***Age*:** The disease commonly occurs between the ages of 20 to 35 years.

Genital lesions: Genital lesions produce a characteristic 'balanitis circinata' over the glans penis; moreover genital ulcers are also commonly seen.

Oral lesions: Oral lesions are mostly seen over the buccal mucosa, palate and gingiva, etc. and these lesions present painless, aphthous-like ulcers. In addition to this a tongue lesion is often seen that resembles the typical "geographic tongue'. Moreover there may be presence of few slightly elevated areas of erythema on the oral mucosa. Pruritic spots are also seen on the palate.

Skin lesions: Well circumscribed erythematous erosions with irregular white linear boundary.

HISTOPATHOLOGY

The oral epithelium exhibits hyperkeratosis with elongation of rete-pegs; formation of few micro-abscesses occur in the superficial part of the epithelium. Histologically, the lesion often resembles 'psoriasis'.

TREATMENT

Systemic steroid therapy and administration of antibiotics.

RABIES

Rabies as an acute fatal viral disease of CNS caused by rabies virus that affects all animals and the virus is transmitted by the infected secretions (usually saliva).

Mostly the diseases are caused due to the bite of infected animals like dogs, cats, foxes, wolves and bats, etc.

PATHOGENESIS

After the introduction of the live virus through the skin following animal bite, the virus replicates within the striated muscle cells at the site of inoculation. Then the virus reaches the peripheral nerve and moves centripetally up the nerve to the central nervous system via the nerve axoplasm. In brain it replicates exclusively within the gray matter and then again it passes centrifugally along the autonomic nerves to reach different body tissues like salivary glands, adrenal medulla, liver, kidney, lungs, heart and skin, etc.

The incubation period of rabies is about 10 days to 1 year (mean being 1 to 2 months).

CLINICAL MANIFESTATIONS

The clinical manifestation of rabies can be divided into four stages:

A. Prodromal stage
B. Encephalitic stage
C. Stage of brain stem centers dysfunction
D. Recovery stage(very rare).

The prodromal stage persists for about 1 to 4 days and is marked by fever, headache, malaise, nausea, vomiting, anorexia, sore throat, non-productive cough and paresthesia at the site of inoculation.

The encephalitic stage is characterized by excitation, anger, confusion, hallucination, paralysis of the vocal cord, high fever (105°F), excessive salivation and lacrimation.

There can be excessive sensitivity to bright, loud noise, touch or even gentle breeze, etc.

The stage of brainstem dysfunction presents the features like facial palsies, difficulty in deglutition, foaming from the mouth. One of the most important features of this stage is "hydrophobia"—(the violent, painful, involuntary contraction of diaphragm with accessory respiratory, pharyngeal and laryngeal muscles which is initiated by drinking of liquid or even thinking of any drink).

Most of the patients die following coma and respiratory arrest, and the median survival rate is only about 4 to 20 days.

LABORATORY FINDINGS

- WBC count is elevated up to 17000 to 30000 per cm of blood
- Isolation of virus from saliva
- Mouse inoculation study for viral antigens
- Detection of Negri bodies in the brain tissue
- Fluorescent antibody (FA) staining for viral antigen.

TREATMENT

- The animal should be captured, confined and observed for 10 days and if any illness or abnormality in its behavior is noticed during that period, it should be killed for fluorescent antibody examination and detection of "Negri body" in the brain.
- Local wound should be cleaned by generous scrubbing with soap water and 1 to 4% benzalkonium chloride.
- Passive immunization with antirabies antiserum.
- Active immunization with antirabies vaccine.

FUNGAL INFECTION

CANDIDIASIS

Candidiasis is the most common type of mycotic or fungal infection that occurs in the oral cavity and is predominantly caused by ***Candida albicans***. The disease can also be produced by *C. tropicalis, C. glabrata, C. krusei* and *C. pseudotropicalis,* etc., but far less commonly. Candida is also called monila and hence the disease is known as '**moniliasis**'.

Candidal organisms multiply primarily by the production of buds from ovoid yeast cells.

The candidal organisms are present in the oral cavity, digestive tract and vaginal tract, etc. as normal commensals in many healthy persons; however they become pathogenic due to some local or systemic changes in the body.

PATHOGENESIS

Candidal organisms produce the disease by tissue invasion or by inducing a hypersensitivity reaction or by releasing some potent toxins. They produce large number of opportunistic infections in immunocompromised patients.

Local and systemic conditions predisposing to the development of candidiasis

- Immunologic immaturity in infants or in old aged persons.
- Hormonal disturbances like diabetes mellitus, hypoparathyroidism, oral pills and pregnancy, etc.
- Long term local or systemic steroid therapy
- Xerostomia with Sjogren's syndrome
- Poor oral hygiene
- Chronic denture wearing
- Heavy smoking
- Anemia
- Acidic saliva
- Advanced malignancy, acute leukemia and squamous cell carcinoma, etc.
- Malabsorption and malnutrition—Iron, folic acid and other vitamin deficiencies
- Prolonged broad spectrum antibiotic therapy causing suppression of oral flora.
- Immunosuppression (for example AIDS)
- Chemotherapy and radiotherapy
- Tricyclic antidepressant therapy
- Blood group 'O' individuals (Tend to suffer more)

CLINICAL FEATURES (FIG. 8.27)

Candidiasis occurs mostly as the superficial infection of the mucous membrane or skin but the infection can involve the deeper structures (e.g. esophagus, lungs or endocardium, etc.) in severely debilitated or immunosuppressed persons.

The oral candidiasis can be classified into the following types:

Acute Pseudomembranous Candidiasis

- It is commonly known as "oral thrush" and it appears as a smooth, thick, creamy-white or yellow, soft and friable plaque (pseudomembrane) on the oral mucosa.
- The plaque can be easily wiped off by gentle scraping, which leaves an erythematous, raw, bleeding surface in the underlying area.
- The lesions may occur at any mucosal site.
- They vary in size ranging from small drop like areas to confluent plaques covering a wide surface.

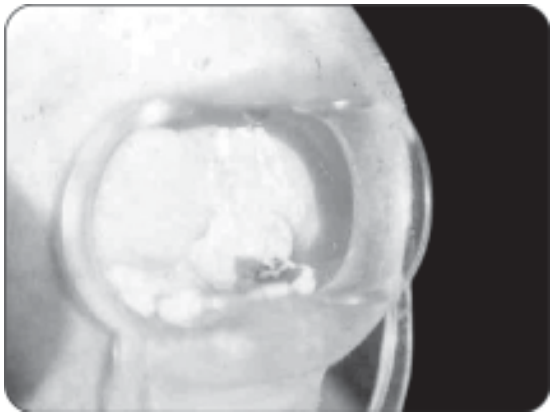


Fig. 8.27: Candidiasis of the cheek

- The plaque consists of fungal organisms, keratotic debris, inflammatory cells, desquamated epithelial cells and fibrin, etc.
- Oral thrush commonly occurs among children, debilitated elderly persons and AIDS patients.
- In neonates, the disease is contracted from birth canal of an infected mother.

Acute Atrophic Candidiasis

- It occurs when the pseudomembranous covering of the oral thrush is lost.
- The lesion presents generalized red, painful, 'peeling patches' over the mucosa, which often causes tenderness, dysphagia and burning sensation, etc.
- The condition is commonly seen on the dorsum of the tongue and palate in patients receiving long term antibiotic or steroid therapy (Figs 8.28 and 8.29).

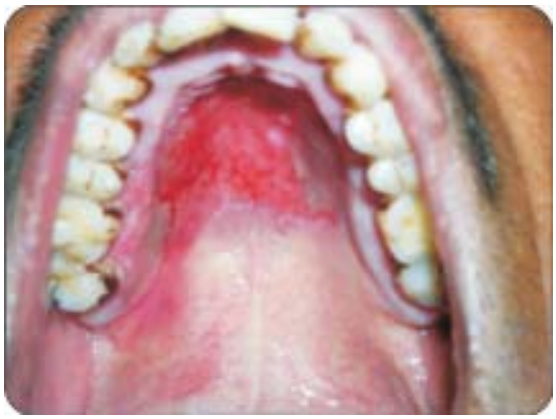


Fig. 8.28: Atrophic candidiasis (palate)

Classification of oral candidiasis

Acute candidiasis	*Chronic candidiasis*	*Systemic candidiasis*	*Mucocutaneous candidiasis*
• Pseudomembranous type • Atrophic type	• Atrophic type • Hypertrophic type • Candida-associated angular cheilitis.	• Candidal endocarditis • Candidal meningitis • Candidal septicemia	• Localized type (oral cavity, face, nails, and scalp,etc.) • Familial type • Syndrome associated candidiasis.

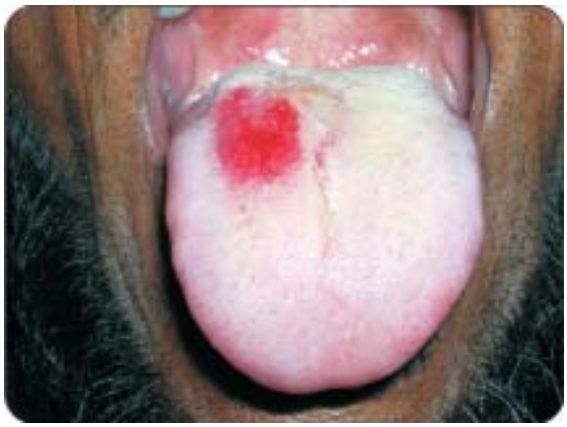


Fig. 8.29: Atrophic candidiasis (tongue)

Chronic Atrophic Candidiasis

- This form of candidiasis is commonly seen in the palatal mucosa of the denture wearing elderly persons.
- The condition is more often seen among females than males.
- The lesion clinically appears as a bright red, edematous, velvety area with little keratinization.
- It is regarded as secondary candidal infection of oral tissues modified by continuous wearing of ill-fitting dentures and associated poor oral hygiene.
- Most of the lesions of chronic atrophic candidiasis are clinically asymptomatic.

Candida–associated Angular Cheilitis

- An important form of chronic atrophic candidiasis is "angular cheilitis". It occurs at the angle of the mouth among persons having deep commissural folds secondary to overclosure of mouth.
- It can also occur among persons with lip-licking habits, denture wearing, or deficiency of riboflavin, vitamin B12 and folic acid deficiency, etc.
- The infection starts due to the colonization of fungi in the skin folds following deposition of saliva due to repeated lip-licking.
- Clinically the patients often have soreness, erythema and fissuring (red cracks) at the corner of the mouth. In some cases the defect can extend over the adjoining skin surfaces. The cracks are often covered with pseudomembrane.
- Under favorable conditions (vitamin deficiency, malnutrition and antibiotic therapy, etc.), lesions similar to angular chelitis could be produced by other organisms like–*staphylococcus aureus or streptococcus-B hemolyticus*, etc.

Chronic Hyperplastic Candidiasis

- It appears as a slightly elevated, indurated, persistent, white plaque or patch on the oral mucosa that often resembles oral leukoplakia.
- The lesions could be bilateral and are mostly seen on the buccal mucosa near the commissure. Some lesions may also develop over the tongue or the palate, etc.
- The patchy areas are of irregular thickness and density and they have a rough, nodular surface.
- These lesions can not be removed by scraping and in some cases there may be presence of erythematous areas within the patch.
- Development of chronic hyperplastic candidiasis is often favoured by certain conditions like smoking, denture wearing and occlusal frictions.
- The hyperplastic tissue is often discolored due to staining from foods and tobacco.

Localized Mucocutaneous Candidiasis

- This is characterized by long standing and persistent candidal infections in the oral cavity, skin, nails and vaginal mucosa, etc.

Familial Mucocutaneous Candidiasis

- It is believed to be transmitted genetically as autosomal recessive trait and most of the patients are mildly affected.
- A triad of mucocutaneous candidiasis, thymoma and myositis has been reported in 1968.

Syndrome-associated Candidiasis

Severe candidiasis (both acute and chronic variety) are well recognized opportunistic infections in immunosuppressed patients, particularly those suffering from AIDS. Depressed cell-mediated immunity is believed to be the cause for the development of these lesions.

Candidiasis Endocrinopathy Syndrome

- Transmitted as autosomal recessive trait.
- Chronic oral candidiasis occurring mostly in the second decade of life.
- Hypoparathyroidism, Addison's disease, diabetes mellitus and hypothyroidism.

SYSTEMIC CANDIDIASIS

Candidal Endocarditis

- Patients who have undergone prosthetic heart valve replacements and those who are using for a long time venous catheters are at risk for developing candidal endocarditis.
- Clinically the patient often develops fever, dyspnea, edema and congestive cardiac failure, etc.
- Candidal growth in the valve may result in the development of major venous embolism.

Candidal Meningitis

- Spread of candidal organisms into the brain results in meningitis, which could be a consequence of oral candidiasis and in such cases, the organisms can be detected from the CSF.
- Patients often develop fever, headache, stiffness in the body and hemiplegia.
- The condition is often fatal.

Candidal Septicemia

- It occurs due to disseminated spread of candidal organisms throughout the body and it can be secondary to severe oral or oropharyngeal candidiasis.
- Clinically the patient often develops fever, chill, nausea, vomiting, shock and coma, etc.
- The condition can be fatal if not treated in time.

HISTOPATHOLOGY OF CANDIDIASIS

Acute Pseudomembranous Candidiasis

- Hyperplastic epithelium with superficial necrotic and desquamating parakeratinized layer.
- Hyperplastic epithelium is infiltrated by candidal hyphae and yeast cells along with PMN.
- Often there is separation between the superficial pseudomembrane and the deeper layers of epithelium.
- The candidal hyphae often appear as a weakly basophilic thread-like structure (Fig. 8.30).
- Lamina propria is infiltrated by chronic inflammatory cells.

Acute Atrophic Candidiasis

- Thin, atrophic, non-keratinized epithelium with occasional presence of candidal hyphae.
- Chronic inflammatory cell infiltration is seen in the epithelium as well as in the lamina propria.
- Histologically these lesions resemble 'oral thrush' without the pseudomembrane.

Fig. 8.30: Photomicrograph of candidiasis

Angular Cheilitis

- Hyperplastic or atrophic epithelium with ortho or parakeratinization.
- Chronic inflammatory cell infiltration in the epithelium as well as in the connective tissue.
- Sometimes microabscess formation in the epithelium.

Chronic Hyperplastic Candidiasis

- Hyperplastic, acanthotic epithelium with parakeratosis.
- Intercellular edema and PMN infiltration sometimes causing separation between different layers of the epithelium.
- Microabscess formation in some cases.
- Atrophy of the epithelium with loss of keratin in the clinically erythematous areas.
- Candidal hyphae invading the parakeratinized layer at right angles to the surface.
- Epithelial displasia may be present in some cases.
- Chronic inflammatory cell infiltration in the underlying connective tissue.
- PAS-stained sections best demonstrate the presence of candidal hyphae in the tissue.

DIFFERENTIAL DIAGNOSIS

- Chemical burn
- Mucous patch of syphilis
- Traumatic ulcer
- Leukoplakia
- Lichen planus
- Discoid lupus erythematosus (DLE).

TREATMENT

Topical and systemic administration of nystat is done in conventional cases.

In immunosuppressed patients, systemic administration of amphotericin-B and fluconazole may be necessary. Removal of primary etiological factors and improvement of oral hygiene is essential

DEEP FUNGAL INFECTIONS

COCCIDIOIDOMYCOSIS

It is deep fungal infection of the lung and caused by *Coccidioides immitis*. The disease is commonly seen in North and South America, where it occurs in endemic form. Since the disease occurs predominantly in the central valley of California, it is often known as 'valley fever'.

CLINICAL FEATURES

- The disease starts with a flu-like illness characterized by fever, malaise, fatigue, headache, myalgia, cough and dyspnea, etc.
- Lymphadenopathy, chest congestion and joint pain, etc. develop after that.
- Pulmonary lesions produce tuberculosis like features , e.g. chest pain, weight loss, persistent cough and low grade fever, etc.
- Granulomatous, verrucous or necrotic ulcers of the skin (more often on the facial skin).
- Large number of cases may be asymptomatic.

ORAL MANIFESTATION

- Granulomatous proliferation of oral mucosa with ulceration and induration.
- Regional lymphadenopathy and occasional jaw swelling.
- Oral lesions heal with scarring.

HISTOPATHOLOGY

- Multiple focal granulomas contaning large number of macrophages, lymphocytes, plasma cells and multiple multinucleated giant cells.
- Liquefaction necrosis and exudation at the margin of the lesion.
- Epithelial hyperplasia with microabscess formation.
- Large double contoured 'spherules' are seen with silver stain.

TREATMENT

Ketoconazole is effective in mild infections. In case of severe or recurrent infections—Amphotericin-B is the drug of choice.

HISTOPLASMOSIS

Histoplasmosis is a deep fungal infection of the lung tissue, which is caused by *Histoplasma capsulatum*. The disease is contracted by inhalation of the airborne spores of the organism.

CLINICAL FEATURES

- Fever, malaise, non-productive cough, dyspnea, anorexia, headache, myalgia and chest pain (in case of pulmonary infections).
- In disseminated cases the disease manifests with hepatosplenomegaly and lympadenopathy.
- Granulomatous lesions and cavitations in the lung.
- Involvement of kidney and bone marrow.
- Granulomatous lesions may also be seen over the skin.
- Calcification of the hilar lymph nodes.
- A large number of cases are asymptomatic in nature.

ORAL MANIFESTATIONS

- Oral lesions occur in the forms of nodules over the mucosa, which frequently undergoes ulceration with raised, rolled borders and induration of the surrounding tissue.
- the ulcers are painful and are often clinically confused with squamous cell carcinoma.
- Most of the oral lesions develop in the gingiva, tongue, palate and buccal mucosa, etc.
- Some lesions may be papular, verrucous or plaque-like.
- Sore throat, pain during chewing, hoarseness of voice and dysphagia are common.
- Granulomatous lesions often cause destruction of the alveolar bone with loosening or exfoliation of teeth.
- Oral lesions of histoplasmosis may occur secondary to HIV infections and in many cases they resemble carcinoma or tuberculous ulcers.

DIFFERENTIAL DIAGNOSIS

- Squamous cell carcinoma.
- Tuberculosis.
- Actinomycosis.
- Leishmaniasis.

HISTOPATHOLOGY (FIG. 8.31)

- Histologically the disease reveals a granulomatous lesion characterized by the formation of multiple, small, granulomas containing histiocytes and the fungi.
- The granulomas are often surrounded by histiocytes, lymphocytes, plasma cells and few scattered multinucleated giant cells.

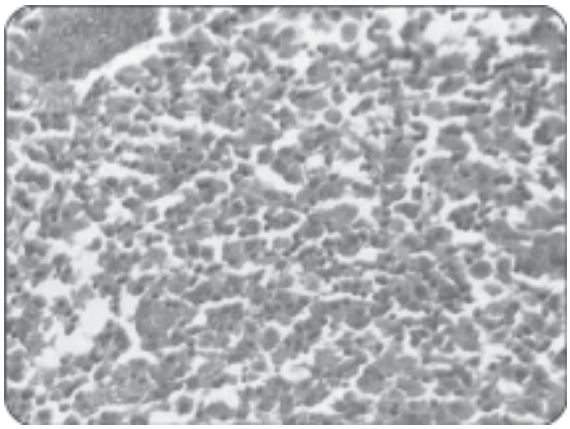


Fig. 8.31: Photomicrograph of histoplasmosis

- Pseudoepitheliomatous hyperplasia can be seen in nonulcerated lesions.

TREATMENT

Administration of Amphotericin-B.

CRYPTOCOCCOSIS

Cryptococcosis is a chronic fungal infection caused by Cryptococcus neoformans. The disease commonly affects the lung, kidney, skin and the mucous membrane. It has a particular tendency to spread to the CNS.

CLINICAL FEATURES

- Cough with mucoid expectoration, pleuritic pain and hemoptysis, etc.
- Pustular lesions which may also discharge pus-like material.
- Papular, nodular or ulcerative lesions over the skin.
- Brain infection results in meningoencephalitis with associated neurogenic symptoms.
- Cryptococcosis may occur as an opportunistic infection in patients suffering from lymphoma, leukemia, diabetes and sarcoidosis, etc.

ORAL MANIFESTATION

- Oral lesions often appear as nodular or granulomatous areas which undergo ulceration within a few days.
- The ulcers are non-healing crater-like; which are often painful.

- These lesions are commonly seen over the hard and soft palate, gingiva, tongue, tonsillar pillars and extraction sockets, etc.
- Some lesions may cause perforation of the palate.
- Occasionally the infection may spread to the salivary glands.

HISTOPATHOLOGY

- Multiple focal granulomas exhibiting epithelioid cells, macrophages, lymphocytes, plasma cells and multinucleated giant cells.
- Encysted Cryptococcal organisms can be seen in PAS stained sections.
- The infective form of the fungus is a budding yeast that exhibits a thick, mucicarmine-positive capsule, which resembles a halo.

TREATMENT

Administration of Amphotericin-B.

NORTH AMERICAN BLASTOMYCOSIS

It is a chronic fungal infection caused by *Blastomyces dermatitidis*.

CLINICAL FEATURES

- Low grade fever, weight loss, cough and purulent sputum.
- Elevated, verrucous crusted lesion (either single or multiple) on the face and hands.
- Lesions heal by scarring at the center.
- Bone involvement is seen in large number of cases.

ORAL MANIFESTATIONS

- Proliferative, ulcerated lesions developing over the palate, lips, tongue, gingiva and maxilla or mandible.
- Loosening of teeth and draining sinuses.
- Oropharyngeal pain and cervical lymphadenopathy.

HISTOPATHOLOGY

- Excessive tissue necrosis with formation of granuloma; which contains macrophages, occasional giant cells and chronic inflammatory cells.
- Microabscess formation is common.
- PAS staining reveals yeast-like organisms.

TREATMENT

Administration of Amphotericin-B.

MUCORMYCOSIS

Mucormycosis or *phycomycosis* is a fungal disease caused by a fungus belonging to the order Mucorales.

CLINICAL FEATURES

- Cervicofacial mucormycosis is characterized by the occurrence of a triad comprising of—uncontrolled diabetes mellitus, periorbital infection and meningoencephalitis.
- Nasal infection with dark blood-stained discharge.
- Facial pain and swelling is common with occasional facial nerve paralysis.
- Necrosis of nasal septum and turbinates.
- Sinusitis involving paranasal sinuses.
- Visual disturbances.

ORAL MANIFESTATIONS

- Maxillary sinusitis with swelling alveolar ridge and palate are the commonest manifestations of this disease.
- Paresthesia of the branches of trigeminal nerve is also common.
- Ulcerative lesions on the palate are the common oral manifestation of this disease.
- The area looks black or gray and often there is perforation of the bone.

RADIOGRAPHY

Radiograph of the maxillary sinus appears opaque with irregularity of the bony wall; the appearance often raises suspicion about a malignant lesion.

HISTOPATHOLOGY

- Necrosis of the involved tissue with chronic inflammatory cell infiltration.
- Thrombosis of the blood vessels in the affected area.

TREATMENT

Administration of Amphotericin-B.

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CHAPTER 9

Dental Caries

DENTAL CARIES

DEFINITION

Dental caries can be defined as '**a microbial disease of the calcified tissues of tooth, characterized by demineralization of the inorganic portions and destruction of its organic structures'.**

Dental caries is a complex, continuous, dynamic biological process of tooth decay, comprising periods of progression alternating with periods of arrest or even partial repair.

It has neither any dramatic or recognizable starting point, nor any end point, unless that is regarded as an acute pulpitis resulting in excruciating pain.

The periods of the disease activity in dental caries vary widely in their duration and intensity between different populations groups, between different individuals and within a single patient at different ages or even throughout the day. Even within a single mouth, individual sites of each tooth vary greatly in their susceptibility.

Like any other infectious disease the progress of dental caries depends upon a constantly changing balance between the nature and intensity of the injurious stimulus on one hand, and the nature and quality of the host's biological responses on the other; many factors influence this balance.

The initiation of a carious lesion at a given tooth surface, be it enamel of the crown or cementum of the exposed root surface, is customarily explained as a series of **physico-chemical phenomena**.

Acids produced by **fermentation** of **carbohydrates** by the plaque **bacteria**, cause **subsurface demineralization** of tooth enamel; and this is considered as the earliest defining manifestation of caries progression.

EPIDEMIOLOGY OF DENTAL CARIES

Dental caries has been recognized throughout history and exists around the world with variable frequency.

The epidemiological studies on dental caries have been very useful in the determination of the need for, and effectiveness of, the dental treatments.

The most common epidemiological measure of dental caries is the **DMF** index (**decayed**, **missing** or **filled** teeth); this is a measure of the number of teeth that are diseased, missing or filled at the time of examination.

DMF may be reported as the number of teeth (**DMFT**) or surface affected (**DMFS**). These measures are cumulative because they not only indicate the number of missing or filled teeth; but also reveal the total number of teeth removed in the past as well as the total number of restorations done in the mouth. In addition to this, the index also states number of teeth having active caries and the number of their surfaces involved.

According to the target of WHO, no country should have a DMFT of 3 at the age of 12 by the year 2000 AD.

In the earlier days, it was a trend that the people from the developed countries, e.g. USA, UK, Australia, New Zealand, Western Europe, Scandinavia and North America use to have more dental caries in comparison to the people of the underdeveloped or developing countries from Africa and Asia.

The basic reason behind this fact was that the people from the developed countries used to take more **refined foods** that contained **large amounts of easily fermentable sugars**, especially the sucrose.

Moreover, people of these countries could also afford to take frequent **in-between** meals that contained large amounts of sugar.

Both these factors contributed greatly to their higher incidences of caries, whereas at the same time, the people from Africa and Asia, etc. did continue to take their traditional foods, which were usually more fibrous and unrefined in nature and were not readily fermentable, thereby, contributed very little to the causation of dental caries.

In the western world, there has been a sharp increase in the disease activity in the first half of the century. However, since early 1970s, there has been a steady decrease in the prevalence of caries among the population of these countries because people have undertaken a wide range of caries preventive measures.

Important measures to prevent caries

- Extensive water fluoridation.
- Use of antibiotics.
- Increased oral hygiene awareness.
- Increased parental care.
- Improvement in the preventive dentistry.
- More availability of skillful dental professionals.

However, the recent reports indicate that the people from the underdeveloped countries are showing higher incidences of dental caries. The basic reason behind this fact is that the people from the underdeveloped countries now a days have also adopted more of urbanized lifestyle and westernized pattern of food habits.

The people of the Asian and African continents have diverted from the so called traditional food habits and have widely adopted the so called easily fermentable and highly sugar-containing diets; which highly increases the risk of caries in them.

Moreover, the people of Asian and African continents, though, have access to the high sugar-containing foods; they have the least access to the caries prevention measures available either individually or socially.

PATHOPHYSIOLOGY OF DENTAL CARIES

The pathophysiology of dental caries is a very complex reaction and it cannot be explained in terms of a single event or observation.

For this purpose, the process of dental caries is often explained with the help of many theories.

Major theories of dental caries

- Acidogenic theory
- Proteolytic theory
- Proteolytic chelation theory
- Sucrose chelation theory
- Autoimmune theory.

ACIDOGENIC THEORY

This theory is also known as **Miller's chemico-parasitic theory** as it was first postulated by WD Miller in the year 1889 and it proposes that "acids formed due to the fermentation of dietary carbohydrates by oral bacteria lead to progressive decalcification of the tooth structures with subsequent disintegration of the organic matrix".

Therefore, acidogenic theory states that the process of dental caries involves two stages:

Initial stage: Production of organic acids occurs as a result of fermentation of carbohydrates by the plaque bacteria.

Late stage: The acids cause decalcification of enamel followed by dentin and thereby cause total destruction of these two structures along with dissolution of their softened residues.

The final result is the loss of integrity of the tooth structures at a particular point on the surface with formation of a cavity.

According to Miller, there are four important factors, which can influence the process of tooth destruction in the process of dental caries and these factors are as follows:

A. **Dietary carbohydrates**
B. **Microorganisms**
C. **Acids** and
D. **Dental plaque.**

ROLE OF CARBOHYDRATES IN DENTAL CARIES

Numerous epidemiological studies have shown that the fermentable dietary carbohydrates play an important role in the causation of caries, especially the readily fermentable types of

carbohydrates, e.g. glucose, sucrose and fructose, etc. Among them sucrose is implicated to be the most potent one. These sugars are easily and rapidly fermented by cariogenic bacteria in the oral cavity to produce acids at or near the tooth surface and cause dissolution of the hydroxyapatite crystals of the enamel followed by the dentin.

The evidences that support the role of carbohydrates in the causation of caries include the following:

- Increased prevalence of caries in developing countries due to westernization or urbanization of the society and an increase in the availability of refined carbohydrates (sucrose) in the diet.
- Decrease in the prevalence of caries during World War-II because of sugar restrictions followed by rise of caries incidence to previous levels, when sucrose became available once again.
- **'The Hope Wood House Study'**— In children's home in Australia; where sucrose and white breads were eliminated from diet, the children had low caries rate. However, the caries index was increased dramatically when these children moved out of the said house and started taking conventional carbohydrate-rich diet.
- Patient with **hereditary fructose intolerance**, who cannot tolerate fructose or sucrose develop little or virtually no caries.

TYPES OF CARBOHYDRATE AND THE CARIES RISK

Dietary carbohydrates undoubtedly cause caries, however, the rate of caries attack always depends upon the forms of carbohydrate, which are taken and the frequency of intake of such carbohydrates.

- The risk of caries attack increases greatly if sugar is taken repeatedly in between two major meals. It provides an almost constant supply of carbohydrate to the plaque bacteria for fermentation and subsequent production of acids.
- Risk of caries incidence increases greatly if the dietary sugar is sticky in nature, which can remain adhered to the tooth surfaces for a longtime after taking the meal.
- The glucose, sucrose and fructose, etc. are rapidly diffused into the plaque due to their low molecular weight and, therefore, make themselves easily available for fermentation by the plaque bacteria.
- However, the principal carbohydrates available in human diet are sucrose and starches.
- Following the ingestion of these sugars, the pH of the plaque falls to 4.5 to 5 within 1 to 3 minutes and it takes another 10 to 30 minutes to return to neutrality. This pH alteration can be recorded with the help of a graph called **Stephen's curve**. The critical pH of plaque is 5.5 and tooth demineralization starts if the pH drops below this level.
- The **Stephen's curves demonstrate the pH curves of plaque in response to sugars**. These curves are similar in shape in both caries-prone and caries-active individuals. However, as the starting pH is often lower in mouth of the caries-prone persons, the fall of pH will be greater for them after taking sucrose and also the pH will remain depressed below critical level for a longer period of time in them.

Different types of carbohydrate and their cariogenicity

Compound	Nature	Cariogenicity
Sucrose	Disaccharide	Highest cariogenecity
Galactose	Disaccharide	Less cariogenic than sucrose
Glucose, fructose	Monosaccharide	Less cariogenic than sucrose
Lactose	Monosaccharide	Less cariogenic than sucrose
Xylitol, sorbitol, mannitol and laccitol	Sugar alcohols	Noncariogenic
Saccharin, aspartine, thaumatin and cyclamate	Nonsugar sweeteners	Noncariogenic

- Interestingly, if there are repeated intakes of sugar during this period in the form of **in between meals**, the pH will fall further and it will take an even longer time to return back to neutrality. The continuous and prolonged fall in the plaque pH results in more tooth demineralization.

Sucrose: The most potent cariogenic carbohydrate

Sucrose is the most important cariogenic carbohydrate. It is disaccharide and forms about one-third of our carbohydrate diet.

- It has the maximum capacity to produce acids and promote tooth decay.
- The caries producing microorganisms, especially the *Streptococcus mutans*, readily use up sucrose to synthesize an **extracellular insoluble polysaccharide** with the help of their enzyme glucosyl transferase.
- The disaccharide bond of sucrose contains enough energy to react with the bacterial enzymes to synthesize extracellular polysaccharide.
- This sticky polysaccharide is called **dextran** and **it helps in adhering or binding the plaque firmly** on to the tooth surface to enable a direct contact between the acids and the tooth and thus cause more tooth decay.
- Sucrose promotes colonization of tooth by ***S. mutans***.
- Its small molecules help it to diffuse readily into the plaque.
- Bacterial metabolism of sucrose is very rapid as compared to any other carbohydrate.
- When sucrose is fermented by cariogenic bacteria and there are production acids, they quickly start to demineralize the tooth.
- Sucrose is also readily converted into **intracellular 'glucan-like' polymers**, which can also be metabolized into acids in future at the time of dietary restrictions of sucrose.

- Besides dextran, other extracellular polysaccharides are also synthesized by the cariogenic bacteria, for example, the **glucan**–synthesized from glucose, and **levan**–from fructose, etc. Fortunately, both of these are soluble and weakly adhering substances; and can be easily removed from the mouth by simple mouth rinses. Therefore, glucan and levan play a far less significant role in caries formation as compared to dextran.
- The role of dietary carbohydrates in the formation of caries can further be established by the fact that, when the dietary sucrose is replaced by **sorbitol, xylitol, mannitol** or **lactitol,** etc. the nonfermentable carbohydrates; the possibility of caries formation is greatly reduced.
- Starches produce little or no caries because they are very slowly diffused into the plaque and they also require extra cellular amylase; to become hydrolyzed before they can be assimilated and metabolized by plaque bacteria.
- Moreover, nonsugar sweeteners, e.g. saccharin, aspartine and thaumatin, etc. are noncariogenic.

ROLE OF MICROORGANISMS IN DENTAL CARIES

Goadby in 1903 stated that caries occurs due to combined action of many common bacteria; some of which are acid producers and some are dentin liquefiers. Since the time of Miller (1889) most investigators acknowledged that microorganisms cause decalcification of tooth by means of carbohydrate fermentation with subsequent acid production.

The common cariogenic microorganisms

- *Streptococcus mutans*
- *Streptococcus sanguis*
- *Streptococcus mitior*
- *Streptococcus salivarius*
- *Streptococcus milleri*
- *Pepto-streptococcus*
- *Lactobacillus acidophilus*
- *Actinomyces israelii*
- *Actinomyces viscosus*
- *Actinomyces nasulandii*

The evidence for the role of bacteria in the genesis of dental caries can further be established by the following facts:

- If the mouth becomes free of bacteria, as in germ free animals, the dental caries will never develop.
- Use of antibiotics effectively reduces the caries incidence in humans as well as in animals.

- Oral bacteria can demineralize tooth enamel *in vitro* and produce lesions similar to the naturally occurring dental caries.
- Specific bacterial groups (known for their cariogenic potential) can be isolated and identified from the carious lesions.

Essential qualities of cariogenic bacteria

- Should be able to produce acids
- Should be able to produce a low pH in the mouth (usually < 5) to demineralize the tooth
- Should be able to survive and continue to produce acid at low levels of pH
- Should be able to attach strongly on to the tooth surface (even the smooth surface)
- Should be able to synthesize insoluble, sticky polysaccharides, e.g. dextran and glucan, etc.

A large number of microorganisms play their individual roles in the development of dental caries and among them the most important one is the *Streptococcus mutans*.

Laboratory culture of *S. mutans*

S. mutans produces a grayish-white colony in glucose agar medium; the colony is about 1 mm in diameter, firm and it typically slides along the surface of the medium. The bacterial colony is distinctive in its appearance of being sunk into the agar, as if it had eaten its way into the medium.

This organism is mostly responsible for the initiation of enamel caries and moreover, it plays at least three very important roles to facilitate caries formation, which are as follows:

- It can readily ferment the dietary carbohydrate to produce acids, which subsequently cause tooth destruction.
- The organism can synthesize **dextran** from sucrose, the latter helps in adhering the plaque bacteria as well as the acids, on to the tooth surface to cause persistent tooth demineralization.
- *Streptococcus mutans* also has the ability to adhere and grow even on hard and smooth surfaces of tooth.

What makes *Streptococcus mutans* the most potent cariogenic bacteria

There are some very important characteristics of *Streptococcus mutans* that give the organism more edge over others in terms of caries production

- *S. mutans* produces acids from fermentation of sucrose, glucose, lactose, mannitol and mucin, etc.
- It is present in large numbers in normal saliva, always ready to attack the tooth as soon as the suitable carbohydrates are available
- *S. mutans* can be isolated in pure culture from the dentin of carious tooth
- It can survive at a pH as low as 4.2
- *S. mutans* synthesizes extracellular insoluble polysaccharide 'dextran'; which helps in adhering plaque bacteria to the tooth surface to enable more tooth decay
- *S. mutans* can produce caries in a tooth in laboratory environment
- It can adhere to acquired pellicle and thus facilitates in plaque formation
- *Streptococcus mutans* also has the ability to adhere and grow even on hard and smooth surfaces of tooth.

Besides *Streptococcus mutans*, other streptococci, which are cariogenic, include *S. sanguis*, *S. mitior*, *S. salivarius*, *S. milleri* and *Peptostreptococcus*, etc.

- The actinomycotic group of organisms namely the *Actinomyces israelii*, *Actinomyces viscosus* and *Actinomyces nasulandii*, etc. are the important organisms that produce caries in the root portions of the teeth. Among these organisms, *A. viscosus* is considered to be the most active agent to cause root caries.
- The *Lactobacillus acidophilus* organisms were considered to be important cariogenic organisms in the past, due to their presence within the carious cavities in large numbers.
- However, recent studies indicate that these organisms cannot adhere on to the smooth surfaces of teeth and are therefore not capable of producing smooth surface caries. However, these organisms are important for the progression of 'dentinal' caries.

- Presence of *Lactobacillus* organisms in the carious cavities in large numbers may also be simply because of their acidophilic nature (they exist comfortably in acidic environments). However, higher *Lactobacillus* counts in saliva also indicate the presence of more active carious lesions in the oral cavity.

ROLE OF ACIDS IN DENTAL CARIES

During the process of caries formation, a large variety of acids are produced in the oral cavity due to the bacterial fermentation of dietary carbohydrates. These acids are lactic acids, aspartic acids, butyric acids, acetic acids, propionic acids and glutamic acids, etc. These acids can cause demineralization of enamel and followed by dentin and eventually cause the tooth decay.

- Metabolism of carbohydrates (especially sucrose) by *Streptococcus mutans* and *Lactobacillus acidophilus* produces organic acids, which result in a highly localized drop in the pH at the 'plaque-tooth interface'.

Important acids which are produced to cause tooth decay in caries

- Lactic acid
- Aspartic acid
- Butyric acid
- Acetic acid
- Propionic acid
- Glutamic acid.

- **A drop in local pH below 5.5 causes demineralization of tooth surfaces**.
- In caries active individuals, the pH at the tooth surface remains below the critical pH of 5.5, for 20 to 50 minutes following a single exposure to sucrose.
- Moreover, it is very important that repeated intakes of sweet snacks in between the meals can result in an almost continuous acid attack on the tooth surfaces.
- Below the critical pH of 5.5, the tooth minerals act as buffers and they loose calcium and phosphate ions into the plaque. This type of buffering activity initially helps to maintain the local pH at nearly 5.5.
- However, when the local pH falls to about 5.0, subsurface demineralization is inevitable in the enamel, which results in the formation of **incipient caries (where the surface of the enamel is intact but it has started to demineralize deep and below the surface enamel,** the process is known as **subsurface demineralization).**

Plaque pH and tooth demineralization

pH 5.5 or above	No demineralization of tooth
pH 5 to 4.5	Subsurface demineralization of enamel
pH 4 to 3	Surface demineralization of enamel

- When the pH is lowered farther and it goes to the level of about 3.0 to 4.0, the surface of the enamel begins to get etched and resorbed. Such types of repeated acid attacks due to prolonged and continuous fall of pH result in cavitations on the tooth surface.

Factors determining the 'rate of acid demineralization' of tooth in caries

- Rate of acid production—Faster the rate more is the decay
- Volume of production of acid—More volume of acid more decay
- Type of acid—Some acids produced by carbohydrate fermentation is strong and some are weak in their tooth demineralizing capacity.
- Degree of fall of pH—Lower the fall of pH greater the decay
- Persistence of acid attack on tooth—Longer the acids remain on tooth greater the decay
- Localization of acids on the tooth surface—Dextran helps to keep the plaque and acids firmly held on to the tooth surface and this cause more decay
- Repetition of acid production (through in between meals)—Means more decay
- Protection of acid if acid on the tooth surface remains under the cover of plaque and does not get neutralized by the buffering action of saliva, it causes more tooth decay
- Surface quality of tooth enamel—Weaker the enamel faster the decay

ROLE OF BACTERIAL PLAQUE IN DENTAL CARIES

Plaque is a thin, transparent film produced on the tooth surface and it consists predominantly of microorganisms suspended in salivary mucins and extracellular bacterial polysaccharides (glucans). There is also presence of desquamated epithelial cells, leukocytes and food debris, etc. in it.

Stages of plaque formation on teeth

- Deposition of cell-free, structureless acquired pellicle.
- Thickening of acquired pellicle due to further deposition salivary glycoproteins following bacterial stimulation.
- Colonization of *S. mutans* and *S. sanguis* within 24 hours.
- Progressive build-up of plaque substance by bacterial polysaccharides.
- Colonization of filamentous and other organisms as the plaque matures.

Acquired pellicle is a component of the dental plaque, which is made by the salivary glycoprotein and is formed just prior to the bacterial colonization.

- One hour after the formation of acquired pellicle, some organisms such as *S. sanguis*, *A. viscous*, *A. naeslundii* and *Peptostreptococcus*, etc. become attached to it. These organisms are called '**pioneering organisms**' in dental caries.
- These initial organisms lack in caries producing potential since they are mostly aerobic in nature and produce very little amount of acid by the fermentation of the carbohydrates.
- As the plaque matures with time, *S. mutans* group becomes more predominant within the plaque. These organisms rapidly metabolize the carbohydrates and produce organic acids.
- As discussed earlier, production of organic acids (mainly the lactic acids) cause drop in the pH at the 'plaque-tooth interface' and this results in enamel demineralization.
- Demineralization of enamel begins in the pH range of 5.0 to 4.5 and with every additional single sucrose exposure or rinse. The pH will be lowered or depressed for nearly another 1 hour.
- The enzyme glucosyl transferase helps in the synthesis of an extracellular matrix, which facilitates the adhering of *S. mutans* to the acquired pellicle because the extracellular matrix makes *S. mutans* colonies more tenacious in nature.

How dental plaque helps in the initiation of dental caries

- It harbors the cariogenic bacteria on the tooth surface.
- Rapid production of high amounts of acids within the plaque occurs through fermentation of carbohydrates by cariogenic bacteria.
- Plaque helps to hold these acids on to the tooth surface for a long duration.
- Increased thickness of plaque does not allow the salivary buffers to enter into it to neutralize the acids produced by the cariogenic bacteria.
- Plaque protects the acids produced by the cariogenic bacteria from getting neutralized in two ways—(a) It has diffusion limiting property that does not allow acids to escape and (b) Moreover, the same property of plaque does not allow the buffering agents from saliva to enter into it and cause neutralization of acids.
- Continued sugar production from bacterial intracellular polysaccharides helps to maintain a low pH and facilities more tooth decay. All these purposes served by the dental plaque enhance the tooth decay.

LIMITATIONS OF ACIDOGENIC THEORY

Although the acidogenic theory of dental caries has got a wide acceptance, it has the following limitations:

- It cannot explain subsurface demineralization.
- It fails to justify the rampant caries.
- It cannot explain the caries in impacted tooth.

PROTEOLYTIC THEORY

- The proteolytic theory of dental caries was first proposed by Gottelib in 1944 and this theory states that, the **proteolytic enzymes liberated by cariogenic bacteria cause destruction of**

the organic matrix of enamel. As a result of that, the inorganic crystals of the enamel get detached from one another and finally the whole structure collapses, leading to a cavity formation.

- The concept of proteolytic theory was further extended by Pincus in 1949 and he proposed that the "sulfatase enzyme" liberated by gram-negative bacilli, hydrolyze the sulfated mucosubstances of enamel matrix and thereby liberate sulfuric acid, glutamic acid and aspartic acid, etc. which dissolve the mineral portion of the enamel.
- The scope of the proteolytic mechanism in initiating the enamel caries is very limited because the organic (protein) content of enamel matrix as such, is very scanty. However, this mechanism can be a more appropriate one in cases of dentinal and cemental caries.

LIMITATIONS OF PROTEOLYTIC THEORY

- The carious lesion cannot be reproduced *in vitro* by the proteolytic mechanism.
- Proteolytic bacteria are very uncommon in the oral cavity.
- This theory cannot explain the role of sucrose, pH and fluoride, etc. in dental caries.

PROTEOLYTIC CHELATION THEORY

The proteolytic chelation theory explains the process of dental caries in the following way, **during caries, first of all proteolytic breakdown of the organic portion of the enamel matrix takes place. Following this, a chelating agent is formed by the combination of proteolytic breakdown products, acquired pellicle and food debris, etc which facilitates tooth decay. The whole process is helped by the bacterial enzymes which facilitates tooth decay.**

The **chelating agent**, which is formed, is **always negatively charged** (mostly due to its protein content) and **it releases the positively charged calcium ions (Ca^{++}) from the enamel or dentin.** This process is called **chelation,** and it eventually results in tooth decay. So, the chelation can be defined as a process that involves the complexing of a metallic ion to a complex substance by a coordinate covalent bond, which results in a highly stable, poorly dissociated and weakly ionized compound called **chelate**.

The proteolytic chelation theory explains that the destruction of the organic matrix of the enamel as well as its mineral parts both occur simultaneously and interdependently.

SUCROSE CHELATION THEORY

Sucrose chelation theory proposes that **'very high concentration of sucrose in the mouth of a caries active individual may result in the formation of complex substances like calcium saccharates and calcium complexing intermediaries, etc. by the action of phosphorelating enzymes'. These complexes cause release of the calcium and phosphorus ions from the enamel and thereby result in tooth decay.**

This theory is unlikely to be a significant because once the sucrose is in the oral cavity, it readily gets metabolized to form acids, and there is hardly any scope for formation of calcium saccharates, etc. Moreover, for the formation of calcium saccharate, a very high level of pH is required, the range which is never achieved in the oral cavity.

AUTOIMMUNE THEORY

The autoimmune theory of dental caries suggests that a few odontoblast cells at some specific sites, within the pulp of a few specific teeth are damaged by the autoimmune mechanisms. For this reason, the defense capacity and integrity of the overlying enamel or dentin in those specific areas are compromised, and they can be the potential sites for caries development in future.

CONTRIBUTING FACTORS IN DENTAL CARIES

A large number of factors influence the caries process directly or indirectly and they are as follows:

Intrinsic factors: Tooth factor

Extrinsic factors: These include the following:

- Saliva factor
- Diet factor

- Systemic factors
- Immunity.

TOOTH FACTOR

Not all the teeth in the dental arch or all surfaces of the individual tooth are equally susceptible to caries. Moreover, the rate of progression of caries is not always equal in every tooth.

Therefore factors influencing the site of attack and the rate of caries progression in a tooth depend upon several factors which are as follows:

Composition of Tooth

- There is an inverse relationship between enamel solubility and the mineral ion concentration of the enamel surface. If the enamel surface is highly mineralized due to the presence of Ca^{++}, F^{-}, Zn^{++} and Fe^{+++}, etc. in higher concentrations, the chance of caries formation becomes less.
- If the solubility of the surface enamel is higher the chance of caries formation is more. It is particularly true that tooth decay is more in case the susceptible tooth has hypomineralized enamel.
- Increased permeability of the enamel surface also increases the possibility of caries development and it can be seen in case of a tooth having hypoplastic enamel.
- A graded increase in the mineral content of enamel with age may account for an increased resistance to caries in older individuals.

Effective Pulp-dentin Complex

If the functional status of the pulp-dentin complex within the tooth remains very sound, the rate of tooth destruction is less. The complex actually resists the progress of caries and subsequent invasion of pulp by forming reparative dentin.

Morphology of Tooth

Presence of deep, narrow and retentive pits and fissures on the tooth surface may contribute to a higher caries incidence. Because these developmental surface defects of a tooth not only favor the colonization of plaque microorganisms but also protect them from the attack of the body's own immune system.

Position of Tooth

The malaligned, rotated or out of position teeth in the dental arch are attacked by caries more frequently as there is more possibility of plaque accumulation in these regions and moreover, these teeth are difficult to keep clean.

SALIVA FACTOR

The saliva factors play a very important role in the prevention of dental caries.

Flow rate: When the salivary flow rate is adequate in the oral cavity, it causes cleaning of the bacteria from the tooth surface by its **flushing action** and thus the chances of caries formation remain less. However, when the salivary flow rate is decreased (xerostomia), the caries incidence becomes higher.

Key salivary factors in dental caries

Factors associated with low caries	Factors associated with high caries
• High flow rate • Proper salivation • Normal viscosity • Buffering capacity • Salivary enzymes • Fluoride action • Salivary immunoglobulins • Remineralization • Direct antibacterial action	• Low salivary flow rate • Desalivation (xerostomia) • Too high or too low viscosity • Lack of salivary buffering action • Salivary glycoproteins may contribute to plaque formation • Sucrose in saliva may be used up by the plaque bacteria to produce caries.

Desalivation: When there is decrease in the amount of salivary secretion, an increased caries incidence is obvious; because saliva helps in cleaning the cariogenic carbohydrates from mouth. That is why patients suffering from **xerostomia** (dry mouth due to decreased salivary secretion) have increased caries susceptibility as compared to a normal individual.

Viscosity: When viscosity of saliva is increased, there will be more and more deposition of plaque on the tooth surfaces since the thick saliva fails to produce adequate cleaning action. On the other hand if the salivary viscosity is too low, the normal contents of minerals and bicarbonates, etc. will be less in it and this type saliva will not be able to produce adequate anticaries functions.

Buffering capacity: High concentrations of salivary bicarbonate ions cause neutralization of acids produced by the cariogenic bacteria by their buffering action and this results in a decrease in the rate of tooth decay. Whenever the buffering action of saliva is suppressed, the acid demineralization of tooth due to caries becomes high.

Moreover, saliva also contains urea and sialine, etc. These chemicals become hydrolyzed to produce ammonia and the later agent can cause rise in the salivary pH. This rise in pH can counter the acid attacks on the tooth surface during the progression of caries. Moreover, the buffering capacity of saliva is often enhanced with increased salivary flow rate.

Salivary enzymes: Salivary 'amylase' causes breakdown of starch (residual carbohydrates) from the tooth surface and make them more soluble. As a result, these are easily washed away from the mouth.

Fluoride action: Saliva acts as a vehicle for fluoride ions, which enter into the plaque and prevent tooth decay.

Salivary immunoglobulins: Salivary immunoglobulins (IgA and IgG) inhibit the cariogenic bacteria especially the *S. mutans*, by facilitating their destruction process through phagocytosis and thus eventually reduce the possibility of caries.

Remineralization of damaged tooth surface: Calcium and phosphate ions present in the saliva help in the partial repair of tooth damaged by caries and this process called remineralization of tooth. Remineralization can control the rate of tooth destruction in caries and this process starts when the salivary pH is above 5.5.

Direct antibacterial action: Several antibacterial agents are found in saliva like lysozyme, thiocyanate, lactoferrin and lactoperoxidase, etc. These agents cause destruction of the cariogenic bacteria by their direct antibacterial action and thereby reduce the caries incidence in the mouth.

ROLE OF FLUORIDES IN THE PREVENTION OF DENTAL CARIES

The fluoride reduces the caries incidence in the following mechanisms:

- During the development of tooth, systemic fluorides cause conversion of the hydroxyapatite crystals of enamel into fluoroapatite crystals and thereby reduce the solubility of enamel; the fluoroapatite crystals are highly resistant to the bacterial induced acid demineralization.
- Fluorides help in the remineralization of incipient carious lesions by redepositing or by reprecipitating the mineral ions lost from the tooth surface during acid–demineralization.
- Fluorides prevent the activity of the enzyme "glucosyl transferase" which is essential for the formation of extracellular polysaccharides (dextran, levan, etc.) and thereby reduce the bacterial (cariogenic) adhesion on to the tooth surface.
- The fluoride ions can limit the rate of carbohydrate metabolism by the cariogenic bacteria and thereby reduce the acid attacks on the tooth.
- Fluorides inhibit the enzyme 'enolase' which is essential for carbohydrate metabolism; and thus prevent the carbohydrate degradation and acid production.
- In high concentrations, the fluoride ions can be directly toxic to the *Streptococcus mutans.*

DIET FACTOR

Physical Nature of Diet

If the diet contains sufficient amount of fibrous foods that help to keep the teeth clean as well as stimulates the salivary flow, the chances of caries formation will be less. Whereas more and more intake of soft and sticky foods increases the possibility of caries development.

Composition of the Diet

- Presence of phosphates in the diet (either organically bound or inorganic) can reduce the incidence of caries.
- Traces of molybdenum and vanadium in the diet may reduce the incidence of caries.
- The diet that contains adequate amounts of vegetables, vitamin (A, D, K and B-complex) and minerals, etc. is often associated with a low caries incidence.
- Increase in the proportion of fat in the diet may cause reduction in the cariogenic effect of sugar.

SYSTEMIC FACTOR

Some people hereditarily have an increased tendency to develop caries while other people show just the reverse tendency.

IMMUNITY

Immune mechanism plays an important role in the prevention of caries in humans. It is associated with the formation of serum and salivary antibodies as well as initiation of some degrees of cell-mediated immune response. It is important to mention that most of the immune-mediated protective activities are specifically directed against the *S. mutans* organisms, which are considered as the most important bacteriologic agents for the causation of dental caries.

Experimental immunization of rats and monkeys with *S. mutans* using both live and dead organisms as well as cell wall preparations, has shown to produce the following:

- IgG, IgA and IgM clones of antibodies in the serum.
- It induces some cell-mediated immune response.

Both of these mechanisms result in a significant reduction of caries.

The immune-mediated prevention of caries is mostly associated with the reduction in the number of *S. mutans* organisms in plaque. The humoral and cell-mediated immune systems gain access into the oral cavity either via the gingival cervicular fluid or via the saliva.

- The salivary immune mechanism probably acts through secretory IgA, which prevents *S. mutans* from adhering to the tooth surface.
- The gingival crevicular immune mechanism involves both humoral and cell-mediated immune systems and therefore, exerts a strong immunologic response.
- In crevicular immune system, the immunoglobulins (IgG, IgM and IgA), complements, neutrophil leukocytes, sensitized lymphocytes and macrophages, etc. are secreted through the gingival crevicular fluid and reach the tooth surfaces.
- The IgG antibodies act as opsonins, they facilitate phagocytosis and cause death of the *S. mutans* by neutrophil leukocytes and macrophages.
- Experimental evidences suggest that immune activity exerted by gingival crevicular system is much stronger than the response obtained through the salivary immune system.

CLINICAL ASPECTS OF DENTAL CARIES

CLINICAL TYPES

Pit and Fissure Caries (Fig. 9.1A)

- This type of lesion occurs in the developmental pits and fissures of the teeth (especially if these areas are deep, narrow and retentive in nature).
- The teeth and their specific areas or surfaces affected by the pit and fissure caries include occlusal surfaces of molars and premolars, buccal and lingual surfaces of molars and lingual surfaces of maxillary incisors.
- The lesions usually appear brown or black, with little softening and opaqueness of the surface. When the lesion is examined by a fine

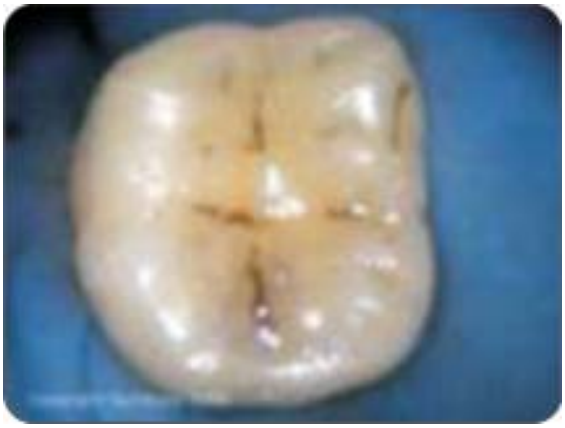

Fig. 9.1A: Pit and fissure caries

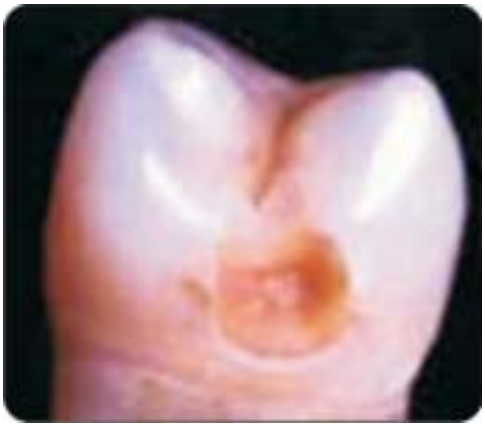

Fig. 9.1B: Smooth surface caries

explorer tip, a "catch point" is often felt, where the explorer tip catches the area.

- The lesions are smaller in the beginning but become wider as they spread towards the dentin due to the typical orientation of the enamel rods.
- When the lesions reach the dentinoenamel junction (DEJ), they spread laterally to cause undermining of the enamel.
- The enamel directly bordering the pit or fissure may appear opaque and bluish-white as it becomes undermined.

Incipient Caries

Definition

Initial carious lesion limited to the enamel is called incipient caries and is characterized by a virtually intact surface but a porous subsurface.

- This type of carious lesions are characterized by the presence of an intact enamel surface, but there is destruction of the enamel below the surface layer which is called "subsurface demineralization".
- Clinically, incipient caries presents a "chalky-white" appearance of the tooth surface and it is only found when the surface of the tooth is dry and the typical chalky-white condition disappears if the surface of the tooth becomes wet.
- The incipient caries is a reversible process and the lesion can be cured due to remineralization by salivary mineral ions.
- Incipient caries can be prevented by topical fluorides, which help to maintain the integrity of enamel undermined by dentinal caries.

Smooth Surface Caries (Fig. 9.1B)

- This type of carious lesion occurs in relation to the smooth surfaces of teeth, e.g. proximal surfaces or gingival areas of the buccal and lingual aspect of tooth.
- Smooth surface caries most commonly occurs in the proximal surface of the teeth just below the contact point.
- The lesion beings as a well-demarcated, chalky-white opacity of enamel with no loss of continuity of the surface.
- The white spot lesion becomes pigmented yellow or brown and it often extends buccally and lingually.
- The surrounding enamel becomes bluish white as the lesion continues to progress.
- The surface of the affected enamel becomes rough and later on, there is formation of a cavity.

Rampant Caries (Fig. 9.1C)

This is an acute fulminating type of carious process, which is characterized by simultaneous involvement of multiple number of teeth (may be all teeth) in multiple surfaces.

- Rapid coronal destruction occurs within a short span of time, causing early involvement of the pulp.

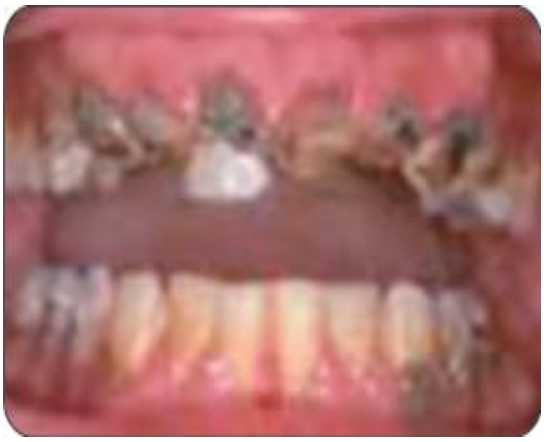

Fig. 9.1C: Rampant caries

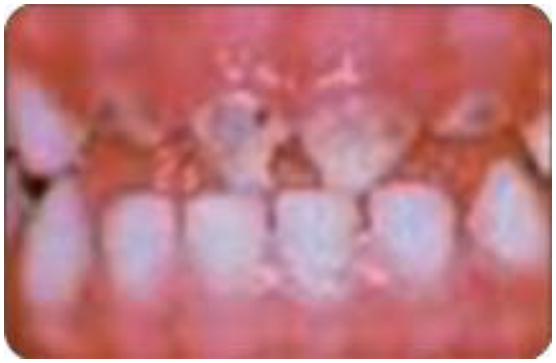

Fig. 9.1D: Nursing bottle caries

- The common age of occurrence of rampant caries is about 4 to 8 years for the deciduous teeth and 11 to 19 years for the permanent teeth.
- Interestingly, the rampant caries can occur in persons with no previous history of dental caries and in those persons who maintain a good level of oral hygiene regularly.
- Moreover, rampant caries attacks those surfaces of teeth, which are otherwise considered immune to the disease.

Nursing Bottle Caries (Fig. 9.1D)

- This is also another type of acute carious lesion, which occurs among those children who take milk or fruit juices by the nursing bottle, for a considerably longer duration of time, preferably during sleep.
- As the child takes large amounts of easily fermentable sugars along with the milk, the sugar facilitates the cariogenic bacteria to produce caries at a rapid pace by fermenting those sugars.
- Nursing bottle caries commonly occurs in the upper anterior teeth (as these are constantly coming in contact with the sweetened milk); while the lower teeth are not usually affected as they remain under the cover of the tongue.
- Both the nursing bottle caries and rampant caries cause early pulp involvement because they spread at a very rapid pace and as a result, the pulp hardly gets any time to protect itself by forming reparative dentin.

Chronic Caries

This type of caries progresses at a slower pace and it rarely causes pulp involvement (unless the tooth is left untreated for many years) because the pulp gets sufficient time to produce secondary dentin or reactionary dentin to protect itself.

Arrested Caries (Fig. 9.1E)

Arrested caries is a lesion whose progression is ceased after the initial development. It can occur both in enamel and in dentin.

Arrested caries of enamel

Arrested caries in enamel may occur when the carious process stops before cavity formation. It occurs when the adjacent carious tooth (from which the disease has actually spread to this new tooth) is lost or is extracted, so that the carious lesion in the new tooth becomes easily accessible for cleaning and plaque control measures. It is commonly seen in smooth surfaces of tooth. Remineralization occurs from saliva or due to topical fluride applications.

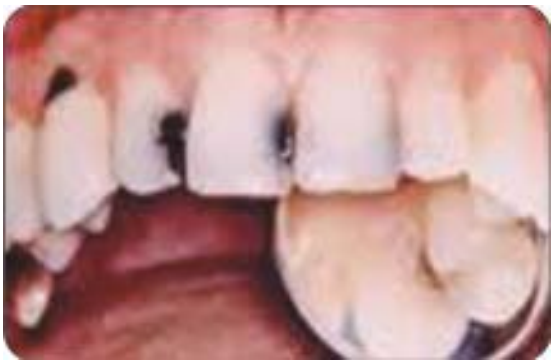

Fig. 9.1E: Arrested caries

Arrested caries of dentin

The arrested caries of dentin usually occurs when a carious cavity becomes wide open; so that it gets exposed to the cleaning measures like tooth brushing, salivary secretions and mastication, etc. The arrested caries presents a hard, black or brown-colored dentinal surface at its base (**eburnated dentin**). Its surface is highly mineralized due to remineralization from oral fluids and has increased fluoride content.

Recurrent Caries

Recurrent caries refers to a carious lesion that begins around the margins or at the base of a pre-existing defective restoration.

Forward Caries

When a carious lesion progresses unidirectionally from enamel into the dentin and pulp, it is called a forward caries.

Backward Caries

These lesions also initially progress from enamel into the dentin, where they spread laterally and involve a wide area. Later on, these lesions proceed in a backward direction from dentin back to enamel and affect the enamel once again at a different location.

Root Caries

These are carious lesions, which involve the cemental wall of the exposed root surfaces of teeth.

Important features of root caries (Fig. 9.1F)

- The development of such lesions is preceded by exposure of the roots of the affected teeth in the oral environment either due to aging or due to gingival recession.
- Because of the roughness of the cemental wall, plaque accumulates readily in the absence of adequate oral hygiene measures and once the root caries begin's it progresses very fast.
- Cementum is invaded along the direction of 'Sharpey's fibers' and microorganisms spread along the incremental lines.
- Cementum is destroyed beneath the plaque over a wide area.

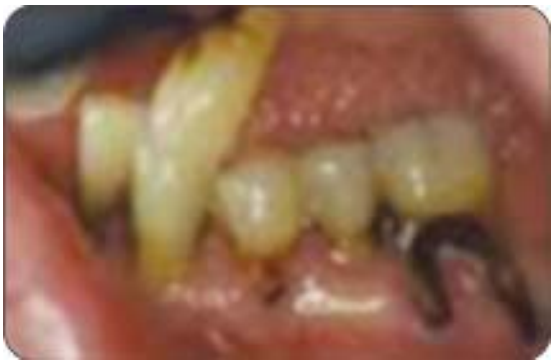

Fig. 9.1F: Root caries

- The dentin is progressively destroyed by a combination of both demineralization and proteolysis.
- Involvement of pulp occurs within a few days (mostly because of the softer nature of the cementum and dentin).
- Clinically, these lesions are extensive, shallow and saucer-shaped, with ill-defined margins.
- The actinomycotic groups of organisms are mostly responsible for the causation of root caries. However, *S. mutans* and *Lactobacillus acidophilus*, etc. may also be associated with this disease.
- Microradiograph reveals subsurface demineralization of the root, which extend to the dentin. Surface remineralization is also seen in some areas.
- The lesions often have soft surfaces with brownish discoloration of the affected area.
- There may be formation of sclerotic dentin as the caries progresses into the dentin from cementum.
- Sometimes, the carious lesion may encircle the entire root of the affected tooth.

Radiation Caries

Patients receiving large doses of radiation for the treatment of malignant lesions in the head and neck region, often develop a specific type of large "caries-like lesions" in the cervical areas of the teeth. These lesions begin a few weeks to few months after radiotherapy. They often surround the entire crowns of the affected teeth, gradually weaken them and even sometimes can cause amputations of tooth.

The exact cause of radiation caries is not known, but it may be due to the reduced salivary secretions, secondary to the radiotherapy.

RADIOLOGICAL FEATURES OF DENTAL CARIES

Radiographs are often (not always) helpful in the detection of dental caries and usually the intraoral periapical (IOPA), panoramic and bitewing radiographs are advised for this purpose.

The bitewing radiographs are especially indicated for the detection of proximal caries. Usually, the pit and fissure caries radiographically appears as a "triangle-shaped" radiolucent area, with its base located towards the dentinoenamel junction. On the other hand, the smooth surface caries also produces a triangle shaped radiolucent area, but its base is located towards the surface of the tooth.

In these lesions if the enamel radiolucency is extending up to the DEJ, it is considered that the tooth will have a cavity and there is definite involvement of the underlying dentin. Whereas if the enamel radiolucency does not extend to the DEJ, there should be no clinically detectable cavity in the tooth.

The root caries on the radiograph usually produces a U-shaped radiolucent area with irregular margin.

HISTOPATHOLOGICAL ASPECT OF DENTAL CARIES

ENAMEL CARIES

For the microscopic examination of enamel caries, ground section preparations are used because the decalcified sections of enamel become useless owing to the very high concentration minerals in this tissue. The ground section preparation is examined by transmitted or polarized lights.

HISTOLOGIC FEATURES OF EARLY ENAMEL CARIES (FIG. 9.2)

- There will be loss of interprismatic or interrod substances with increase in the prominence of the enamel rods.
- Appearance of transverse striations of the enamel rods due to segmental demineralization.
- Dark lines often appear at right angles to the enamel rods, suggesting segments.

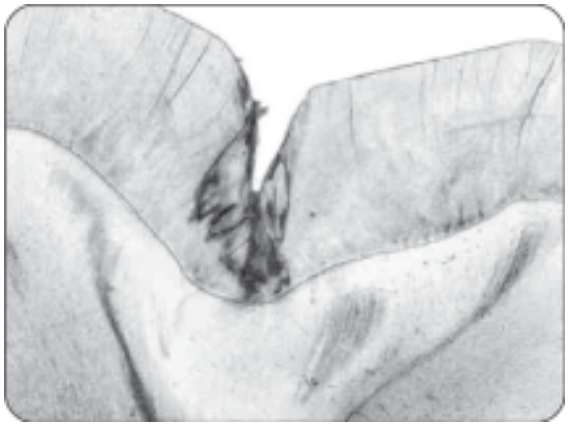

Fig. 9.2: Photomicrograph of enamel caries

- Accentuation of the incremental striae of Retzius often occurs.

HISTOLOGIC FEATURES OF ADVANCED ENAMEL CARIES

Advance enamel caries microscopically presents several zones in the tissue, which are as follows:

Zone I: Translucent Zone

- It is the deepest zone in the carious enamel and is the first recognizable histological change at the advancing front of the lesion.
- This zone is slightly more porous than the normal sound enamel and contains 1% by volume of spaces (the pore volume), which is 0.1% in sound normal enamel.
- The pores are larger than the usual smaller pores seen in normal enamel. Dissolution of mineral occurs mainly at the junction of prismitic and interprismitic enamel.

Zone II: Dark Zone

The dark zone is located just superficial to the translucent zone and its dark appearance is due to the excessive demineralization of the enamel due to caries.

- This zone is narrower in rapidly advancing caries and it is wider in slowly advancing lesions.
- This zone contains 2 to 4% pore volume.
- Some pores are larger but other pores are smaller than those of the translucent zone.

- This zone also reveals some degrees of remineralization of the carious enamel.

Zone III: Body of the Lesion

This zone is situated between the dark zone and the surface layer of enamel, and it represents the area of greatest demineralization.

- It has a pore volume of between 5 to 25%.
- This zone contains apatite crystals larger than those of the normal enamel.
- Large crystals result from reprecipitation of minerals dissolved from deeper zones.
- With continuing acid attacks on the enamel, there may be further dissolution of minerals both from the periphery of the apatite crystals and their cores.
- The lost minerals in the enamel are often replaced by unbound H_2O and organic matters.
- This zone shows increased prominence of the striae of Retzius.

Zone IV: Surface Zone

Initially, the surface zone of a carious enamel remains comparatively unaffected despite subsurface demineralization and also to the surface remineralization.

- It is about 40 µm thick.
- However, in untreated cases the surface enamel often gets destroyed and a cavity is formed.
- Surface remineralization results from active precipitation of mineral ions derived from both plaque and the saliva.

Ultrastructural studies (of enamel caries): Ultrastructural studies suggest that the initial dissolution of enamel begins along prism boundaries and later on there is demineralization occuring both within and between the prisms, which results in an increase in the intercrystalline gap.

Along with dissolution there is also remineralization of enamel and change in enamel crystal structures due to the combined effects of demineralization and remineralization of enamel.

HISTOLOGY OF DENTINAL CARIES (CARIES IN DENTIN)

The dentinal caries histologically presents five zones in the tissue, which are as follows:

Zone I (Normal Dentin)

- This zone represents the innermost layer of the carious dentin and here the dentinal tubules appear normal.
- There is evidence of fatty degeneration of the Tomes processes.
- No crystals in the lumen of the tubules.
- No bacteria in the tubules.
- Intertubular dentin has normal cross-banded collagen and normal dense apatite crystals.

Zone II (Sub-transparent Dentin)

- This is the zone of dentinal sclerosis and it is characterized by the deposition of very fine crystal structures within the dentinal tubules at the advancing front.
- Superficial layer shows areas of demineralization and damage of the odontoblastic processes.
- No bacteria in the tubules.
- This dentin is capable of remineralization.

Zone III (Transparent Dentin)

- This zone appears **transparent** and this is because of the demineralization of dentin due to caries.
- It is softer than normal dentin.
- Further loss of mineral ions from intertubular dentin.
- Large crystals within the lumen of the dentinal tubules.
- No bacteria in tubules.
- Cross-banded intertubular collagen still intact.
- This zone is capable of self-repair and remineralization.

Zone IV (Turbid Dentin)

- This zone is called the "turbid dentin" and is **marked by the widening and distortion of the dentinal tubules, which are packed with microorganisms**. There is very little amount

of mineral present in the dentin and moreover denaturation of collagen fibers also takes place.
- This zone cannot undergo self-repair or remineralization.
- Must be removed before restorative treatment.

Zone V (Infected Dentin)

- This is the outermost zone of the carious dentin and is characterized by complete destruction of the dentinal tubules (as a result of their severe expansion due to accumulation of a large number of microorganisms and their by-products).
- The expanded tubules cause compression and bending of the adjacent tubules and eventually destroy them.
- In this zone, the areas of decomposition of dentin, which occur along the direction of the dentinal tubules, are called the **liquefaction foci of Miller**.
- In some areas, the cariogenic microorganisms spread laterally and large bacteria-filled clefts develop at right angles to the direction of the tubules due to decomposition of dentin. These clefts are called the **transverse clefts**.
- The mechanism of formation of transverse clefts is not clearly known, they may follow the course of incremental lines, or result from the coalescence of liquefaction of adjacent tubules.
- Transverse clefts may also arise by extensive proteolytic activity along the interconnecting lateral branches of odontoblastic processes.
- In zone V, bacteria may no longer remain confined within the dentinal tubules and they invade and destroy the peri- and intertubular dentin. In the process, the entire dentinal structure becomes destroyed (Fig. 9.3).

PROTECTIVE RESPONSES OF DENTIN AND PULP AGAINST CARIES

Hectic odontoblastic activity takes place in the dentin-pulp complex in order to protect the tooth from the invasion of caries.

Following are the protective responses from the pulp-dentin complex:

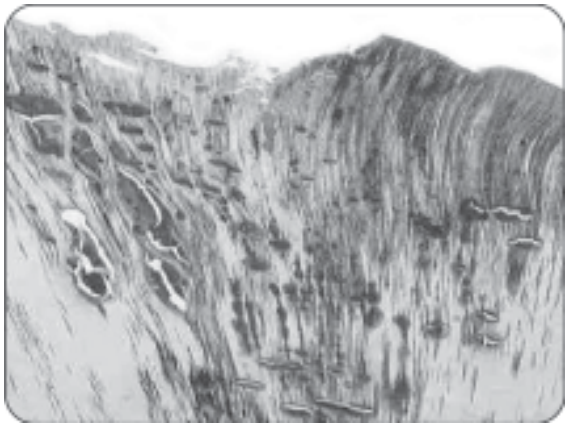

Fig. 9.3: Photomicrograph of dentinal caries showing bacterial invasion within the dentinal tubules

TUBULAR SCLEROSIS

Peritubular dentin reduces the size of the individual dentinal tubules and thus prevents the bacterial penetration.

REGULAR REACTIONARY DENTIN

Reactionary dentin develops on regular basis as a result of localized, nonspecific mild irritation to the odontoblast cells. However, this dentin seems to develop mostly during caries attack in a tooth.

In regular reactionary dentin a layer of dentin forms at the surface of the pulp chamber deep to the progressive front of dentin caries and it contains normal tubular structures.

It is often hypermineralized as compared to the primary dentin and it delays the pulp exposure by increasing the depth of the tissue between carious dentin and the pulp.

IRREGULAR REACTIONARY DENTIN

This type of dentin forms under moderate to severe insult by caries and this irregular reactionary dentin contains only few irregularly shaped and tortuous tubules. Sometimes, the dentinal tubules can be even absent.

DEAD TRACTS

The dead tracts form when the odontoblast cells die and their tubules become sealed off. They often prevent the further progression of caries in dentin towards the pulp.

CARIES ACTIVITY TESTS

A number of caries activity tests have been evolved to help detect the presence of oral conditions associated with increased risk of caries. However, no single test can be relied upon to predict the caries susceptibility of a person with a high degree of confidence. Caries activity tests are more useful than clinical examinations since these can predict the need for preventive treatment before the caries has actually started.

SNYDER TEST

Snyder test is the qualitative determination of acidogenic organisms in the mouth; it measures the ability of salivary microorganisms to produce organic acids from a carbohydrate medium. **Glucose-agar media containing an indicator dye (bromocresol green) is used for this test.** The indicator dye changes from green to yellow in the range of pH from 5.4 to 3.8.

Paraffin-stimulated saliva (0.2 ml) is added into the medium, change of the medium from green to yellow is indicative of the degrees of caries activity.

Results

If the color of the medium changes from green to yellow within 24 hours, caries susceptibility of the patient should be considered very high.

If the similar color change occurs within 48 hours, the patient is considered to have a definite caries susceptibility.

If the color change occurs in 72 hours, a limited caries susceptibility is indicated.

Finally, if the color change does not occur in 72 hours, the patient should be considered caries immune.

SALIVARY REDUCTASE TEST

Salivary reductase test measures the activity of reductase enzyme present in salivary bacteria. Paraffin-stimulated saliva is collected in a plastic container and an indicator dye "diazoresorcinol" is added to it, which colors the saliva blue.

The reductase enzyme liberated by the cariogenic bacteria causes color changes in the medium from blue to other colors, which indicates the caries "conduciveness" of the patient.

Results

Changes of color	Caries conduciveness
No change in color in 15 minutes	Nonconducive
Color changes from blue to orchid in 15 minutes	Slightly conducive
Color changes from blue to red in 15 minutes	Moderately conducive
Color changes from blue to red immediately on mixing	Highly conducive
Color changes from blue to colorless in 15 minutes	Extremely conducive

SALIVARY BUFFERING CAPACITY TEST

Salivary buffering capacity test is a chair side test to measure the buffering capacity of the saliva. A special kit called "dento buff" is used for this test, which contains a small vial of weak HCl and a color indicator chart.

If one milliliter saliva is put into the acid solution, its pH will rise gradually depending upon the buffering capacity of the saliva, and this change of pH is measured by the accompanying color chart.

Results

If the buffering capacity of saliva is normal, the final pH of the solution will rise up to 5 to 7, and if the buffering capacity is low, the pH will rise up to 4 only.

However, it is understood that more is the buffering capacity of saliva, less will be the acid demineralization of the tooth due to caries.

MICROBIOLOGICAL TEST

Microbiological test helps to measure the number of *Streptococcus mutans* and *Lactobacillus acidophilus* per microliter of saliva.

Two samples of paraffin-stimulated saliva (1 ml each) are collected from the patient, these are diluted 10 times and each is cultivated in two different special media: (i) Rogosa's SL agar medium for *Lactobacillus,* and (ii) Mitis salivarius agar medium for *Streptococcus mutans.*

After incubation, the number of colonies that developed in two separate media are counted and then are multiplied by 10 (dilution factor) to estimate the number of bacteria in 1 ml of saliva.

Result

If the count is more than 10,00,000 *S. mutans* and more than 1,00,000 *L. acidophilus*, the caries susceptibility of the individual should be considered very high.

If the count is less than 1,00,000 *S. mutans* and less than 1,000 *L. acidophilus*, the individual is considered less susceptible to caries.

S. MUTANS DIP-SLIDE METHOD

This test measures the number of *S. mutans* colonies in modified MSA; the saliva is collected for 5 minutes and is poured over the agar-coated slide. Slides are then dried and bacitracin disks are placed in the middle of the inoculated agar about 1 cm from each other. The slide is then incubated in a tube containing CO_2 for 48 hours. A zone of inhibition 10 to 20 mm in diameter is formed around each bacitracin disk. *S. mutans* presents small blue colonies with the zone of inhibition.

Result

The colony density is compared with a model chart and classified as 0 (negligible), 1 (less than 100,000), 2 (100,000-1000, 000) and 3 (more than 1000,000) *S. mutans* colony forming units/ml of saliva.

ENAMEL SOLUBILITY TEST

Popularly known as 'Fosdick calcium dissolution test'; in this test patient's saliva is mixed with glucose and thereafter measured amount of (in milligram) powdered enamel is mixed with it and kept for 4 hours.

Acid which is produced due to fermentation of glucose by the cariogenic bacteria present in the saliva cause is dissolution of powdered enamel. The test measures the amount of enamel powder dissolved during the 4-hour period.

METHODS OF CARIES PREVENTION

The dental caries can be prevented by the following methods:

Limit substrate

- Eliminate sucrose from the diet or reduce its amount.
- Eliminate sucrose from the "in-between" meals and snacks.

Modify oral microflora

- Bactericidal mouth-rinse by chlorhexidine
- Topical fluoride treatments
- Antibiotic treatment by vancomycin and tetracyclines

Plaque disruption—by brushing and floosing, etc.

Modify tooth

- Systemic fluorides
- Topical fluorides
- Maintain a smooth surface of the tooth

Stimulate salivary flow

- Eat noncariogenic fibrous foods that require lots of chewing.
- Use sugarless chewing gums.
- Administer sialogogues

Restore tooth surface

- Restore all cavitated lesions
- Seal pits and fissures at caries risk
- Correct all defects, e.g. marginal crevice, proximal overhangs.

CARIES VACCINE

Dental caries fulfills the criteria of an infectious disease and the possibility of preventing it by vaccination has been persuaded over a long period of time. The rationale is that immunization with *Streptococcus mutans* should induce an immune response, which might prevent the dental caries in the following ways:

- It will prevent the ability of the microorganisms to colonize on to the tooth surface.
- It can alter the pattern of polysaccharide metabolism by the bacteria and thereby reduce their adhering capacity on to the tooth surface.
- It can reduce ability of microorganisms to produce acids also.
- It can reduce caries by helping in the process of killing the cariogenic microorganisms.

The caries vaccines are usually given at the age of about 6 months, before the eruption of the deciduous teeth. Oral administration or subcutaneous injection of killed *Streptococcus mutans* can induce the formation of specific IgA, IgG and IgM in the blood.

Passive immunization against caries can also be done by injecting specific IgG class of antibody against the *S. mutans*.

Although the caries vaccine is theoretically very convincing, it has failed to gain a wide range of acceptance because these vaccines produce some cardiotoxicity in humans by cross-reacting with the heart tissue.

The enzyme glucosyl transferase converts sucrose into glucans, which are important for accumulation of *S. mutans* on the tooth surfaces. Antibodies against glucosyl transferase enzyme have been tested in experimental animals and it has been observed that these antibodies can reduce the accumulation of plaque and the incidences of caries.

However, this mechanism is more effective in rodents and it has got little effect on primates.

Experimental Caries in Animals

Dogs have been used as experimental animals for producing experimental caries; however, no caries could be produced in this way probably because dogs are naturally immune to caries.

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CHAPTER 10

Diseases of Dentin-Pulp Complex and Periapical Tissues

PULPAL DISEASES

Dental pain is probably one of the most common sufferings as experienced by patients with various dental diseases. Large numbers of patients take refuse to the dentist only when they are cornered by the misery of pain in the tooth.

Dental pulp has the unique importance in this regard, as it is the main component part of tooth, where the pain actually begins form. Pulp is the soft delicate connective tissue that occupies the central portion of the tooth and it has got two parts namely the pulp chamber (the coronal portion) and the root canals (the radicular portion).

The cellular constituents of pulp include the odontoblasts cells (which form dentin) the fibroblasts (which form and maintain the pulp matrix) and undifferentiated mesenchymal cells (from which the connective tissue cells of the pulp are derived) besides this, dental pulp also contains macrophages and lymphocytes. The macrophages remove bacteria from pulp and interact with other inflammatory cells during inflammation. The lymphocytes (mainly–T lymphocytes) in the dental pulp are associated with immune defense systems. The extracellular component of pulp or the pulp matrix consists of collagen fibers and ground substance. The fibers found in the pulp are mainly the type I and type III collagen in about 55:45 ratio. The ground substance in pulp is composed of glycosaminoglycans, hyaluronic acid, chondroitin sulfate, glycoproteins and water. The function of ground substance is to support the pulpal cells and to act as the medium of transport for nutrients and metabolites. Beside the afferent and efferent blood vessel, the pulp is richly innervated by numerous nerve fibers, which enter the pulp through the apical foramina. The nerve bundle entering the pulp consists mainly of sensory fibers of the trigeminal (fifth cranial) nerve and sympathetic branches from the superior cervical ganglion. Each bundle contains both myelinated and non-myelinated axons.

The myelinated fibers are of two types namely the Aα fibers and Aβ fibers, whereas the non–myelinated fibers are designated as C-fibers. Physiologically the Aα fibers are responsible for transmitting the sharp localized pain in the pulp and the Aβ fibers are responsible for transmitting the mechanical, thermal and tactile sensations. The C-fibers are associated with the transmission of dull, diffuse pain in the dental pulp.

DENTIN-PULP COMPLEX

Dentin is the vital and cellular hard tissue, ultimately and inseparably related to the ground substance to the dental pulp. It is important to note that the dentin and the pulp together act as a unit called the "Dentin-Pulp complex", while responding to the injurious stimuli of various nature in the tooth.

ETIOLOGY OF PULPAL DISEASES

A large number of factors causing injuries to the dentin-pulp complex have been identified, which may be of either acute or chronic in nature. As a general rule, the response to the injurious stimuli, which can cause damage or necrosis to cells varies with the stimulus intensity and with the defense capacity of the body.

The dentin-pulp complex responses to injuries or stimuli in similar ways to other vital tissues elsewhere in the body but some aspects of its responses are the consequences of its unique structure. As the pulpal tissue is lying within the solid confinement of dentinal walls and because its entire blood supply depends upon the smaller blood vessels passing through the tiny apical foramina, (often it makes the pulpal tissue a little

more extravulnerable) moderate degree of injury to pulp often elicits an exaggerated amount of damage.

Factors causing injury to the pulp

A. Physical Factors

Acute Injury

- Accidental blow to the tooth.
- Heating due to grinding.
- Cavity preparation without water spray.
- Vigorous polishing with rotary instruments.
- Root planning in periodontal therapy.
- Large metallic restoration with inadequate insulation.

Chronic Injury

- Attrition due to abrasive foods or bruxism.
- Abrasion due to abnormal tooth brushing.

B. Chemical Factors

Medicaments or materials applied to dentin surface may cause damage to the pulp by diffusion through the dentinal tubules.

C. Microbial Factors

- Dental caries with bacterial invasion of dentin and pulp.
- Bacterial invasion into the pulp from a fractured tooth, where the dental pulp is exposed to the oral environment.
- "**Anachoretic infection**" of the pulp occurs, when bacteria present in the circulating bloodstream tend to accumulate in the pulp and cause infection.

CLASSIFICATION OF THE PULPAL DISEASES

Inflammatory Diseases

- Focal reversible pulpitis.
- Acute pulpitis.
- Chronic pulpitis.
- Chronic hyperplastic pulpitis.

Other Miscellaneous Conditions of the Pulp

- Aerodontalgia
- Necrosis
- Reticular atrophy
- Calcifications
- Pulpal metaplasia.

RESPONSE OF DENTIN AND PULP TO INJURIOUS STIMULI

Being a vital and cellular tissue, dentin always plays a major role in protecting the dental pulp from various injurious stimuli. The dentinal activity that helps to safeguard the pulp from noxious stimuli is as follows:

I. Indirect pulpal response through dentinal changes.
II. Direct pulpal response.

INDIRECT PULPAL RESPONSE THROUGH DENTINAL CHANGES

It is achieved through two processes:

A. Dentinal sclerosis
B. Formation of reparative dentin.

A. *Dentinal Sclerosis (Transparent Dentin)*

- It is produced by the rapid laying down of peritubular dentin.
- Dentinal sclerosis reduces dentin permeability and thereby minimizes the risk of pulpal damage from chemical or bacterial agents.
- Crystals of calcium phosphate may also be deposited within the dentinal tubules as a response to slowly progressing caries.
- Dentinal sclerosis can also occur as a normal aging process.

B. *Reparative Dentin*

- Reparative dentin is produced only by those odontoblast cells, which are directly affected by the injurious stimuli, and not by the entire odontoblast cells of the dental pulp.
- If the intensity of the injurious stimulus is high, the reparative dentin is deposited rapidly and exhibits sparse, irregular tubular pattern with frequent cellular inclusions.
- When the stimulus is less active, reparative dentin is deposited less rapidly with regular tubular pattern and minimum cellular inclusions.
- In most of the areas, there is no continuity between dentinal tubules of reparative dentin and the overlying primary or secondary dentine. This minimizes dentin permeability and provides more protection to the pulp.

DIRECT PULPAL RESPONSE TO INJURIOUS STIMULI

- The pulpal tissue tries to eliminate or neutralize the damaging factors and initiate tissue repair.
- Cellular damage to the pulpal tissue results in the release of vasoactive and chemotactic mediators in the area.
- Vasoactive mediators produce vasodilatation and the chemotactic agents attract specific inflammatory cells to the injured tissue.
- Pulpal tissue also produces immunoglobulines, e.g. IgG, IgM, IgA and complement C3 and C4 in response to the bacterial antigens of dental caries.

FOCAL REVERSIBLE PULPITIS

Focal reversible pulpitis or pulp hyperemia is a mild, transient, localized inflammatory reaction in the pulp, which can be treated by conservative means, without involving any form of direct pulp therapy.

Etiology of focal reversible pulpitis

- Slowly progressing chronic carious lesion.
- Stimuli of short duration, e.g. cutting dentin while cavity preparation.
- Metallic restoration without proper thermal insulation.
- Chemical irritation to the pulp (e.g. acid etching in cervical margin of tooth).
- Excessive pressure by orthodontic appliances.f. Severe attrition or abrasion of tooth with minimal dentin thickness.

CLINICAL FEATURES

- The tooth with focal reversible pulpitis is **sensitive to thermal changes**, especially to cold.
- Pain often results while drinking cold fluids or when ice or cold air is applied to the tooth.
- The pain is of very short duration and it disappears as soon as the thermal irritant is withdrawned.
- Pain also results when the tooth is exposed to extremely high temperatures.
- **Young people develop focal reversible pulpitis more often than the older individuals** because of the more reparative capacity of the pulp tissue among the former group.
- Pulpal stimuli, which cause reversible pulpitis in young people often causes irreversible pulpitis to the older individuals because of the less pulpal tissue viability.
- The affected tooth responds to stimulation by electric pulp tester at a lower level of current (including a lower pain threshold) when compared with an adjacent normal tooth.
- The involved tooth often has large carious lesions or restoration with improper insulation.

HISTOPATHOLOGY

Histologically, focal reversible pulpitis presents the following features (Fig. 10.1):

- Acute inflammatory reaction in the pulp limited to the odontoblastic or subodontoblastic regions, adjacent to the irritated dentinal tubules.
- Dilatation of pulpal blood vessels with increased vascular permeability.
- Edema in the pulp with infiltration by the polymorphonuclear leukocytes in the area.
- Odontoblast cell nuclei may be displaced into the dentinal tubules due to either increased local tissue pressure or due to abnormal dentinal fluid movements during injury.
- Few odontoblast cells could be damaged in the localized area of injury.
- Thrombosis of pulpal blood vessels may occur in some cases.

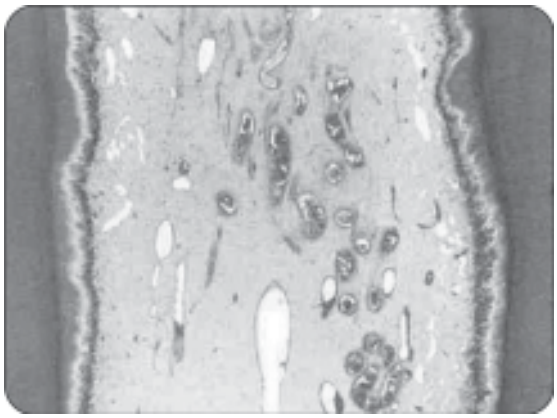

Fig. 10.1: Photomicrograph of focal reversible pulpitis

- Repair takes place by redifferentiation of odontoblast cells, which are damaged and sometimes with deposition of reparative dentin.

TREATMENT

Treatment of focal reversible pulpitis is mostly directed towards elimination of the primary irritating factors and restoration of tooth wherever necessary.

Reversible pulpitis due to dental caries is usually treated by the following means:

- Effective dietary change.
- Sealing of the exposed dentinal surface.
- Excavation of carious dentin followed by placement of a suitable dressing material (e.g. zinc oxide–engenol).

ACUTE PULPITIS

Acute pulpitis is an irreversible condition characterized by acute, intense inflammatory reaction in the pulpal tissue.

MODE OF DEVELOPMENT

Acute pulpitis can occur in the following pathways:

- As an extension of the focal reversible pulpitis.
- As a *de novo* condition, where the inflammation is acute from the beginning.
- As an acute exacerbation of the chronic pulpitis.

Etiology of acute pulpitis

- Caries progressing beyond the dentinal barrier and reaching the pulp.
- Pulp exposure due to faulty cavity preparation.
- Blow to tooth with subsequent damage to pulp.
- Excessive heating of tooth during cavity preparation without water spray.
- Chemical irritation to the pulp.
- Cracked tooth syndrome.
- Tooth or teeth coming in the line of fracture when the jaw is traumatized.
- Anachoretic infection to the pulp.
- Recurrent caries around a pre-exiting restoration.
- Metallic restoration in a tooth without proper thermal insulation.

CLINICAL FEATURES

Acute pulpitis is often considered as one of the most dreaded disease of tooth because of the horrific nature of pain involved in it. The disease usually presents the following features:

- The **tooth is extremely sensitive to hot and cold stimuli**; however the pain in acute pulpitis can start spontaneously in the absence of any stimulus.
- A short and severe "**lancinating**" type of pain is often elicited from the affected tooth.
- Application of hot or cold stimuli causes an increase in the intensity of pain and such type of pain persists for a longer duration even after the stimuli are removed.
- As the dental pulp is located within the solid confinement of dentinal walls, intra-pulpal pressure builds-up quickly and so is the pain, since there is lack of escape route of inflammatory exudates during pulpal inflammations.
- In the initial stages of acute irreversible pulpitis the pain can be localized or rather the patient can identify the offending tooth, however in the more severe later stages the pain becomes regional and the patient is unable to identify the offending tooth.
- The intensity of pain increases during sleep because there is an increase in the local blood pressure in head and neck region in supine position, which results in increased flow of blood in the pulp chamber. More flow of blood in the pulp chamber causes more compression of the nerves resulting in more pain.
  If the entrance to the pulp opening is not wide, acute pulpitis not only causes an excruciating pain but also helps in quickly spreading the inflammation throughout the pulp with subsequent necrosis.
- Acute pulpitis **is often associated with micro-abscess formation** in the pulp along with **liquefaction degeneration**.
- . When drainage is established, small amount of pus exudes from the opening, which has a noxious odor.
- The affected tooth responds to a lower level of current, if electric pulp tester is used.

- Pain subsides when the drainage is established or when the pulp undergoes complete necrosis.
- The tooth is neither mobile and nor tendered to percussion; unless the pulpal inflammation has spread beyond the root apex into the periapical region.
- Patients with acute pulpitis are often apprehensive and moderately ill.
- When intrapulpal pressure becomes very high during acute inflammation, it can cause collapse of the apical blood vessel. This phenomenon is known as **"pulp-strangulation".**

HISTOPATHOLOGY

Acute pulpitis presents the following histopathological features (Fig. 10.2):

- Severe edema in the pulp with vasodilatation.
- Moderate to dense infiltration of polymorphonuclear leukocytes.
- Focal or complete destruction of the odontoblast cells at the pulp dentin border.
- Many **micro-abscess formations**, characterized by areas of liquefaction degeneration in the pulp being surrounded by dense band of neutrophils and microorganisms (Fig. 10.3).
- In severe cases, there may be **complete liquefaction and necrosis of the pulp with total destruction of the odontoblastic cell layer**. This phenomenon is known as **acute suppurative pulpitis.**
- Death of the pulp may also be accompanied by tissue dehydration. This condition is known as "**dry gangrene of the pulp**".

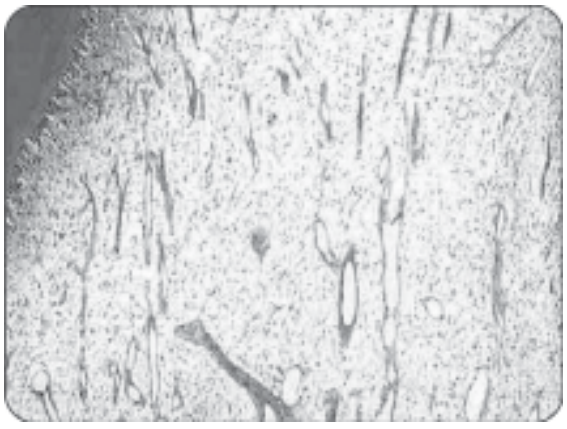

Fig. 10.2: Photomicrograph of acute pulpitis

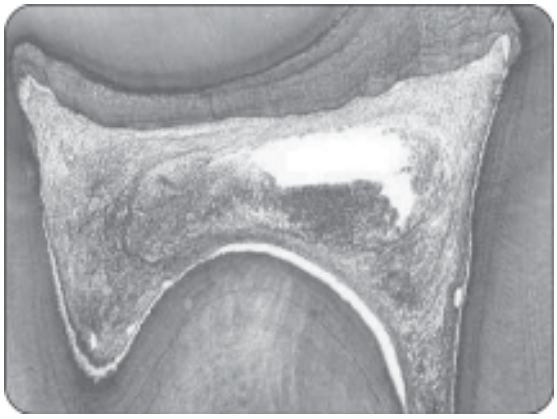

Fig. 10.3: Photomicrograph of pulp abscess

TREATMENT

As acute-pulpitis is an irreversible condition no treatment can be accomplished without an active and surgical pulp therapy, which could range from partial to complete removal of pulp.

The treatment modalities are as follows:

- Drainage of exudate or pus from the pulp chamber.
- Direct pulp capping.
- Root canal treatment (RCT).
- Extraction of tooth.

CHRONIC PULPITIS

Chronic pulpitis is a condition characterized by a low grade, often persistent inflammatory reaction in the pulpal tissue with little or no constitutional symptoms.

ETIOLOGY

Etiology for chronic pulpitis is same as that of the acute pulpitis but here the irritants are of low virulence.

MODE OF DEVELOPMENT

- Chronic pulpitis mostly occurs as a chronic inflammatory reaction in the pulp from the very beginning.
- Occasionally, it may be present as a quiescent phase of the pre-existing acute pulpitis.

CLINICAL FEATURES

Generally in chronic pulpitis the signs and symptoms are much milder in comparison to the acute pulpitis.

- The tooth with chronic pulpitis **may be asymptomatic** for quiet some time.
- In other cases there may be an **intermittent dull and throbbing pain** in the tooth.
- The tooth is less sensitive to hot and cold stimuli.
- The tooth usually responds to a higher level of current when electric pulp tester is used. It happens due to degeneration of most of the nerve fibers in the chronically inflamed pulp.
- Even if the pulp is exposed to the oral environment through a large open cavity in the tooth, still a very little pain is felt.
- Manipulation of the chronically inflamed pulp by small instruments often elicits bleeding but the maneuver causes little pain.

HISTOPATHOLOGY

- The chronic inflammatory response in the pulp is characterized by cellular infiltration by lymphocytes, plasma cell and macrophages, etc.
- The chronic nature of the inflammation may continue for a long-time with occasional periods of acute exacerbations.
- Blood capillaries are prominent and few microorganisms are also found in the pulpal tissue.
- Prolonged chronic inflammation may encourage fibroblastic activity in the pulp with formation of collagen bundles.
- Persisting chronic pulpitis may cause diffuse or solitary areas of calcification in the pulp.
- Chronic inflammation in the pulp in some cases may result in internal resorption of the tooth.

TREATMENT

- Root canal treatment or
- Extraction of tooth.

PULP POLYP (CHRONIC HYPERPLASTIC PULPITIS)

Pulp polyp is an **unusual type of hyperplastic granulation tissue response** in the pulp, which is characterized by an **overgrowth of the tissue outside the boundary of the pulp chamber as a protruding mass.**

PATHOGENESIS

Pulp polyp exhibits an intense proliferation of the pulpal connective tissue and this type of hyperplastic tissue growth depends on several factors, which are as follows:

Contributing factors for pulp polyp

- Persistence of balance between injurious agents and tissue resistance.
- Presence of a low grade sustained inflammation.
- Pulp tissue should be well-vascularized with excellent tissue reactivity.
- The carious cavity should be wide open.
- The patients must be young with good body resistance.
- The apical foramen of the affected tooth must be wide so that pulpal strangulation and complete necrosis due to inflammation does not occur.

If all these factors are favorably present, a tooth with chronic pulpitis many progress further into chronic hyperplastic pulpitis. However, the incidence rate is quite low.

CLINICAL FEATURES

- Pulp polyp clinically appears as a **small, pinkish-red, lobulated mass, which protrudes from the pulp chamber and often fills up the carious cavity.**
- The teeth in which pulp polyp commonly develops are often the deciduous molars and first permanent molars.
- **The condition is obviously seen in either children or young adults.**
- The affected **tooth always has a large open carious cavity**, which is present for a long duration.
- The lesion bleeds profusely upon provocation.
- If traumatized, the pulp polyp becomes ulcerated and appears as a dark red, fleshy mass with fibrinous exudate on the surface.
- The involved tooth is usually painless but it may be sensitive to thermal stimuli.
- Although pulp polyp is a purely connective tissue growth, it may be sometimes superficially epithelized.

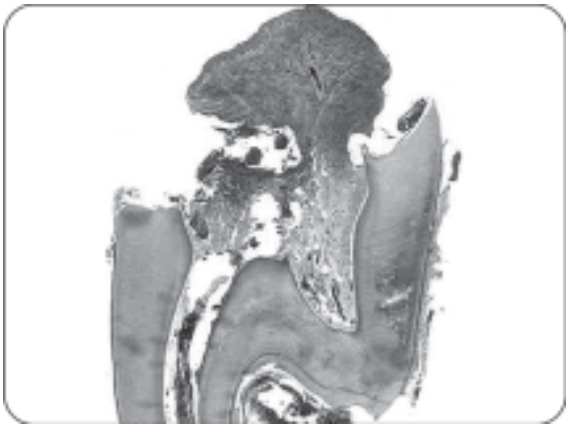

Fig. 10.4: Photomicrograph of pulp polyp

HISTOPATHOLOGY

Pulp polyp histologically presents the following features (Fig. 10.4):

- The hyperplastic pulpal tissue lesion presents the features of a granulation tissue mass, consisting of numerous proliferating fibroblasts and young blood capillaries.
- There may be edema and hyperemia of the pulpal tissue. Moreover, focal areas of pulp necrosis, which are surrounded by area of fibrosis, are often seen.
- Inflammatory cell infiltration chiefly by the lymphocytes, plasma cells and sometimes polymorphonuclear neutrophils in the tissue are common.
- Reparative secondary dentin may be formed adjacent to the dentinal wall of the affected tooth.
- Stratified squamous type epithelial lining is often observed on the surface of the pulp polyp, which resembles oral epithelium.
- The epithelial cells on the surface of the polyp are believed to be **the desquamated epithelial cells, which came either from the buccal mucosa, gingiva or from the salivary gland ducts.**
- These cells are carried via saliva and are transplanted on to the surface of the pulp polyp.
- When the pulp polyp is present for a long-time, persistent rubbing of the buccal mucosa against the lesion may help in the grafting of epithelial cells on its surface.
- The epithelized surface of the pulp polyp may sometimes show even well-formed retes peg-formation.

TREATMENT

Treatment is done either by root canal treatment or by extraction of the affected tooth.

AERODONTALGIA

Aerodontalgia is an unusual type of dental pain, which occurs as an effect of change in the altitude.

CLINICAL FEATURES

- Aerodontalgia affects some persons who, experience pain in the tooth during high altitude flight or during deep sea diving.
- At ground levels the tooth is completely asymptomatic.
- . In some cases the pain may not start readily during flight or during diving, instead it may occur few hours or days later.
- The condition may be related to subclinical pulpitis.
- Sometimes, similar problem may happen in an endodontically treated tooth with improper obturation of the canals.
- The entrapped air in the improperly obturated root canals may expand during flight or during diving (due to alteration in the atmospheric pressure), which creates pressure in the periapical nerve bundles and produce pain.

PULP NECROSIS

Pulp necrosis may occur either due to pulpitis or due to injury and subsequent occlusion of the apical blood vessel.

- A coagulative type of necrosis of the pulp occurs due to ischemia.
- When the necrosis follows pulpitis, the breakdown of inflammatory cells may lead to liquifactive degeneration in the pulp.
- The necrosed pulp may become secondarily infected by putrefactive bacteria from caries.
- The gangrenous necrosis of pulp is usually associated with a foul odor, when the pulp chamber is opened for endodontic therapy.

- In sickle cell anemia, blockage of the pulpal vessel by sickled or defective RBCs may result in pulp necrosis.

DIAGNOSIS OF PULPAL DISEASES

Several clinical tests are performed for the evaluation of pulpal disease, which are as follows:

History

- Pulpitis history often reveals the state of the disease. History of intense pain in the tooth, which continues even after the removal of stimulus, indicates an irreversible pulpal damage.
- If the pain or sensitivity comes down as soon as the stimulus is withdrawned, the condition is probably a reversible pulpitis.
- A tooth having dull pain of late but has passed through previous bouts of sharp acute pain, indicates either chronic pulpitis or pulp necrosis.

Clinical Examination

Clinical examination of tooth either visually or with hand instruments may help in establishing the diagnosis of the pulpal diseases.

- Carious exposure in a tooth can be easily detected by clinical examination.
- Similarly a fractured tooth with pulp damage can also be detected by this method.
- Change in the color of the tooth can spell-out if the pulp is vital or not.

Radiographic Examination

Intraoral periapical radiographs or bitewing radiographs, etc. can help in establishing a diagnosis in pulpal disease (Fig. 10.5). Although these findings are not always perfect, radiographs can often indicate if the carious infection has reached to the pulp or if the pulpal inflammation has already progressed beyond the apical foramen into the periapical tissue.

Clinical Test for Evaluation of Pulp Response (pulp vitality tests)

If the dental pulp is not in a healthy state it will generate abnormal responses to different stimuli and this can help in making a diagnosis of the pulpal disease.

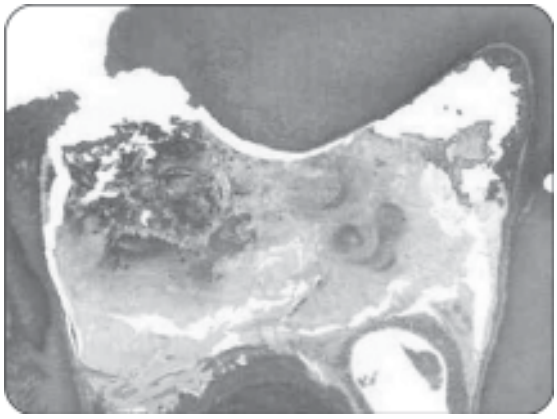

Fig. 10.5: Photomicrograph of necrotic pulp

Bacteriology of pulpal infections: The commonly encountered microorganisms in the dental pulp during acute or chronic pulpitis are as folows:

(I) ANAEROBIC ORGANISMS

Gram-negative rods

Bacteroides buccae
Bacteroides denticola
Bacteroides endodontalis
Bacteroides gingivalis
Fusobacterium nucleatum
Wolinela recta
Selenomonous sputigena

Gram-negative cocci

Veillonella parvula

Gram-positive rods

Actinomyces israelii
Actinomyces odontolyticus
Eubacterium alactolyticum
Eubacterium brachy
Eubacterium lentum
Eubacterium nodatum
Lactobacillus catenaforme
Lactobailus minutus

Gram-positive cocci

Streptococcus constellatus
Streptococcus intermedius
Streptococcus morbillorum
Peptostreptococcus anaerobius
Peptostreptococcus magnus
Peptostreptococcus prevotii.

Pulp vitality tests

- ***Heat test:*** Sensitivity to heat may be tested by application of hot water or heated gutta-percha stick on the suspected tooth. A tooth having pulpitis will respond to a lower level of heat as compared to a normal tooth. Therefore, it is always important that the response gathered from a suspected tooth should always be compared with a normal tooth from the some arch or the opposing arch.
- ***Cold test:*** Selective application of cold water or water ice or dry ice can help in assessing the pulpal health. This is by far the most reliable method of pulp testing.
- ***Percussion:*** Sensitivity to percussion indicates periapical inflammation in a tooth, this can happen in pulpitis only when the inflammatory process has extended beyond the tooth apex into the periapical area. Percussion sensitivity should be carried out both in vertical and in horizontal direction.
- ***Palpation:*** Palpation of the apical tissues may elicit tenderness or it may reveal soft or hard tissue swelling, which are indicative of periapical inflammations.
- ***Pressure:*** Gentle pressure on the tooth often helps to diagnose fracture or cracked tooth syndrome. It can also give indication regarding the presence of periapical inflammation.
- ***Electrical pulp test:*** The electric pulp testing reveals the varying degrees of sensory reply in the pulp, which alters in different inflammatory states. In reversible pulpitis the pulp gets stimulated at a lower level of current as compared to that of a normal pulp (because of lower pain threshold). In irreversible pulpitis the threshold level is further lowered and the pulp responds to an even lower level of current. In chronic pulpitis the pulp responds to a higher level of current (as compared to normal pulp) and it happens due to the decreased number of sensory nerve fibers in the pulp as a result of necrosis.
- ***Laser Doppler flowmetry:*** It can be used as an advanced diagnostic aid for accurate diagnosis of pulpal pathology.

(II) AEROBIC AND FACULTATIVE ANAEROBIC ORGANISMS

Gram-negative rods

Capnocytophaga ochracea
Eikenella corrodens
Campylobactor sputorum

Gram-positive rods

Actinomyces naeslundii
Actinomyces viscosus

Gram-positive cocci

Streptococcus mutans
Streptococcus milleri
Streptococcus mitior
Streptococcus sanguis

Factors causing retarded healing of the pulp tissue following injury

There are many factors both physiological and pathological which reduce the healing capacity of the pulpal tissue. And because of this pulp becomes less able to withstand mechanical chemical or inflammatory insults.

The factors are as follows:

- Decrease in the vascularity and cellularity of pulp in advanced age.
- Fibrosis and calcification in the pulp.
- Decrease in the volume of pulp tissue due to continuous dentin deposition
- Obliteration of the pulp canal due to injury causes decrease in the blood supply to pulp and the residual pulp tissue eventually dies.
- Chronic periodontal disease can cause more and more deposition of reparative dentin and therefore reduce the size of the pulp chamber and diameter of root canal.
- Gross calcification in the pulp tissue due to hereditary disorders, e.g. dentinogenesis imperfecta may reduce the ability of pulp to survive injury.
- Developmental anomalies of tooth, e.g. dens-invaginatus, may provide an easy access for progression of dental caries towards the pulp.
- Systemic diseases, e.g. diabetes, anemia and nutritional deficiency, etc. cause a general reduction in the host defence mechanism and therefore have an obvious effect on pulp as well.
- Radiotherapy in the jawbones with subsequent effect on the tooth pulp.

DISEASES OF THE PERIAPICAL TISSUES

PRIMARY ACUTE APICAL PERIODONTITIS

Primary acute apical periodontitis mostly occurs as a result of extension of the pulpal inflammation into the periapical tissues. The lesion may also occur as a result of occlusal trauma and in such cases the pulp is vital.

CLINICAL FEATURES

- Moderate pain and sensitivity in the tooth.
- **Slight extrusion of the tooth** due to escape of inflammatory exudates into the apical periodontal ligament.
- The most important and determining feature is the severe pain on slight pressure during mastication. It happens because normal chewing pressure becomes too heavy for the tooth as it is extruded or raised occlusally due to apical inflammation.
- There is discomfort in the tooth initially and gradually it becomes more and more tendered, even to mere touch.
- **Thermal changes (hot and cold) do not aggravate the pain.**
- As the disease progresses, the inflammation becomes more and more severe with formation of pus in the apical region, at this stage the pain is very intense and is throbbing in nature.
- The gingiva overlying the affected root may be red and tendered.
- Acute apical periodontitis due to pulpal infection is not reversible and mostly turns into chronic apical periodontitis or periapical granuloma.
- Sometimes the exudates may penetrate the overlying bone and periosteum and cause soft tissue swelling and even cellulitis.
- Intrestingly once the facial swelling develops the pain in the offending tooth becomes less due to relief of pressure in the periapical region of the tooth.
- The regional lymph nodes are often enlarged and tendered.

Possible complications:

- Periapical abscess formation
- Regional lymphadenopathy
- Cellulitis
- Development of periapical granuloma.

TREATMENT

Extraction or endodontic treatment of the diseased tooth.

PERIAPICAL GRANULOMA (CHRONIC APICAL PERIODONTITIS)

DEFINITION

Periapical granuloma is a localized mass of granulation tissue around the root apex of a non-vital tooth, which develops in response to a low grade infection or inflammation.

Etiological factors in periapical granuloma

- Extension of the pulpal inflammation or infection beyond the root apex.
- Occlusal trauma.
- Orthodontic tooth movements with excessive uncontrolled force.
- Acute trauma due to blow on the tooth.
- Perforation to the root apex during endodontic therapy.
- Spread of periodontal infection into the root apex.
- Chemical irritation.

PATHOGENESIS

Most of the periapical granulomas develop due to the spread of pulpal infections beyond the root apex. The root canal of a non-vital tooth is an ideal environment for bacterial growth because it protects the organisms from normal body defenses, as well as it provides them with good nutrition. In case of periapical granuloma a balance between the pathogenicity of bacteria within the canal and the defense capacity of the periapical tissue is established.

Inflammation in the periapical region causes destruction of the apical periodontal ligaments, adjoining alveolar bone and cementum, etc.

Later on, these tissues are replaced by a mass of "**granulation tissue**". The granuloma increases in size due to the gradual resorption of the surrounding bone by chemical mediators like—osteoclast activating factor (OAF) and collagenase, etc. which are released by the chronic inflammatory cells.

CLINICAL FEATURES

- The offending tooth produces sensitivity to percussion, which occurs due to edema, hyperemia and inflammation of the apical periodontal ligaments.
- There can be mild pain and discomfort in the tooth during chewing solid foods.
- Patient may give a previous history of pain in the tooth (earlier when pulpitis was present), which had subsided thereafter.
- The involved tooth is always non-vital and it does not responds to thermal or electric pulp testers.
- The tooth may be slightly elongated from its socket and is tendered to the chewing pressure.
- In many cases, periapical granuloma may be asymptomatic throughout its course.
- There may be severe pain and sensitivity in the tooth during acute exacerbations of the disease.

RADIOLOGICAL FEATURES

- Most of the lesions are detected incidentally during routine radiographic examinations.
- In the initial stages, periapical granuloma radiographically shows **widening of the periodontal ligament space of the tooth.**
- Fully developed lesions usually produce a well-defined, radiolucent area of varying size, which appears to be in continuity with the root apex.
- Sometimes, the radiolucent lesion is well-demarcated from the surrounding normal bone by a thin sclerotic margin.
- In other cases, the radiolucency blends gradually with the surrounding tissue.
- Long-standing periapical granuloma may show **varying degrees of root resorption and loss of apical lamina dura.**

HISTOPATHOLOGY

Histologically, periapical granuloma presents the following features (Fig. 10.6):

- The lesion appears as a granulation tissue mass consisting of proliferating fibroblasts, endothelial cells and numerous immature blood capillaries.
- Chronic inflammatory cells, e.g. macrophages, lymphocytes and plasma cells, etc. are often present in the lesion.
- Some lesions show the presence of epithelial islands, cholesterol clefts and foam cells.
- Giant cells are also found on rare occasions.
- The plasma cells often produce immunoglobulin (IgG, IgM, IgA and the IgE, etc.). Besides this, there is also presence of T lymphocytes in the lesion.
- Although periapical granuloma is a **"sterile"** lesion, it is often observed that few bacteria (e.g. *Actinomyces israelii, Actinomyces naeslundii* and *Arachnida proprionica*) are almost always present in the lesion and they are not affected by the cellular immune mechanism.
- The epithelial cell rests of Malassez, a natural component of the periodontal ligament, proliferate in response to chronic inflammation and these proliferating cells later on may undergo cystification to produce radicular cyst.
- The bony tissue at the periphery of the lesion is usually lined by osteoclast cells with areas of bone resorptions.
- Resorption of cementum and dentin often occurs as a result of the chronic inflammation

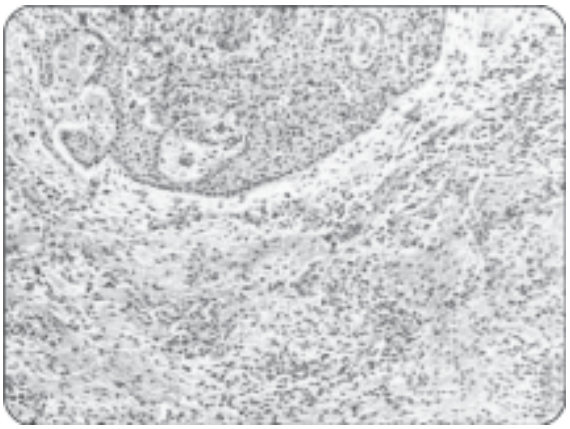

Fig. 10.6: Photomicrograph of periapical granuloma

but in some areas along the root, cementoblastic activity may predominate leading to hypercementosis like reaction.

TREATMENT

The lesion is treated either by extracting the tooth or by performing root canal treatment in the tooth with apicoectomy or apical curettage.

SEQUELAE

Sequelae of periapical granuloma:

- If the granuloma continues to enlarge, resorptions of root apex or apical bone may occur.
- Acute exacerbation may produce (acute apical periodontous) with severe pain, discomfort and tenderness to percussion.
- Suppuration in the periapical granuloma may lead to acute periapical abscess formation.
- Proliferation of epithelial cell rest of malassez may lead to development of radicular cyst.
- Low-grade infection from periapical granuloma may cause osteosclerosis (bone apposition) in the apical region of tooth.
- Similar low-grade infections may cause hypercementosis in the affected tooth as well.

ACUTE EXACERBATION OF CHRONIC PERIAPICAL GRANULOMA (PHOENIX ABSCESS)

- Most of the periapical granulomas clinically remain quite as long as the balance between the bacteria contained within the root canal and body's defense in the granuloma is maintained.
- If this balance is lost somehow, an explosive type of acute exacerbation occurs in the pre-existing chronic lesion, which is known as "phoenix abscess".
- Clinically phoenix abscess presents severe pain, local swelling, extreme tenderness in the tooth upon pressure and sometimes facial cellulitis, etc.
- The intense pain in phoenix abscess may result from excessive accumulation of purulent exudates.
- Treatment is done by drainage either via the root canal or by an incision over the localized swelling. Antibiotics are always given to control the infection.

PERIAPICAL ABSCESS (DENTOALVEOLAR ABSCESS)

DEFINITION

Periapical abscess can be defined as a localized, acute or chronic suppurative infection in the periapical region of a non-vital tooth.

Etiological factors of periapical abscess

- Extension of pulpal infection into the periapical tissue.
- Fracture of tooth with pulp exposure.
- Accidental perforation of the apical foramen during root canal treatment, which results in entry of pulpal microorganisms into the periapical area.
- Extension of periodontal infection into the periapical tissues.
- Secondary bacterial invasion into the pre-existing periapical granuloma or cyst or scar.
- Anachoretic infection of the periapical tissues.

PATHOGENESIS

Periapical abscess often results from a mixed bacterial infection caused by strict anaerobes, e.g. *Prevotella* and *Porphyromonas*, etc. Anaerobic streptococci and staphylococci also play major roles in causing the disease.

CLINICAL FEATURES

- Periapical abscess is a common odontogenic infection and constitutes about 2 percent of all apical radiolucencies.
- Acute abscess produces **severe pain in the affected tooth**.
- There will be **localized swelling and an erythematous change in the overlying mucosa**.
- The **pain aggravates during percussion or when pressure is applied with the opposing tooth.**
- Pressure from purulent exudates and inflammatory infiltrates in the periapical area often causes extrusion of the tooth from its socket.
- The associated tooth is non-vital and sometimes it can be mobile also.
- The affected area of the jaw may be tendered on palpation.

- Elevated body temperature and localized lymphadenitis are common findings in periapical abscess.
- **Application of heat on the tooth intensifies pain, whereas application of cold relieves the pain temporarily**.
- If prompt treatment is not given, the abscess penetrates the cortical plate of bone (mostly buccal) and invades into the adjacent soft tissues, thereby causing cellulitis.
- Pus discharging sinus often develops on the alveolar mucosa over the affected root apex and sometimes on the skin overlying the jawbone.
- If the host resistance is high or the virulence of the organisms involved in periapical abscess is low, a chronic stage of the abscess sets in, which mostly remains asymptomatic.
- Unlike the acute lesions, chronic periapical abscess usually produces mild, dull pain and it also produces **intraoral or extraoral pus discharging sinuses**.
- Infections from the acute periapical abscess often spread to the facial spaces, leading to space infections.
- Infection of the facial spaces may be further complicated by the development of septicemia, Ludwig's angina and cavernous sinus thrombosis, etc.
- In periapical abscess, spread of periapical infections into the medullary spaces of bone may produce **osteomyelitis** in some patients.

RADIOLOGICAL FEATURES

As the **acute periapical abscess** develops quite rapidly, there is **little time for the lesion to cause any significant amount of bone resorption that could be detected radiographically.** Therefore, radiographic changes in acute abscess are minimum and are limited to only slight thickening of the periodontal ligament space in apex region of the involved tooth.

However, in **chronic periapical abscess**, radiographs often reveal **small radiolucent areas at the root apex with poorly defined margins.**

HISTOPATHOLOGY

Histologically, periapical abscess presents the following features:

- The lesion appears as a zone of liquefaction necrosis, which is made up of proteinaceous exudates, necrotic tissue and a large number of viable or dead neutrophils (pus).
- The adjacent tissues surrounding the liquefaction zone have many dilated blood capillaries and infiltration with neutrophils.
- Inflammatory change is also observed in the periodontal ligament and adjoining bone–marrow.
- Bony trabeculae in the periapical region may show empty lacunae, which results from the death of the osteocytes.
- In chronic periapical abscess the inflammatory cell pattern is different and in these lesions often exhibit infiltration by lymphocytes, plasma cells and macrophages, etc.
- Areas of bone destruction are also accompanied by areas of fibrosis as well as bone regeneration in chronic lesions.

vii. Pus discharging sinus in chronic abscess is often lined either by a granulation tissue or by a squamous epithelial lining.

TREATMENT

For the treatment of acute periapical abscess standard principles of management of acute inflammation are as follows:

- Drainage is established either through an opening in the tooth or by an incision over the soft tissue swelling at the apex region.
- Antibiotics are administered against the offending microorganisms.
- Once the acute phase of the disease is brought under control, the affected tooth is treated either by root canal therapy or by extraction.

OSTEOMYELITIS

DEFINITION

Osteomyelitis can be defined as the inflammation of bone and bone marrow along with the surrounding periosteum. The inflammatory condition involves all the structures of bone, e.g. the bone marrow, haversian systems, periosteum, blood vessels, nerves and epiphyses, etc.

Classification of osteomyelitis

There are various types of osteomyelitic lesions occurring in the jawbones, which can be broadly divided into **two groups—acute osteomyelitis and chronic osteomyelitis**. According to the specificity of the causative microorganisms, osteomyelitis may be of two types—specific osteomyelitis and non-specific osteomyelitis.

Acute osteomyelitis

Most commonly encountered (Nonspecific) lesions in this category include:

- Acute suppurative osteomyelitis
- Acute subperiosteal osteomyelitis
- Acute periosteitis

Chronic osteomyelitis

Nonspecific type

- Chronic intramedullary osteomyelitis
- Chronic focal sclerosing osteomyelitis
- Chronic diffuse sclerosing osteomyelitis
- Chronic osteomyelitis with proliferative periosteitis
- Chronic subperiosteal osteomyelitis
- Chronic periosteitis.

Specific type

- Tuberculous osteomyelitis.
- Syphilitic osteomyelitis.
- Actinomycotic osteomyelitis.

Radiation induced osteomyelitis

Idiopathic osteomyelitis

ETIOLOGY OF OSTEOMYELITIS

Numerous etiologic factors have been identified, which can cause osteomyelitis and these factors are as follows:

- Direct spread of infection from dental pulp into the jawbone.
- Spread of infection into the bone from the pre-existing suppurative odontogenic infections, e.g.
  - Periapical abscess.
  - Periodontal pocket involved in a fractured jaw bone.
  - Infected periapical granuloma
  - Infected periapical cyst.
  - Acute necrotizing ulcerative gingivitis
  - Periodontal abscess.
  - Pericoronitis
  - Infected and fractured tooth/retained root tip.
- Spread of infection following removal of tooth without proper asepsis and antibiotic coverage.
- Compound fracture of the jawbone with exposure of bone outside the skin or mucosa.
- Gunshot injuries in the jaw with soft tissue laceration and exposure of bone.
- Spread of microorganisms from overlying soft tissue (skin or mucosa) infections.
- Post-radiation secondary infection.

Predisposing factors of osteomyelitis

Local Factors

- *Anatomical site of the disease:* The mandibular bone has poor blood supply in comparison to that of the maxilla, besides this it has more compact bony pattern due to which, osteomyelitis occurs far more commonly in mandible than maxilla.
- *Pre-existing bone disease:* Long standing bony disease like Paget's disease of bone, fibrous dysplasia, cystic lesions, osteopetrosis, etc. many render the jaw bones more susceptible to osteomyelitis, when infections occur in the tissue.
- *Radiation injury:* Radiotherapy to the head and neck area often produces obliterative endarteritis, which results in impaired blood supply to the jawbones. Therefore in such conditions possibility of osteomyelitis is increased once the infection in the bone sets in.

Systemic Factors

Predisposing factors (systemic) in osteomyelitis favor the development of the disease by lowering the body resistance to infections. These factors include the following:

- Malnutrition and chronic alcoholism
- Drug addiction
- Anemia, especially sickle cell anemia
- Diabetes (poorly controlled)
- Acute leukemia
- Agranulocytosis
- Syphilis
- Measles and typhoid fever.
- HIV infection and AIDS.
- Extremes of age
- Urinary tract infection.

- Infection to the pre-existing bony diseases, e.g. Paget's disease of bone, fibrous dysplasia and osteopetrosis, etc.
- Phosphorus poisoning
- Anachoretic infections
- Idiopathic factors.

Being an inflammatory disease, development of osteomyelitis depends mainly upon the balance between the virulence and number of microorganisms present in the bone and the local or systemic defense capacity of the patient's body to infection.

However, besides these two main factors there are several other predisposing factors which play determining role in the pathogenesis of osteomyelitis.

MICROORGANISMS INVOLVED IN OSTEOMYELITIS

Osteomyelitis due to specific bacterial infections like tuberculous, syphilitic and actinomycotic group of organisms occurs in the jawbones quite often. Osteomyelitis of the jaws due to non-specific bacterial infections is far more common as compared to the specific types and micro-organisms responsible for this type of infections are as follows:

- **Aerobic organisms**
  - *Staphylococcus aureus*
  - Hemolytic *Streptococcus*
- **Anaerobic organisms**
  - *Bacteroids*
  - Anaerobic *Streptococcus.*

PATHOGENESIS OF OSTEOMYELITIS

In osteomyelitis inflammation and destruction of bone take place by the following mechanisms:

- Infection from the periapical lesions or infected pulp or other foci enters into bone marrow first and from there it extends into the cancellous bony spaces.
- As the infection is established, the lumina of the nutrient vessels of the living bone are occluded by the formation of thrombus. (The thrombus consists of dead or viable neutrophils, microorganisms and necrotic tissue debris, etc.)
- Due to thrombosis of the nutrient vessels and excessive pressure from the inflammatory exudates against the rigid and confined space in the bone, the nutrition supply to the bone cells is completely disturbed resulting in death of cancellous bony trabeculae with formation of '**sequestrum**'.
- The infection then spreads via the Volkmann's canals in the cortical plates and reaches to the external surface of bone below the periosteum, inflammation at this area results in periosteitis.
- Accumulation of more and more exudates and pus cause separation between the cortical plates of bone and the periosteum.
- Further extension of the inflammation may lead to single or multiple sinus tracts formation, which communicate between the bone and the external surface of the skin and mucous membrane.
- As the cortical plates of the bone get the blood supply from the overlying periosteum, separation between the cortical plates and the periosteum results in necrosis of the cortical bone.
- Although the periosteum is infected and elevated from the cortical bone, a few bone-forming cells still survive in it and when the acute phase of the disease subsides, a new layer of bone may form over the sequestrum which completely surrounds it, the enclosed sequestrum is now called the '**involucrum**'.
- Pus discharges from the involucrum through sinuses called cloacae and bathe the surface of the sequestra.

The above mentioned pathogenic mechanisms apply largely to suppurative osteomyelitis. However, there can be several cases of osteomyelitis, which are characterized by simultaneous bone destruction and bone formation (e.g. non-suppurative osteomyelitis and Garre's osteomyelitis, etc.). In these lesions, a balance always exists between the virulence of the pathogenic organism and the host's local and systemic defense mechanism.

ACUTE SUPPURATIVE OSTEOMYELITIS

Acute suppurative osteomyelitis is a serious type of diffusely spreading acute inflammation

of the bone, characterized by extensive tissue necrosis.

CLINICAL FEATURES

Age: Acute osteomyelitis usually occurs after 30 years of age as there is more probability of systemic diseases from this age and onwards and moreover there is also decreased bony resistance to infection (due to reduced vascularity).

Sex: Incidence is more among males than females.

Site: The mandible is involved more often than the maxilla as it has a limited blood supply and it is a dense bone with thicker cortical plates. The mandibular lesions are usually diffuse in nature, while the maxillary lesions are mostly well-localized. Moreover the maxillary lesions are rare and are seen in infants or neonates following birth injuries or severe otitis media, etc.

Bacteriology: *Staphylococci* and *Streptococci* are the organisms, which predominantly cause acute suppurative osteomyelitis of the jaw. However, *Actinomyces israelii, Prevotella, Porphyromonous* and *Bacteroids* can also cause the disease.

CLINICAL FEATURES (FIGS 10.7 TO 10.10)

- Acute suppurative osteomyelitis often causes severe throbbing, deep seated pain and diffuse large swelling of the jaw along with the related soft tissues.
- Often there is loosening and soreness of the regional teeth with difficulty in taking food.

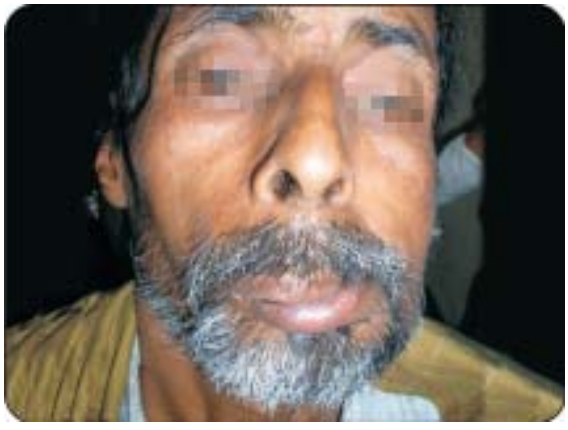

Fig. 10.7: Osteomyelitis-I

Fig. 10.8: Osteomyelitis-II

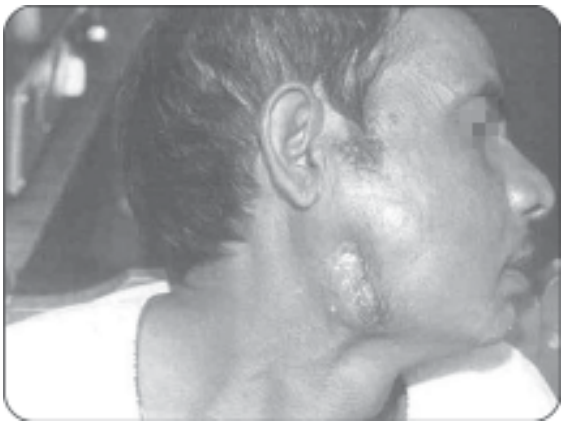

Fig. 10.9: Acute osteomyelitis causing formation of extraoral sinus

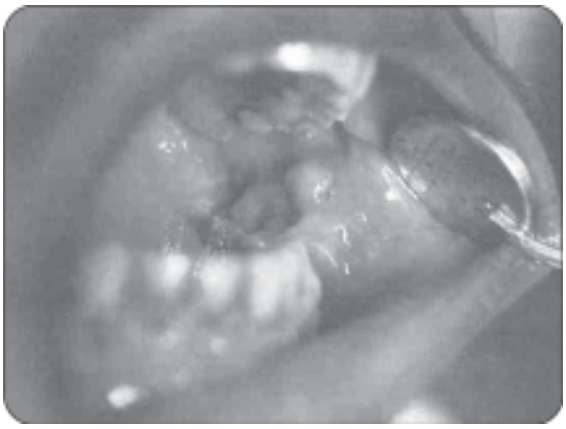

Fig. 10.10: Intraoral view of the same patient showing large area of soft tissue necrosis in mandibular molar region

- The overlying gingiva is often red, swollen and tendered to palpation.
- Excessive muscle edema may cause difficulty in mouth opening and swallowing.
- Patients often complain of excessive salivation and bad breath, etc.

- Multiple intraoral or extraoral pus discharging sinuses often develop and moreover discharge of pus can also be seen from the gingival crevice of the affected teeth or from the socket (Figs 10.9 and 10.10).
- Regional lymph nodes are enlarged and tendered in most cases.
- Paresthesia or anesthesia of the lip (either on the affected side or the entire lip) is a common and characteristic phenomenon.
- Reddening of the overlying skin or mucosa is often seen in advanced stages of the disease.
- In acute suppurative osteomyelitis, patients are slightly febrile and the general symptoms include fever, malaise, anorexia and vomiting, etc.
- In the absence of adequate therapy, metastatic spread of infection to different body systems may become inevitable and it can lead to cellulitis, bacteremia or septicemia, etc.
- Distension of the periosteum occurs due to accumulation of pus and later on whenever sub-periosteal new bone formation occurs, the bony swelling becomes firm or hard.
- Necrotic bone fragment or sequestrum may exfoliate spontaneously from the bony wound (Fig. 10.11).
- Once the acute phase of the disease is over, a chronic phase often sets in, which usually presents much milder clinical symptoms.
- Pathologic fracture may occur sometimes due to weakening of bone as a result of progressive destruction.

RADIOLOGICAL FEATURES (FIGS 10.12 AND 10.13)

- In the initial stage of the disease, when bone destruction is yet to occur, no noticeable radiographic change is observed in the jaw.
- At this stage of the disease, a radionuclide scan may be helpful in documenting the subtle bony changes occurring in the jaw.
- Radiographic changes become more apparent in about ten days time since the onset of the disease and these radiographic changes are characterized by **large areas of radiolucencies in the jaw bone, with ill-defined, moth-eaten margins (Fig. 10.12).**
- **Sequestra** are frequently seen as **multiple radiopaque foci of diminished radiodensity** within the lesion.
- The sequestra become more sharply defined as they are gradually separated from the normal bone.
- Peripheral bone reaction at the margin of the lesion is not evident in case of early acute lesions, however, in the chronic stages of the disease, sub-periosteal new bone formation may be seen in the jaw (especially in young patients).
- In case of subperiosteal new bone formation, the radiograph reveals **thin, curved strip of radiopacity on the outer surface of the bony cortex.**
- The **involucrum** radiographically appears as a **gray shadow** on the outer surface of the cortical plate.

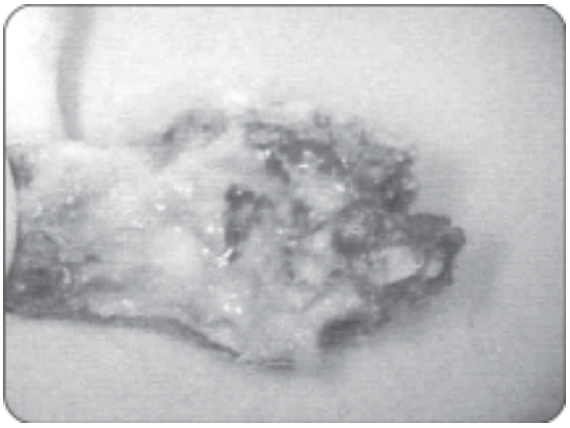

Fig. 10.11: A piece of dead bone (sequestrum)

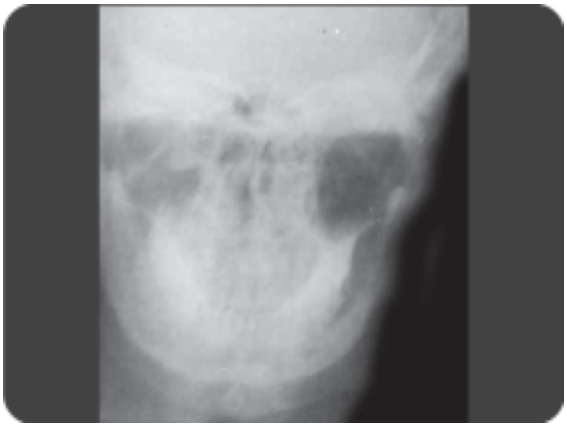

Fig. 10.12: Acute suppurative osteomyelitis causing large area of bone destruction on left side of mandible

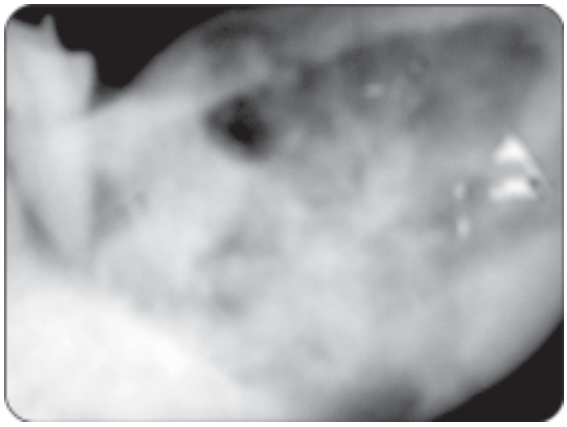

Fig. 10.13: Radiograph of osteomyelitis

- Sometimes, **"cloacae"** (a hole formed during the process of sinus development) may be seen as dark shadow traversing the bony opacity.

HISTOPATHOLOGY (FIG. 10.14)

- In acute suppurative osteomyelitis, the bone marrow undergoes liquefaction and a purulent exudates occupy the marrow space.
- Thrombosis of the blood vessels also occurs in the medullary spaces.
- A large number of acute inflammatory cell infiltrations occur in the Haversian canal and the periphery of the bone, which predominantly contains polymorphonuclear neutrophils (PMN) with occasional presence of lymphocytes and plasma cells.
- Bony trabeculae exhibit reduced osteoblastic activity with loss of osteocytes from the lacunae along with increased osteoclastic resorptions, which often produces scalloping at the bony margins.

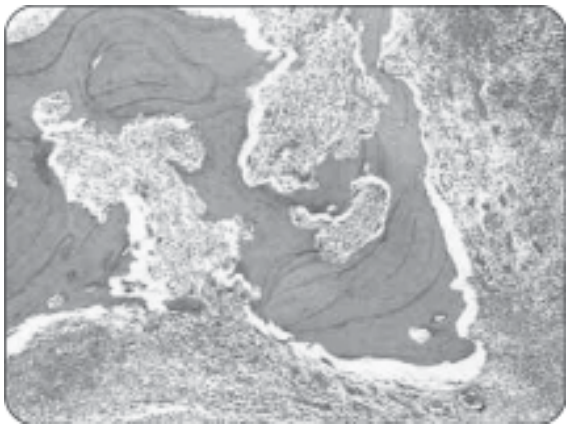

Fig. 10.14: Photomicrograph of acute osteomyelitis

- Bacterial colonies are often seen within the marrow tissue of the inflamed bone.
- Some areas of the affected bone undergo complete necrosis with degeneration of both osteoblast cells (bordering the bony trabeculae) and osteocyte cells (inside the lacunae) and therefore results in the development of **sequestrum**.
- **Sequestrum** therefore is a dead or necrosed fragment of bone, which is separated from the remaining viable bone.
- Sequestrum gradually undergoes spontaneous resorption or it may exfoliate through mucous membrane or skin.
- When the sequestrum becomes surrounded by new vital bone, the mass of enclosed non vital bone is called **involucrum**.
- Sometimes the infection in the bone becomes walled off. This may lead to a localized abscess formation **(Brodie's abscess).** The abscess may remain within the bone as a sterile lesion or it may act as persistent source of infection.

DIFFERENTIAL DIAGNOSIS

- Metastatic tumor in the bone with secondary infection.
- Primary intra-alveolar carcinoma.
- Primary mesenchymal malignant neoplasm.
- Primary lymphoma of bone.
- Intraosseous salivary gland neoplasm.

TREATMENT

- Incision and drainage of the inflammatory exudates and pus.
- Antibiotic therapy.
- Removal of the sequestrum.
- Elimination of the primary source of infection, e.g. offending tooth, etc.

CHRONIC SUPPURATIVE OSTEOMYELITIS

Depending on the severity of symptoms and the course of the disease over the time, suppurative osteomyelitis is divided into two varieties—acute and chronic. The disease, which is persisting for more than a month, is called chronic suppurative osteomyelitis.

- Chronic suppurative osteomyelitis may be the sequelae of acute suppurative osteomyelitis, in which proper treatment is either not done or inadequately done.
- The disease may also arise primarily as a chronic, low-grade inflammatory reaction in the bone, without any pre-existing acute phase.
- It is generally believed that lower levels of virulence of the causative microorganisms, e.g. Staphylococci, Bacteroids and Actinomyces, etc. are mostly responsible for the development of chronic suppurative osteomyelitis.

ETIOLOGY

Nonspecific microorganisms like staphylococci, streptococci, Bacteroids and Actinomyces, etc. mostly cause the disease.

CLINICAL FEATURES

- The molar area of mandible is more frequently affected.
- In case of chronic suppurative osteomyelitis, the **pain is usually mild and dull** vague in nature even if the disease is very extensive.
- Patients often give **history of dull vague pain in the jaw for several weeks**, which had started following an acute tooth abscess, tooth fracture or extraction, etc.
- Pain is usually mild and insidious in nature, which does not always correspond to the real severity of the disease.
- Jaw swelling is a common feature but mobility of teeth and sinus tract formations, etc. are rare.
- On rare occasions sinus tracts may develop both intraorally and extraorally with intermittent discharge of purulent materials.
- Anesthesia and paresthesia of the lip are very uncommon.
- Acute exacerbations of the chronic disease may occur from time to time.
- Sequestrum is often found, which protrudes from the ulcerated skin or mucosal surfaces.

RADIOLOGY

- Radiographically chronic suppurative osteomyelitis mostly presents a **"moth-eaten" radiolucent area in the bone with poorly defined margins.**
- Within the radiolucent area **multiple radiopaque foci are evident**, which represent areas of **"sequestrum"** formations.

Radiographically chronic osteomyelitis may present at least four different images, which are as follows

A. An ill-defined radiolucency in the bone with ragged borders.
B. A radiolucency with multiple radiopaque foci within it, the later structures represent sequestra.
C. A dense zone of radiopacity with faint radiolucency at the margin.
D. A "salt and pepper" radiographic effect in the bone.

HISTOPATHOLOGY

Chronic suppurative osteomyelitis often presents the following features (Fig. 10.15):

- Chronic inflammatory reaction in the bone with accumulation of exudates and pus within the medullary spaces.
- The lymphocytes, plasma cells and macrophages, etc. predominate among the inflammatory cells.
- Osteoblastic and osteoclastic activity occur parallely with formation of irregular bony trabeculae having reversal lines.
- Sequestrum may develop in the later stages of the disease.

TREATMENT

- Administration of antibiotics after bacterial culture and sensitivity testing.
- Surgical intervention in order to remove the sequestrum (saucerization of the bone).

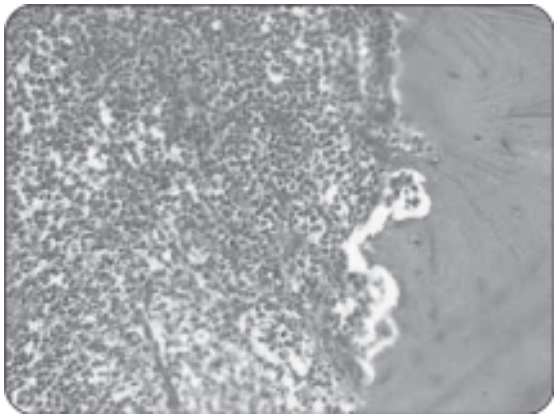

Fig. 10.15: Photomicrograph of chronic osteomyelitis

CHRONIC FOCAL SCLEROSING OSTEOMYELITIS (CONDENSING OSTEITIS)

DEFINITION

Chronic focal sclerosing osteomyelitis or condensing osteitis is a rare non-suppurative inflammatory condition of bone characterized by **sclerotic bone formation around the root apex of a nonvital tooth.**

PATHOGENESIS

The condition develops as a result of chronic persistent inflammation in the bone, where resistance of the tissue against infection is very high or where the virulence of the infective organisms is low.

A low-grade inflammation in the jaw bone causes stimulation of the osteoblast cells, which results in the formation of dense trabecular bone in the area and this process is known as osteosclerosis.

Osteosclerosis with additional bone formation may sometimes results in decreased marrow spaces.

ETIOLOGY

The disease often occurs in young individuals, having low grade sustained inflammation in the bone.

The common conditions, which can precipitate chronic focal sclerosing osteomyelitis, include the following:

- Chronic pulpitis.
- Traumatic malocclusion.

CLINICAL FEATURES

- The disease fsfrequently develops in children or young adults before the age of 20 years.
- **Mandibular first molars are mostly involved** with this condition. However, mandibular second molars or premolars can also be involved on rare occasions.
- The condition is mostly asymptomatic and there is no bony expansion seen.
- Majority of the lesions are discovered incidentally during routine radiographic examination of the jawbone.
- The **associated tooth is non-vital** and usually presents a large carious lesion, it is mostly asymptomatic or is associated with occasional mild pain.
- The disease can also occur in relation to a non-carious tooth and in such cases, traumatic malocclusion is the most likely factor, which is precipitating the disease.
- When the associated tooth is removed, the lesion may remain within the jaw for an indefinite to period of time without symptoms.

RADIOLOGICAL FEATURES

The lesion radiographically presents the following features:

- **Well-circumscribed radiopaque mass with uniform radiodensity; seen around the root apex of a nonvital tooth.**
- **There is no radiolucent border around the lesion** as may be seen in cemento-osseous dysplasia.
- The affected tooth exhibits an apical inflammatory process with **widening of periodontal ligament space.**
- The radiopacity is not separated from the root apex and the root tips are usually identified within the radiopaque lesion.
- A residual area of condensing osteitis that is seen after resolution of the inflammatory focus is known as '**bone scar**'.
- In case the lesion is found in edentulous jaw, there are always positive histories that an infected tooth was earlier removed for that area.
- The border of the lesion is usually well-defined or sometimes the border may be ragged.
- The radiodensity of the lesion is much higher as compared to the surrounding normal bone.

HISTOLOGICAL FEATURES

- There is usually presence of a dense mass of sclerotic bone in the lesion with little or no interstitial marrow tissue.
- Wherever the bone marrow is present it is usually fibrotic and is often infiltrated by chronic inflammatory cells.

DIFFERENTIAL DIAGNOSIS

- Mature cementoma
- Peripheral osteoma
- Complex odontoma
- Cementoblastoma
- Osteoblastoma
- Bony exostoses
- Metastatic tumor.

TREATMENT

- The affected tooth should be treated endodontically or it should be removed.
- No treatment required for the bony lesion.
- Biopsy may be necessary to rule out metastatic malignancy.

DIFFUSE SCLEROSING OSTEOMYELITIS

DEFINITION

Diffuse sclerosing osteomyelitis is a different entity form the small, isolated lesions of focal sclerosing osteomyelitis. It is mainly confined to the mandible and it typically involves a large section of the bone.

ETIOLOGY

Diffuse sclerosing osteomyelitis is a proliferative reaction in response to a low grade inflammation or infection in the jaw bone.

The infections in such cases are usually wide spread or diffuse in nature and are derived either from the periodontal tissue or from the periapical tissue.

These infections are usually subclinical in nature. Investigators have identified two bacteria in association with this disease, which are namely the *Propionibacterium acnes* and *Peptostreptococcus intermedium*.

CLINICAL FEATURES

- Diffuse sclerosing osteomyelitis is usually seen among elderly people.
- It is mostly seen among blacks and racial groups.
- More common among females.
- Mandible is mostly affected in diffuse sclerosing osteomyelitis especially in edentulous areas. The disease can affect the maxilla as well and even sometimes all four quadrants of both jaw could be affected at a time.
- The disease is usually asymptomatic but sometimes the patients may complain of a vague pain in the jaw with foul taste in the mouth.
- Acute exacerbation may occur in the lesion, which often produces mild pain, suppuration and fistulas tract formation, etc.
- SAPHO syndrome—It is a special entity characterized by chronic multifocal osteomyelitis with hyperostosis and osteitis of the bone. The condition is associated with negative bacterial culture and is nonresponsive to antibiotic therapy.

RADIOGRAPHIC FEATURES

- Radiograph shows areas of diffuse or nodular sclerosis of the bone.
- The appearance may be similar to the **"cotton-wool" radiopacities** seen in Paget's disease of bone.
- The border between the sclerotic bone and the normal bone is not well-demarcated.

HISTOPATHOLOGY

- Diffuse sclerosing osteomyelitis shows formation of dense irregular bone within a hypocellular fibrous stroma (Fig. 10.16)
- Bony trabeculae often reveal multiple reversal and resting lines.
- Patchy distribution of chronic inflammatory cells is often found in the marrow tissue.

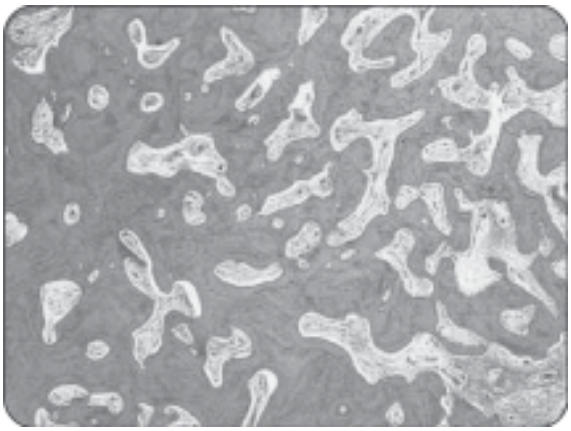

Fig. 10.16: Photomicrograph of sclerosing osteomyelitis

DIFFERENTIAL DIAGNOSIS

Diffuse sclerosing osteomyelitis is to be distinguished from the following lesions:

- Paget's disease of bone
- Osteopetrosis
- Cementomas
- Gardner's syndrome
- Late stage of fibrous dysplasia.

TREATMENT

No treatment is required as the disease is often asymptomatic and is too extensive for surgical removal. In case of acute exacerbations, surgical debribement and removal of the sequestrum is done along with antibiotic therapy.

CHRONIC OSTEOMYELITIS WITH PROLIFERATIVE PERIOSTITIS (GARRE'S OSTEOMYELITIS)

DEFINITION

Garre's osteomyelitis represents a reactive periosteal osteogenesis in response to low-grade infection or trauma. The condition was first authentically reported in 1893 by German physician C Garre and it is characterized by focal gross thickening of the involved bone due to sub-periosteal new bone deposition (**duplication of the cortex**).

Predisposing factors for the development of Garre's osteomyelitis

- Chronic periapical abscess.
- Chronic periapical granuloma with secondary infection.
- Infected periapical cyst.
- Perifollicular infection in an erupting tooth or impacted tooth.
- Chronic parotid abscess.
- Chronic periodontal infection.
- Other chronic infections in the soft tissue overlying the jaw.
- Chronic trauma in the jaw bone.
- Mechanical irritation in the jaw from dentures.

PATHOGENESIS

It is usually believed that a low-grade, sustained infection or inflammation of the jaw bone, which is occurring in a young person with high degree of body resistance and excellent tissue reactivity, may often precipitate Garre's osteomyelitis.

It is therefore understandable that the above-mentioned factors contribute to a strong osteogenic potential of the periosteal osteoblast cells in the affected jaw bone.

Generally in Garre's osteomyelitis, a low-grade chronic inflammation spreads through the cortical bone of the jaw and it initiates a proliferative reaction in the periosteum, leading to sub-periosteal new bone formations.

It is important to note that an acute and intense type of inflammation or infection in the jaw bone usually does not produce Garre's osteomyelitis, since this type of infection does not permit sufficient time for the bone to undergo any sub-periosteal osteogenesis.

CLINICAL FEATURES

***Age*:** Children and young adults (mean age is 13 years).

Sex: There is no sex predilection.

Site: Mandible is commonly involved in Garre's osteomyelitis in its posterior part. Maxilla can be affected on rare occasion.

PRESENTATIONS

- The involved jaw bone often presents a **grossly carious, nonvital tooth (mostly lower first permanent molar tooth).**
- The tooth is always associated with periapical or sometimes other inflammatory foci.
- There is thickening and swelling of the affected bone with little or no pain.
- The size of the swelling may be ranging from centimeters to a lesion spanning the entire length of the mandible.
- The thickness of the bone may be up to 1 cm.
- Occasionally slight tenderness or a vague pain may be felt in the affected area of bone.
- The overlying skin and oral mucosa appears normal.
- Garre's osteomyelitis is generally a solitary lesion, however multifocal lesions are also sometimes reported.
- Slight pyrexia and moderate leukocytosis may be present but the erythrocyte sedimentation rate (ESR) is normal.

RADIOGRAPHIC APPEARANCE

- Garre's osteomyelitis radiographically presents a central jaw lesion with a **mottled, predominantly radiolucent** appearance, the lesion often has **few radiopaque foci**.
- The affected periosteum forms several layers of reactive vital bone and as a result the expanded cortex of bone radiographically exhibits **many concentric or parallel opaque layers**, which often produce a typical "**onion skin**" appearance.
- These concentric bone laminations may be as many as 12 in numbers, these are roughly parallel to each other and the underlying cortical surface of bone.
- The standard occlusal radiograph reveals a smooth, convex, bony overgrowth on the outer cortex of the jaw. This is often called *'duplication' of the cortex*.
- Few newly formed bony trabeculae are often oriented perpendicular to the **"onion skin"** layers.

Common diseases associated with periosteal new bone formation in the jaw

- Osteomyelitis
- Trauma
- Cyst
- Malignancy, e.g. osteosarcoma
- Fracture of bone.

HISTOPATHOLOGY

- The lesion histologically presents areas of newly formed bone, consisting of multiple osteoids and primitive bony tissues in the subperiosteal region.
- Parallel rows of highly cellular and reactive woven bones are seen.
- Osteoblastic activity dominates the outer surface of bone while both osteoblastic as well as osteoclastic activities can be observed in the central part of bone.
- The marrow spaces contain fibrous tissue showing patchy areas of chronic inflammatory cell infiltration.
- On rare occasions there may be presence of small sequestra.

DIFFERENTIAL DIAGNOSIS

- Ossifying fibroma
- Immature fibrous dysplasia
- Ewing's sarcoma
- Osteoblastic osteosarcoma
- Osteoma
- Fracture callus
- Metastatic tumor of the jaw bone
- Pulse granuloma.

TREATMENT

- Elimination of the causative agent.
- Extraction of the offending tooth and antibiotic therapy.
- The cortical swelling undergoes spontaneous physiologic remodelling and does not required any additional surgical intervention.

GIANT CELL PERIOSTITIS WITH HYALINE CHANGE (PULSE GRANULOMA)

DEFINITION

A large variety of foreign materials can be implanted into the oral tissues, some which can initiate a granulomatous reaction. Such reactions are characterized by chronic inflammation and subsequent formation of a ring-shaped hyaline eosinophilic structure in the tissue and few giant cells.

The term "pulse granuloma" has been coined since vegetable materials especially pulses are believed to cause these disease more often than others. The disease occurs when the vegetable material is introduced into the oral tissue via extraction socket or surgical flaps or open root canals, or through ulceration in the oral mucosa.

CLINICAL FEATURES

- Clinically the lesion is either dome-shaped or multinodular and it is usually soft or firm in consistency.
- Mucobuccal fold is the most common site for the development of pulse granuloma and often there is thickening of the periosteum due to proliferative periostitis.
- Pain is not a prominent feature unless there is suppuration.

Classification of endodontic-periodontic lesions

According to Simon, the endodontic-periodontic lesions are classified into four types:

- *Primary endodontic lesions:* Here the infection originates in the pulp, which later on extends via the accessory canals or apical canals into the periodontium and produce a resultant inflammation there. Clinically and radiographically the disease simulates periodontal defects. Endodontic treatment alone usually solves the problem.
- *Primary endodontic lesions with secondary periodontal involvement:* If prompt endodontic therapy is not done in a situation, where the pulpal infection has already spread into the periodontium, then periodontal tissue breakdown will occur. Treatment in such cases will involve both endodontic as well as the periodontal therapy.
- *Primary periodontal lesion with secondary endodontic involvement:* If an accessory root canal comes in the path of a progressive periodontal infection, then the pathogenic organisms from the periodontium may take entry into the pulp via such canals and results in secondary pulpal infections and necrosis. Moreover infection along the root may also reach to the apex and cause retrograde infection of the dental pulp via the apical foramen. Treatment will be both periodontal and endodontic in such cases.
- *True combined lesion:* Periodontal and endodontic lesions may arise independently in a tooth and at some stage both these lesions may coalesce together to establish a true combined endodontic-periodontic disease. Dual therapy for both lesions required but prognosis is mostly poor.

HISTOPATHOLOGY

- Fibrosis in the submucosa with presence of granulation tissue showing few inflammatory cells.
- Multiple ring-like hyaline structures are found, which are enclosing connective tissue including blood vessels.
- Multinucleated giants are presents.
- Pulse granuloma produces multiple compartmentalized spaces containing giant cells.
- Oil-granuloma produces many empty vacuoles.

TREATMENT

Local excision is the treatment of choice.

ENDODONTIC-PERIODONTIC LESIONS

Sometimes infections of the pulpal origin may spread into the periodontal tissue and likewise the periodontal infections may also sometimes spread to involve the dental pulp secondarily. Therefore, a possibility is always there for the development of a combined endodontic-periodontic lesion, which is facilitated by two important factors.

- Dynamic nature of both pulpal and periodontal diseases.
- Communication between pulp and periodontium via accessory canals or the apical foramen.

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CHAPTER 11

Spread of the Oral Infection

An infective process involving the tooth and its supporting structures is known as odontogenic infections.

In the oral cavity, a large number of such odontogenic infective lesions are often encountered, which originate either from the gingival tissue or from the periapical sites.

Infections from the gingival tissue often involve the deeper periodontal ligaments and the supporting alveolar bone and they may eventually progress to the periapical region of tooth.

In most instances of periapical infections, the microorganisms are derived from the necrosed dental pulp as a sequel of dental caries.

The common odontogenic infections which are often encountered in the oral cavity include **pericoronitis, periodontal abscess, periapical abscess, subperiosteal abscess and the osteomyelitis of various types.**

Once the odontogenic infections reach the bone or muscle or mucosa or lymph nodes, etc. they may either resolve spontaneously or spread to the local or the distant sites.

Factors determining spread of oral infections to distant sites

- Virulence of the microorganisms.
- Immunity of the host.
- Anatomical site of the initial infection.

FACTORS RELATING TO ORGANISMS

Some organisms producing odontogenic infections are more virulent than others, moreover, a few organisms, e.g. *Streptococcus aureus* can produce enzymes like hyaluronidase and fibrinolysins, etc. which help in the spread of infection into distant areas by breaking tissue barriers.

FACTORS RELATING TO THE HOST

If the host or the patient has a high degree of body resistance, the distant spread of infection from the oral cavity is less likely to occur and vice versa.

FACTORS RELATING TO THE SITE OF INFECTION

The site of initial involvement of the odontogenic infection also determines whether it will remain localized or will make a distant spread.

The thinner cortical plates of bone or loose tissue spaces around the wound may offer little resistance to the spread of infection, therefore, infections from such areas may often spread diffusely.

However, thicker cortical plates of bone and tough tissue sites (e.g. areas of muscle attachments) may actually prevent the spread of distant spread of infection.

SPACE INFECTIONS

Odontogenic infections often spread through natural pathways into potential tissue spaces situated between different planes of fascia.

Infections into the various tissue spaces are known as the 'space infections'. Such infections in the vicinity of the jaw bones can be divided into two broad groups, namely, those related to the maxilla and those related to the mandible.

SPACE INFECTIONS RELATED TO MAXILLA

CANINE FOSSA INFECTION

Source of infection: Maxillary canine tooth.

Clinical Features

- Pain and tenderness over infraorbital region.
- Elevated body temperature
- Submandibular lymphadenopathy.

Treatment

- Extraction or endodontic treatment of the involved canine tooth.
- Antibiotic therapy.

PALATAL SPACE INFECTION

Source of Infection

Maxillary lateral incisors and infection via palatal roots of maxillary molars.

Clinical Features

Pain and an extremely tendered swelling over the palate.

Treatment

- Antibiotic therapy
- Extraction or endodontic treatment of the involved tooth.

INFRATEMPORAL SPACE INFECTION

Boundary	Infratemporal space is bordered by the following structures:
Anteriorly	Maxillary tuberosity
Posteriorly	Lateral pterygoid muscle, condyle of the mandible, temporalis muscle.
Laterally	Tendon of the temporalis muscle, coronoid process of mandible
Medially	Lateral pterygoid plate, inferior belly of the lateral pterygoid muscle.

Contents of Infratemporal Space

- Pterygoid plexus
- Internal maxillary artery
- Mandibular nerve, myelohyoid nerve
- Lingual nerve, buccinator nerve and chorda tympani nerves
- External pterygoid muscle.

Source of infection: Infected maxillary molar teeth.

Infected needles or solution used for injection of the maxillary tuberosity.

Clinical Features

- Trismus and pain
- Swelling of the eyelids when postzygomatic fossa is involved.
- Dysphagia due to involvement of pharynx.
- Swelling in the preauricular region, which may extend up to the cheek.

Treatment

- Surgical drainage
- Antibiotic therapy
- Extraction or endodontic treatment of the offending tooth.

PTERYGOMANDIBULAR SPACE INFECTION

Pterygomandibular space is the inferior portion of the infratemporal space.

Boundary: The space lies between the internal pterygoid muscle and the ramus of the mandible.

Sources of Infection

- Pericoronitis of mandibular third molar tooth.
- Infected needles or injection into the space.

Clinical Features

- Severe trismus
- Radiating pain
- Swelling of the lateral-posterior region of soft palate may be seen.

Treatment

- Drainage
- Antibiotic treatment
- Treatment of the offending third molar tooth.

TEMPORAL POUCH INFECTION

Source of Infection

Secondary infections from the submasseteric, pterygopalatine and infratemporal spaces.

Maxillary molars are the common offending teeth.

Clinical Features

- Pain and trismus
- Swelling may be an occasional feature.

Treatment

- Surgical drainage
- Antibiotic therapy.

PAROTID SPACE INFECTION

Parotid space is a compartment formed by splitting of the investing layer of deep cervical fascia.

Contents

- Parotid glands
- Extra- and intraglandular lymph nodes
- Facial nerve, auriculotemporal nerve
- Posterior facial vein
- External carotid, internal maxillary and superficial temporal arteries.

Source of Infection

Secondary infections from lateral pharyngeal and submasseteric spaces.

Clinical Features

- A smooth, painful swelling in front and below the external ear.
- Fever, chills, etc.
- Sometimes, the entire side of the face may be swollen.

Treatment

- Surgical drainage
- Antibiotic therapy.

SPACE INFECTIONS RELATED TO MANDIBLE

MENTAL SPACE INFECTIONS

Source of Infection

Mandibular anterior teeth.

Clinical Features

- A tense painful swelling in the chin region.
- This kind of swelling can also occur in the localized nonodontogenic infections.

Treatment

- Surgical drainage
- Antibiotic therapy
- Treatment of the offending tooth.

SUBMENTAL SPACE INFECTION

Boundary: Anteriorly the midline of mandible, posteriorly the anterior border of the submaxillary space and inferiorly by the myelohyoid muscle.

Source of Infection

Mandibular anterior teeth.

Clinical Features

- Painful swelling in the submental area.
- Occasionally dyspnea and dysphagia.

Treatment

- Antibiotic therapy
- Extraction or endodontic therapy to the offending tooth.

SUBMANDIBULAR SPACE INFECTION

Boundary: Submandibular or submaxillary space is bordered by the following structures:
Medially—Hyoglossus and digastric muscles.
Laterally—Superficial fascia and skin.
Superiorly—Posterior portion of hyoglossus muscle.

Contents: Submandibular salivary gland and lymph nodes.

Source of infection: Infected mandibular molars.

Clinical Features

- Submandibular space infection is the most common of all space infections in the orofacial region (Figs 11.1 to 11.3).

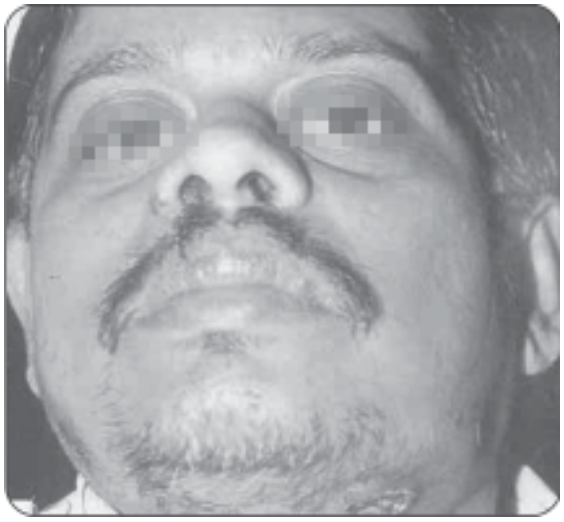


Fig. 11.1: Submandibular space infection resulting in extraoral sinus formation

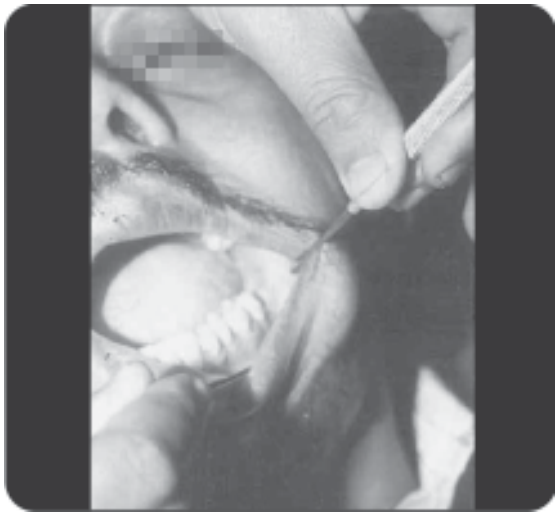


Fig. 11.2: Intraoral view of the same patient

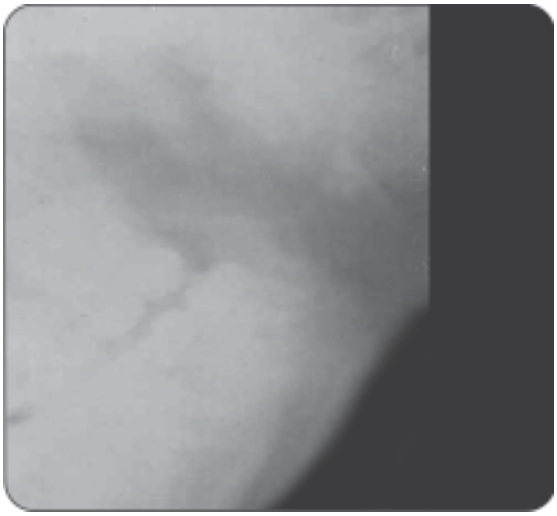


Fig. 11.3: X-ray reveals periapical radiolucency in mandibular molar region

- Fever, chill and anorexia.
- Pain with swelling near the angle of the mandible.
- Submandibular space infection often results in lymph adenitis in the submandibular lymph node and sialadenitis in the submandibular salivary gland.
- Infections from the submandibular space may extend to the sublingual and submental spaces, and rarely to the lateral pharyngeal spaces.
- Involvement of the pharynx and the larynx may cause dyspnea and dysphagia.
- Distant spread of infection from the submandibular space may result in infections of the cranial fossa or of the mediastinum.

Treatment

- Surgical drainage
- Antibiotic therapy
- Treatment of the offending tooth
- Tracheotomy may be required in cases of airway obstruction.

SUBLINGUAL SPACE INFECTION

Boundary: Sublingual space is situated above the submandibular space and it is bordered by the following structures:
Superiorly—Mucosa of the floor of the mouth.
Inferiorly—Mylohyoid muscle.
Antero-laterally—Body of the mandible.
Posteriorly—Hyoid bone.
Medially—Median raphae of the tongue.

Source of Infection

- Mandibular teeth except second and third molars.
- Sublingual infections may be transported from the submandibular space.

Clinical Features

- Swelling of the floor of the mouth
- Airway obstructions in severe cases
- Dysphagia
- Infections can spread to involve the tongue.

Treatment

- Drainage
- Antibiotic therapy
- Elimination of the source of infection.

LATERAL PHARYNGEAL SPACE INFECTION

Lateral pharyngeal or parapharyngeal space is situated deep in the neck and infection of this space often terminates fatally.

Boundary
Anteriorly—Buccopharyngeal aponeurosis, parotid gland and pterygoid muscles.
Posteriorly—Prevertebral fascia.
Laterally—Carotid sheath.
Medially—Lateral wall of the pharynx.

Source of Infection

- Mandibular third molar.
- Infection of the palatine tonsils, mastoid air cells and parotid glands.

- Infection may also come from the retromandibular space.

Clinical Features

- Pain, trismus with fever and chill.
- Dysphagia and dyspnea due to involvement of the pharynx and larynx.
- Infection from lateral pharyngeal space may spread to the mediastinum via the prevertebral fascia.

Complications

- Septicemia
- Respiratory paralysis
- Thrombosis of the internal jugular vein
- Erosions of the internal carotid artery.

Treatment

- Surgical drainage
- Antibiotic therapy
- Elimination of the primary source of infections
- Maintenance of airway patency.

RETRO-PHARYNGEAL SPACE INFECTION

Boundary

Anteriorly—Wall of the pharynx.

Posteriorly—Prevertebral fascia.

Laterally—Lateral pharyngeal space and carotid sheath.

Source of Infection

Lateral pharyngeal space.

Clinical Features

- Pain, swelling and dysphagia, etc.
- Retropharyngeal space infection may spread to the mediastinum as the prevertebral fascia extends to the posterior mediastinum.

INFECTION OF THE SPACE OF BODY OF MANDIBLE

Boundary: A natural tissue space exists around the body of the mandible as it is enclosed by a layer of fascia derived from the outer layer of deep cervical fascia.

Inferiorly—The fascia attaches on the inferior border of mandible and then covers its body from both buccal and lingual side.

Superiorly—It becomes continuous with the alveolar periosteum and muscles of the facial expression having attachment to the mandible.

Contents

- Body of mandible excluding the ramus, along with the covering periosteum.
- Fascia and muscle attachments.
- Teeth and periodontium.

Source of Infection

- Mandibular teeth.
- Periodontal infection of the regional teeth.
- Blood-borne infections.
- Infection following fracture of mandible.
- Extension of infection from neighboring tissue spaces.

Clinical Features

- The odontogenic infections perforate either the buccal or the lingual cortical plates of mandible before they spread to the mandibular body space.
- The clinical manifestation varies and it depends upon factors like the source of infection, which cortical plate (buccal or lingual) has been perforated and at what level of the bone.
- If infections from incisors, cuspids and bicuspids are spreading into the space by perforating the buccal cortical plate, an induration, swelling and fluctuation of the labial sulcus will be observed.
- When infections from the same sources are perforating the lingual cortical plate, swelling of the floor of the mouth will occur.
- Infections from mandibular molar teeth when perforate the buccal cortical plate above the attachment of buccinator muscle, a swelling of the oral vestibule is seen.
- If buccal perforation takes place below the level of attachment of buccinator muscle, a swelling of the covering skin over mandible is noticed.

- When infections of mandibular molars and premolars perforate the lingual cortical plate of bone above the level of attachment of the mylohyoid muscle, swelling of the floor of the mouth occurs.
- If lingual perforation occurs below the myelohyoid attachment, the infection spreads either into the submandibular space or into the lateral pharyngeal space.

Treatment

- Drainage
- Antibiotic therapy
- Treatment of the infected tooth or the other primary source.

SUBMASSETERIC SPACE INFECTION

Boundary: Submasseteric space is bordered by the following structures:

Medially—Lateral surface of the mandibular ramus.

Laterally—Masseter muscle.

Anteriorly—Retromolar fossa.

Posteriorly—Parotid gland.

Source of Infection

- Mandibular third molars
- Infection from this tooth passes through the retromolar fossa and moves into the submasseteric space.

Clinical Features

- Pain and swelling due to subperiosteal abscess formation.
- Trismus.

Treatment

- Surgical drainage
- Antibiotic therapy
- Treatment of the infected third molar.

Sequelae of odontogenic infections

- Localized abscess formation
- Acute cellulitis
- Ludwig's angina
- Cavernous sinus thrombosis
- Bacteremia, septicemia, toxemia and pyemia

CELLULITIS

DEFINITION

Cellulitis is an acute edematous, purulent inflammatory process, which spreads diffusely through different tissue spaces or fascial planes.

PATHOGENESIS

- Acute cellulitis is mostly caused by some unusually virulent bacteria, which often produce hyaluronidase and fibrinolysins, etc.
- Hyaluronidase and fibrinolysins cause lysis of the hyaluronic acid (universal intercellular cement substance) and fibrin respectively, and cause breakdown of the tissue barriers. The enzymes, therefore, help the infective process to spread diffusely into tissue spaces.
- Diminished body resistance in general and tissue resistance in particular of the host, bacterial resistance to antibiotics, favorable anatomic locations, etc. also help in the process development of cellulitis.
- Microorganisms such as *Streptococcus pyogenes* and anaerobes, particularly bacteroides most commonly produce facial cellulitis.
- In acute cellulitis, infection from the lower anterior teeth perforates the lingual cortical plate of bone and moves into the superficial sublingual space, and from there tracks backwards.
- Infection from lower molar teeth, after penetrating the lingual cortical plate reaches the junction of fascial spaces at posterior border of mylohyoid muscle.
- From there the infection may spread forward to reach the sublingual and submandibular space and backwards into the parapharyngeal spaces.

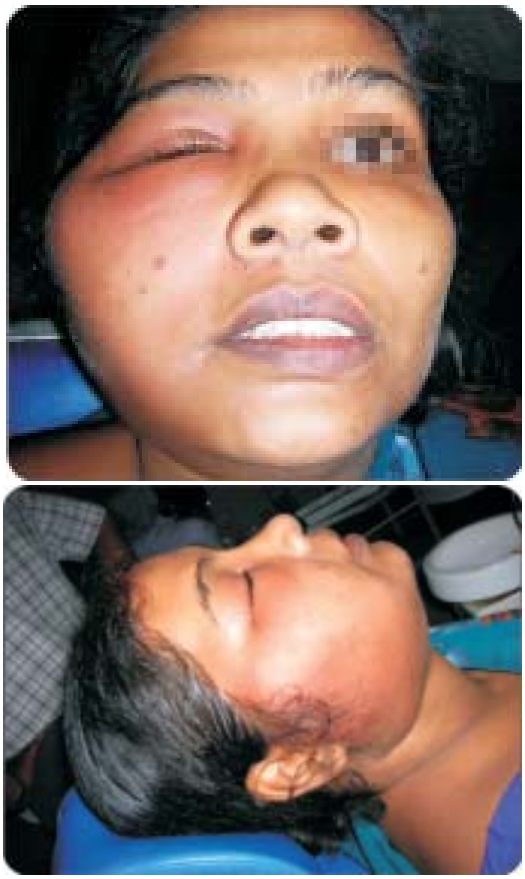
Primary sources of infections for orofacial cellulitis

- Periapical abscess
- Pericoronitis or pericoronal abscess
- Periodontal abscess
- Osteomyelitis
- Infected post-extraction wound
- Gunshot injuries
- Oral soft tissue infections
- Oral infection in HIV
- Bloodborne infections.

CLINICAL FEATURES

Cellulitis clinically presents the following features:

- Development of **a large, diffuse, painful swelling over the face or neck** with facial asymmetry (Figs 11.4 A and B).
- The soft tissue swelling is usually firm and brawny.
- When cellulitis involves the superficial tissue spaces, the overlying skin often appears purplish.
- However, when the infection spreads along the deeper tissue spaces, the skin appears normal.
- Fever, chill, leukocytosis, etc. are often present, which make the patient slightly ill.
- Regional lymphadenopathy frequently develops and in untreated cases cellulitis may spread over a wide area and sometimes involve the entire face.
- Trismus, dyspnea and dysphagia are the common complications.
- Some lesions resolve completely, however, in other cases pus discharging intraoral or extra-oral sinuses may develop.



Figs 11.4A and B: Cellulitis

HISTOPATHOLOGIC FEATURES

- Collection of a large amount of fibrin and serum fluid in the tissue.
- Separation of periosteum and muscles from the bony surface due to accumulation of fluid.
- Acute inflammatory cell infiltration by PMN and occasionally lymphocytes.
- Pus may develop in the later stages of the disease.
- Formation of sinus tracts over skin or mucosal surfaces.

TREATMENT

- Bacteriological examination of the exudate or pus, etc
- Drainage
- Antibiotic therapy
- Elimination of the primary source of infection.

LUDWIG'S ANGINA

DEFINITION

Ludwig's angina is **an overwhelming diffuse, suppurative cellulitis**, which simultaneously involves the **submandibular, sublingual and submental spaces.**

Predisposing factors for Ludwig's angina

- Diabetes mellitus
- HIV infection
- Oral transplants
- Aplastic anemia.

CAUSATIVE MICROORGANISMS

- Hemolytic streptococci are the most frequently encountered organisms to cause Ludwig's angina. However, staphylococci, bacteroides and fusiform bacilli may also be involved.

Primary sources of infections in Ludwig's angina

- Periapical, pericoronal or periodontal infections from mandibular molar teeth
- Gunshot injury or stab wounds in the floor of the mouth with secondary infection
- Infection following fracture of the mandible
- Osteomyelitis of the jawbones
- Infection of the other orofacial soft tissues
- Spread of infection from peritonsillar or parapharyngeal abscesses
- Submandibular sialadenitis.

PATHOGENESIS OF LUDWIG'S ANGINA

- In Ludwig's angina, all the three important spaces in the submandibular region, i.e. the submandibular space, sublingual space and the submental space, are involved simultaneously.
- Although **involvement of these spaces occurs one after the another**, the spread of infection is so rapid as if it is involving all the spaces together.
- Infection from mandibular second and third molar teeth often perforates the lingual cortical plate of bone (buccal cortical plate is usually not perforated in the molar region as it is much harder and thicker as compared to the lingual plate) below the level of attachment of the mylohyoid muscle and spreads to the submandibular space.
- Similarly, infection from mandibular first molar teeth also perforates the buccal cortical plate but above the level of mylohyoid muscle attachment, and, therefore, spreads to the sublingual space.
- Submental space is usually involved by extension of infection from the neighboring spaces.
- Submandibular space infections or inflammations can spread to lateral pharyngeal space, from there it can spread to retropharyngeal space and from there it can even spread to the mediastinum.

CLINICAL FEATURES

- Ludwig's angina produces a rapidly spreading, large, diffuse and **board-like aggressive swelling**; which involves the upper part of neck and floor of the mouth bilaterally with brawny induration.
- The swelling causes **elevation of the tongue**; which may be pushed up against the palate and the patient often has a typical **open mouthed appearance**.
- The enlarged **tongue may protrude outside the mouth** and the condition is called **woody tongue.**
- The swollen area of the neck is firm, painful, nonfluctuant and does not pit upon pressure.
- The **condition is always bilateral** and the patient is often unable to open the mouth, speak or swallow properly.
- Usually, the patient is very toxic with high fever, chill, rapid pulse, dysphagia, sore throat, drooling and fast respiration, etc.
- In untreated cases, cellulitis may spread further and cause a massive swelling in the neck above the hyoid bone; this condition is often known as **bull neck**.
- As the condition deteriorates further there may be development of **edema glottis**; which is a serious condition and can result in death due to asphyxia.
- Other serious consequences of Ludwig's angina include the development of cavernous sinus thrombosis, meningitis, brain abscess and suppurative encephalitis, etc.

DIAGNOSIS

Diagnosis is usually established by the following methods:

- Clinical features of the disease are often very specific.
- Leukocytosis
- Bacterial culture with identification of specific microorganisms.

TREATMENT

- High dose of antibiotics.
- Drainage by incision at the anterior part of the neck.
- Emergency tracheostomy may be required in cases of airway obstructions.

CAVERNOUS SINUS THROMBOSIS (THROMBOPHLEBITIS)

DEFINITION

Cavernous sinus thrombosis is a serious **life-threatening condition** characterized by formation of septic thrombi within the cavernous sinus and its numerous communicating branches.

ROUTES OF SPREAD OF INFECTIONS

External Route

- The veins of the maxillary regions of face anatomically drain into the cavernous sinus and because of this, infections from **upper lip, face, eye and nares**, etc. often reach cavernous

sinus directly through facial and angular veins.
- Since facial and angular veins are **quite longer vessels** and, moreover, they **have no value systems** in them, infections from the outer face spread rapidly to the cavernous sinus via this route.

Internal Route

- Infections from internal structures (especially upper and lower third molar teeth) reach cavernous sinus via the **pterygoid plexus**.
- Spread of infection via the internal route usually occurs at a much slower pace, since the infection has to pass through many small and twisted venous passages of the pterygoid plexus.

Primary sources of infection in cavernous sinus thrombosis

External sources

Infection from face, e.g. lip, face, nares and eye.

Internal sources

- Periapical/Pericoronal/Periosteal abscesses
- Otitis media
- Fracture of skull
- Meningitis
- Septicemia.

CLINICAL FEATURES

- Patients with cavernous sinus thrombosis are often gravely ill and if timely intervention is not done the disease can terminate fatally.
- Headache, fever, vomiting, nausea and chill, etc. are present in the initial stages.
- Patients may also develop **tachycardia, tachypnea, stiffness of the neck and irregular breathing**, etc. with alarming severity.
- Occlusion of the ophthalmic veins causes **photophobia, increased lacrimation, proptosis, chemosis, dialatation of pupil and edema of the eyelids,** etc.
- **Paralysis** of the external ocular muscles, **exophthalmos, fixation of the eyeball,** intraocular hemorrhage and even blindness can occur.
- **Massive swelling of the nose and forehead** areas.
- Complete paralysis of the third, fourth and sixth cranial nerves common.
- Pain above the eye and diminished sensation over the forehead.
- The condition is initially unilateral but, it often becomes bilateral within 2 to 3 days.
- Death may occur due to brain abscess, meningitis, septicemia, toxemia or pyemia, etc.

TREATMENT

- Maintenance of airway in cases of respiratory distress
- High doses of antibiotic therapy
- Drainage
- Anticoagulant therapy.

MAXILLARY SINUSITIS

DEFINITION

Maxillary sinusitis can be defined as the acute or chronic inflammations of the maxillary sinus.

ETIOLOGY

- Maxillary sinusitis often occurs due to direct extension of odontogenic infections and it happens due to the typical anatomical relation and proximity of the teeth to this sinus.
- Usually, periapical abscess in the upper premolar or molar teeth may spread to the maxillary sinus.
- In other situations, broken root fragments of any of these teeth may be pushed into the sinus along with some bacteria.
- However, there are a few other causes of maxillary sinusitis, which are as follows:
  - Common cold
  - Influenza
  - Exanthematous diseases
  - Spread of infections from the neighboring frontal or parietal sinuses
  - Phycomycosis infection
  - Traumatic injury to the maxillary tuberosity followed by secondary infection.

CLINICAL FEATURES

- Acute maxillary sinusitis produces moderate to severe pain in the sinus region with swelling.

- The pain usually increases when digital pressure is applied over the maxilla.
- Patient feels pain in the teeth or in the ear because the sinusitis pain is often referred to these structures.
- Fever, malaise, discharge of pus into the nose with fetid breath, etc. are the other conventional features of acute maxillary sinusitis.
- Chronic maxillary sinusitis presents little or no pain and the disease is often discovered during routine examinations.
- However, sometimes there can be presence of vague pain, stuffy sensation in the face, mild nasal discharge with foul breath.

RADIOLOGICAL FEATURES

- For detailed visualization of the maxillary sinus. Water's view radiographs are specifically needed.
- Acute maxillary sinusitis radiographically does not produce any significant diagnostic findings.
- However, chronic maxillary sinusitis often produces **clouding of the maxillary sinus** on radiographs.
- This clouding of the sinus occurs due to presence of fluid and hyperplastic epithelial tissues, which fill up the entire sinus cavity.

HISTOLOGICAL FEATURES

- In acute maxillary sinusitis, the lining epithelium of the maxillary sinus shows edema, occasional hemorrhage and infiltration by acute inflammatory cells.
- Squamous metaplasia of the ciliated columnar epithelium occurs in rare cases.
- Chronic maxillary sinusitis often produces marked thickening of the lining epithelium with formation of numerous epithelial polyps.
- The polyps fill up the entire sinus cavity and these are made up of hyperplastic, granulation tissue with lymphocytic and sometimes plasma cell infiltrations.

TREATMENT

- Removal of primary sources of infection
- Drainage
- Removal of hyperplastic epithelium by thorough curettage
- Antibiotics may be administered in acute cases.

FOCAL INFECTION

It has been observed since long time that infections from oral cavity can spread to distant parts of the body and produce fresh lesions over there.

Orofacial tissues especially the teeth and the periodontium normally harbor numerous microorganisms, which are otherwise nonpathogenic as long as they are within the oral cavity. However, once these organisms spread to the distant organs of the body, they behave as strictly pathogenic organisms and produce diseases.

Moreover, oral tissues are vulnerable to infections caused by various microorganisms (e.g. bacteria, virus and fungus), which produce a wide variety of lesions in the oral cavity.

Infections from these primary lesions may spread to the distant organs to initiate secondary diseases.

DEFINITION

Focal Infection

Metastases of microorganisms or their toxins from a localized site of infection to any distant part of the body with subsequent injury are called "**focal infections**."

Focus of Infection

Circumscribed area of tissue, which is infected by exogenous pathogenic organisms and is usually located near the skin or mucosal surface is called a **focus of infection**.

MECHANISM OF FOCAL INFECTION

Focal infections mostly occur by the following mechanisms:

- Spread of "pathogenic microorganisms" from their primary site of infection to the distant part of body via the blood vessels or lymphatics.
- Spread of "toxins" liberated by the pathogenic microbes to distant organs either via blood vessels or lymphatics (erythrogenic toxins

liberated by beta hemolytic Streptococci produce diffuse, bright skin rashes in scarlet fever.

Examples of Various Oral "Foci" of Infections

- Periapical abscess (acute or chronic)
- Pericoronitis
- Infected periapical granuloma or cyst
- Periodontal abscess
- Infected dental pulp or root canals
- Infected root fragments of teeth
- Osteomyelitis
- Syphilitic chancre
- Infections in the maxillary sinus, nasal sinus, throat and tonsils, etc.

COMMON CONSEQUENCES OF "FOCAL INFECTIONS" FROM THE OROFACIAL REGION

Several life-threatening systemic diseases can occur due to either 'direct spread of infections or dissemination of toxins' liberated by the oral pathogenic microorganisms into the blood. Following are few examples of these diseases caused by focal infections from the oral and orofacial infective sources:

- Subacute bacterial endocarditis
- Cavernous sinus thrombosis
- Meningitis and brain abscess
- Subdural empyema
- Suppurative encephalitis
- Ocular diseases
- Renal diseases
- Gastrointestinal diseases
- Upper respiratory tract disease
- Dermatological lesions
- Bacteremia, septicemia, toxemia and pyemia
- Rheumatoid arthritis and rheumatic fever.

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CHAPTER 12

Physical and Chemical Injuries of the Oral Cavity

PART I: PHYSICAL INJURIES

FRACTURES OF TEETH

Tooth fracture is a common type of injury and it occurs in a variety of situations, e.g. sudden severe trauma, tooth weakened by a large restoration, non-vital tooth and internal resorptions, etc.

It is important to note that the boys usually have more tooth fractures in comparison to the girls, and class II malocclusion is associated with more cases of anterior tooth fractures.

Classification of tooth fracture

Class I	Simple fracture of the crown that involves enamel with little or no dentin involvement.
Class II	Fracture involving the enamel and dentin but not the pulp.
Class III	Extensive fracture involving considerable dentin and exposing the pulp.
Class IV	Fracture causing loss of vitality of the affected tooth.
Class V	Fracture causing complete loss of the tooth.
Class VI	Fracture of the root with or without the crown fracture.
Class VII	Displacement of the tooth without any fracture of the crown or the root.
Class VIII	Fracture of the crown en mass and its replacement.
Class IX	Fracture involving the deciduous teeth.

ROOT FRACTURE

Root fracture represents a small percentage of total number of tooth fractures. Most cases occur due to trauma between the ages of 10 to 20 years. Most of the root fractures are horizontal in nature and are located in the middle third of the root. Other fractures of root usually occur in the apical third area. Most of the affected teeth become non-vital as soon as the fracture occurs. Some may heal by forming reparative dentin. Nonvital teeth show formation of granulation tissue around the apex with extensive resorption of the root.

CEMENTAL TEAR

Cemental tears are small fractures of the cementum on the root surface, which usually occur as a result of sudden rotational forces. Cemental tears cause detachment of part of cementum, which remains within the periodontal ligament. The condition is usually asymptomatic.

TREATMENT

The fractured vital teeth are easily saved by restoration but in case of fractured nonvital teeth, root canal treatment (RCT) should be done before any restoration is given.

Post and core crown is built on an existing tooth-root, where the crown is lost as a result of fracture.

Sometimes in cases of a vertical tooth fracture, the patients often complain of a sharp pain especially during chewing hard foods but the fracture is not detected by radiographs and this condition is often known as the "cracked-tooth syndrome". It will require extraction of the affected tooth.

BRUXISM

DEFINITION

Bruxism can be defined as the habitual, unintentional grinding or clenching of teeth, it

Causes of premature loss of teeth	
Trauma	• Due to accidents • Psychotic patients • Radiation.
Periodontal diseases	• Aggressive juvenile periodontitis • AIDS related periodontal diseases.
Hereditary conditions	• Acatalasia • Chediac-Higashi disease • Cyclic neutropenia • Dentin dysplasia-type I (Rootless tooth) • Hypophosphatesia • Hypophosphatemia • Lesch-Nyhan syndrome • Papillon-Lefevre syndrome • Down's syndrome.
Immunocompromised states	• HIV/AIDS • Leukemia • Chemotherapy.
Neoplasms	• Benign and malignant neoplasm of the jaws • Lymphomas • Tumor-like conditions.
Miscellaneous factors	• Diabetes mellitus • Histiocytosis–X • Acrodynia • Regional odontodysplasia (ghost teeth) • Osteomyelitis • Vitamin-C deficiency • Langerhan's cell disease.

occurs periodically either during sleep in the night or during day-time. The person, who has the habit of bruxism does grinding or clinching of teeth at inappropriate moments along with repeated tapping. The act causes considerable amount of damage to the teeth and the related structures. About 10 to 20 percent of the general population is affected by this habit.

CAUSES

Local factor: Occlusal disturbances.
Systematic causes: Unrecognized mental tension due to the following reasons:

- Chronic GI upset
- Sleep disorder
- Heredity
- Physical disability
- Endocrine disorder

Psychological factor

- Emotional upsets due to fear, pain, anger, rejection, nervousness or frustrations, etc.
- Persons with aggressive, hurried or overly competitive tendencies.

Occupational cause: Watchmakers and carpenters are prone to have bruxism (as they habitually hold the instruments by the teeth).

Habitual cause: Continuous chewing of pan, tobacco, pencils and finger nails also can cause the defect, etc.

TYPES OF BRUXISM

There are two types of bruxism:
A. Nocturnal
B. Day-time habit

CLINICAL FEATURES

- Severe attrition of teeth with loss of enamel and exposure of dentin (both occlusally and inter-proximally).
- Noise during grinding of teeth.
- Multiple wear facets on the occlusal surface with occasional fracture of cusps or restorations.
- Loosening and drifting of teeth.
- Gingival recession.
- Hypertrophy of the masticatory muscles (predominantly masseter and anterior temporalis).
- Trismus, altered occlusion and indentations at the tongue border.
- Dislocation of the jaw or deviation.
- Facial pain, myalgia and headache.
- Tenderness on palpation of muscles of mastication.
- Sensitivity of teeth.
- Damage and erosion of the mucosa on the inner aspect of cheek.
- A popping or clicking sound in the TM Joint.

TREATMENT

- Removal of the irritating factors (local and systemic).
- Use of occlusal splints.
- Behavior modification.

ANKYLOSIS OF TEETH

Tooth ankylosis is a pathological condition in which the root of the tooth becomes completely united with the bony socket. Many of these teeth fail to erupt in the oral cavity.

PATHOGENESIS

In case of ankylosis, partial resorption of the root occurs due to some reason and later on it is repaired by the deposition of either cementum or alveolar bone. As a result of this, there may be complete obliteration of the periodontal ligament space around the root leading to ankylosis.

CLINICAL FEATURES

- Ankylosis can occur in both deciduous as well as in permanent dentitions and it can develop during any stage of tooth development or tooth eruption.
- The ankylosed teeth usually do not exhibit any clinical manifestations. However, they often produce a **dull, high pitched, muffled sound on percussion, instead of a sharp normal sound.**
- Ankylosed deciduous tooth often blocks the path of eruption of permanent tooth.

Causes of ankylosis of tooth

- Heredity
- Constant occlusal trauma
- Chronic periodontal inflammation
- Sports injury or accident
- Chronic periapical inflammation
- Problems with mineral metabolism or bone growth
- Reimplantation or transplantation of teeth
- Idiopathic.

COMMON SYMPTOMS ASSOCIATED WITH ANKYLOSED TOOTH

- Congenital absence of single or multiple tooth.
- Malocclusion of teeth especially infra-occlusion.
- Abnormal tooth eruption pattern in the jaw.
- Periodontal problems.
- Dental caries.
- Facial skeletal deformity.

RADIOGRAPHIC FEATURES

Radiographically, these teeth often show obliteration of the periodontal ligament spaces around their roots.

TREATMENT

- Orthodontic treatment to help the tooth to erupt.
- Surgical repositioning of the affected tooth may be required.
- Wherever required, these teeth should be extracted by surgical method only.

SUBMERGED TEETH

DEFINITION

A tooth which has not erupted to the point of making contact with the opposing maxillary or

mandibular tooth, during mastication. In other words a submerged tooth is the one, whose relative occlusal movement in the dental arch has stopped during or after the period of active eruption.

CAUSES OF DEVELOPMENT OF SUBMERGED TOOTH

- Genetic cause
- Congenital developmental gap in the periodontal ligament
- Trauma
- Excessive mechanical force
- Disturbed local metabolism
- Congenital absence of permanent successor.

CLINICAL FEATURES

- Submerged teeth are ankylosed deciduous teeth, usually located in the mandibular posterior region.
- They can be single or multiple in numbers.
- The submerged appearance occurs as the occlusal plane of the retained smaller sized tooth is located below the occlusal plane of the rest of the teeth in the arch.
- Thus the submerged tooth always remains out of occlusion as it is static and fails to make any occlusal movement as shown by other teeth in the dental arch.
- These teeth are not movable despite having variable degree of root resorptions
- The normal permanent teeth on either side of the submerged tooth hold it strongly in its position and do not allow it to exfoliate.
- As a result the submerged tooth often gets ankylosed in the jaw.
- In such cases, if the underlying permanent tooth is present below the submerged tooth, it will become either impacted or it may erupt from the buccal or lingual aspect of the submerged tooth in the arch, therefore resulting in local malocclusion.

RADIOGRAPHIC FEATURES

Radiograph reveals obliteration of the periodontal ligament space around the root of the submerged tooth with variable degree of root resorptions. It also reveals missing or impacted permanent successor tooth below the submerged tooth (whenever it happens).

TREATMENT

- Wait and observe for normal exfoliation
- Put a crown on the submerged tooth to raise the occlusal height
- Extract and orthodontically move the permanent successor

TOOTHBRUSH INJURY

Toothbrush injuries are caused by chronic physical irritation from the toothbrush bristles to the marginal and the attached gingiva.

Although any area of the entire dental arch can be involved, these lesions are more often seen in maxillary gingiva over the premolar and canine region (since these are the locations where maximum pressure is exerted during brushing). Moreover, lesions can develop more frequently on the left-sided gingiva if the patient is right handed or vice versa.

CLINICAL FEATURES

- The lesions commonly appear as superficial linear erosions in an erythematous background.
- Some lesions may appear as white, red or ulcerated areas.
- Most lesions produce pain, especially during taking food and some of these lesions can be infected secondarily.
- When the injury is very severe, it can produce deep clefts on the gingival margin with severe gingival recession.
- Accidental injury with a tooth brush may produce large bruise on the floor of the mouth, tongue and cheek, etc.
- On rare occasions the brush can accidentally penetrate even the pharyngeal wall.
- In long-standing cases, there may be irreversible loss of the underlying alveolar bone in the gingiva.

HISTOPATHOLOGY

- This traumatic lesion of the gingiva histologically shows ulceration with focal loss of overlying epithelium.

- The adjacent normal epithelium at the border of the ulcer exhibits hyperparakeratosis and acanthosis.
- The ulcerated area is covered by a superficial zone of granulation tissue.
- The underlying connective tissue shows chronic inflammatory cell infiltration by lymphocytes and plasma cells.

TREATMENT

- Elimination of local factors causing injury (development of proper brushing habit).
- Symptomatic treatment of the injured area.

TOOTHPICK INJURY

Toothpick injury is almost similar to that of toothbrush injury as discussed earlier. It usually results from habitual, overzealous use of common utensils for maintaining oral hygiene.

CLINICAL FEATURES

- It is usually a localized problem and having involvement of only one or two areas of the dental arch.
- Since toothpicks are often inserted into the interproximal areas, the interdental papillae are often damaged or lost.
- Typically, there is a depression involving both buccal and lingual aspects of the gingiva.
- Besides the gingival tissue, toothpick injury also causes injury and subsequent loss of the cementum, dentin and cervical enamel on the mesial and distal aspect of the tooth.
- Patients may have pain and sensitivity in the teeth.
- Habitual toothpick injury causes widening of the interproximal spaces with loss of contact points between two adjacent teeth. This can lead to further accumulation of food particles in the area and thereby resulting in continuation of the habit.

TRAUMATIC ATROPHIC GLOSSITIS

DEFINITION

These are focal sensitive erythematous areas of the tongue due to physical (traumatic) injury or irritation.

CAUSES

- Recent restorations or other changes in oral environment.
- Broken fillings or prosthesis.
- Chipped cusps or sharp incisal edges.
- Extensive calculus in lower anterior teeth.
- Malaligned or crowded teeth.
- Defective prosthesis (loose upper denture, which needs to be reseated again and again by the tongue, can lead to the development of traumatic atrophic glossitis).
- As a symptom of familial dysautonomia or Riley-Day syndrome.

CLINICAL FEATURES

***Site*:** Tip of the tongue and occasionally the lateral margin.

- The affected area shows thinning and reddening of the mucosa.
- The filliform papilla is lost and the fungi form papilla appears enlarged and reddened.
- Patients usually move their tongue repeatedly over the restorations or broken edges in a compulsive manner to explore these areas and thereby injure the tongue.

HISTOPATHOLOGY

- The tongue papilla is thinned and is devoid of filliform papilla.
- The underlying connective tissue exhibits vasodilatation and chronic inflammatory cell infiltration by lymphocytes and plasma cells.

TREATMENT

- Elimination of the irritating factor.
- Stoppage of compulsive tongue movements.

CHRONIC ULCERS OF THE TONGUE

Chronic ulcer of the tongue usually occurs on the middle and posterior third of the lateral border and is often mistaken for squamous cell carcinoma.

CLINICAL FEATURE

Chronic tongue ulcers clinically appear as shallow ulcerations surrounded by a raised rolled border of fibrous tissue and an outer wide zone of indurations.

ETIOLOGY

- ***Traumatic factor:*** The irritating factors are difficult to detect and they can be broken fractured restorations or sharp denture clasps, etc.
- ***Psychological factor:*** Seizures and tongue biting.
- ***Functional cause:*** Chronic tongue ulcers may also occur due to lack of coordination in the tongue movements during mastication.
- ***Medications:*** Some medicines can cause tongue ulcers, e. g. lansoprazole, mouth washes and tooth pastes, etc.
- ***Malnutrition:*** Protein energy malnutrition, deficiency of vitamin B-complex.
- ***Systemic diseases***: Parkinson's disease, crohn's disease, diabetes mellitus, malignancy, etc.
- ***Structural defects in the tongue:*** Chronic tongue ulcers may occur in cases of macroglossia secondary to amyloidosis, hemangioma, lymphangioma, acromegaly and hypothyroidism, etc. In these conditions the large tongue often gets injured or irritated during mastication, which results in ulceration.
- ***Hematological factor:*** Iron deficiency anemia, aplastic anemia and agranulocytosis.
- ***Oral habits***:Excessive consumption of tobacco, alcohol, pan with spices.
- ***Infective conditions:*** Tuberculosis, syphilis, candidiasis and HIV infections, etc.
- ***Immunological abnormality:*** Aphthous ulcers.
- ***Factitious injury:*** Self inflicted injury with subsequent ulceration of the tongue.

TREATMENT

Surgical excision of the ulcer and removal of the local irritating factors. Treatment of the systemic conditions. Histopathological evaluation of the tissue should be done to rule out malignancy because these areas of tongue are prone to develop carcinomas.

TRAUMATIC ULCER

An ulcer can be defined as the breach in continuity of the skin or the epithelium due to molecular cell death.

If an ulcer develops as a result of trauma, it is known as the traumatic ulcer.

CAUSES OF TRAUMATIC ULCER

Traumatic ulcers in the oral cavity may occur due to the following reasons:

- Accidental biting of the mucosa while eating or chewing.
- Injury from the orthodontic or prosthetic appliances.
- Injury from a sharp broken tooth, carious or malposed tooth.
- Toothbrush injury.
- Injury due to iatrogenic causes (e.g. violent rubbing of mucosa with the cotton roll during dental procedures).
- Injury from ill-fitting or misaligned prosthesis.
- Thermal, chemical or electrical injury to the oral mucosa.
- Nocturnal parafunctional habits, e.g. bruxism, cheek biting, thumb sucking.
- Improper feeding of children.
- Factitious injury.
- Xerostomia.

CLINICAL FEATURES (FIG. 12.1)

- Traumatic ulcers frequently develop on the tongue, vestibule, alveolar ridge or palate, etc.
- The lesion often exhibits a solitary, painful ulcer of short duration.
- The ulcers are often covered with a yellow, fibrinopurulent exudate.
- Most of the time, the cause of the ulcer is easily detected from the patient's history.

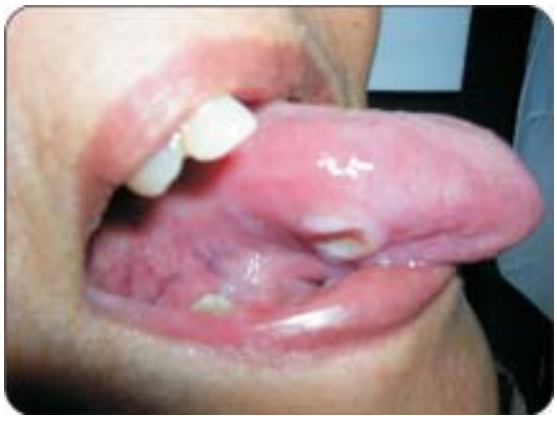

Fig. 12.1: Traumatic ulcer

- There is considerable difficulty in taking foods.
- Secondary infections often make the situation complicated.
- Long standing ulcers may be associated with premalignant or malignant changes.

TREATMENT

Removal of the primary cause and symptomatic treatment will easily cure the condition. Systemic conditions should be duly treated wherever required.

FACTITIOUS INJURIES (SELF-INFLICTED ORAL WOUNDS)

Factitious injuries are self-inflicted injuries caused by the patient himself or herself and these are either habitual or inadvertent. These injuries are commonly seen in persons with disturbed mental state and injuries are purposefully created for 'seeking attention'.

Characteristics of wound in factitious injuries

- Presence of an wound in absence of any recognizable disease or any apparent cause.
- Bizarre shape or outline of the wound.
- Wounds found in the mouth of an otherwise healthy individual.
- Wounds present in areas of mouth easily accessible to patient.
- Clinical appearance of the wound is often inconsistent with the history given by the patient.

Following are the examples of few factitious injuries:

- Cheek and lip biting
- Self extraction of tooth
- Fingernail injuries
- Nasal ulcerations and facial emphysema
- Periorbital ecchymosis
- Persistent oral mucosal and gingival ulcerations
- Mandibular subluxation.

CHEEK AND LIP BITING

These are habitual factitious injuries found in areas of the mucosal soft tissue, which can be grasped between the patient's teeth. The "shaggy" appearing lesions are often found on the buccal mucosa along the occlusal line and also on the inner surfaces of the lips (Figs 12.2 and 12.3).

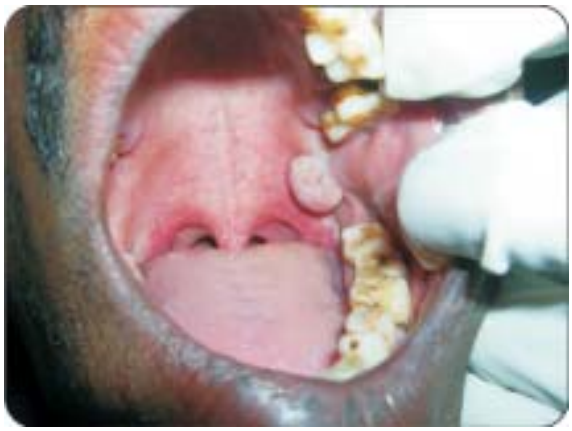

Fig. 12.2: Traumatic fibroma-I

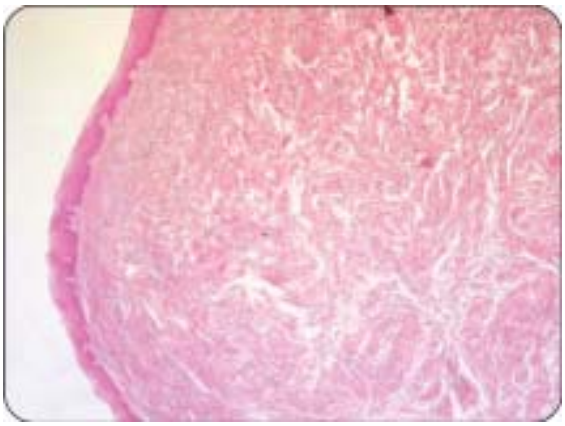

Fig. 12.3: Traumatic fibroma-II

The lesions can be quite painful and they can bleed in case the injury is deep seated.

FINGERNAIL INJURIES

Fingernail injury to the oral tissue is a common type of factitious injury. The patient often habitually irritates the gum and also tries to force the free gingival margin apically.

This results in the formation of vertical clefts on the gingival margin with exposure of the roots.

Fingernail injuries can produce chronic non-healing ulcers. Self-inflicted fingernail injuries may also occur on the lips or on the lingual vestibule.

In some cases, the emotionally disturbed patients may even carefully try to maintain or continue with the factitious wound in their mouth, either by interfering with its healing process or by causing repeated injuries in the same area. They do this for the purpose of drawing attention or compassion from the family members.

DENTURE RELATED INJURIES OR LESIONS

Denture injuries may be either acute or chronic in nature and there are several types of such injuries, which are as follows:

- Traumatic ulcer
- Denture hyperplasia
- Denture stomatitis or sore mouth
- Angular stomatitis (due to improper vertical height in dentures)
- Papillary palatal hyperplasia
- Frictional keratosis
- Pain due to pressure on a buried tooth in the gums.

ACUTE INJURIES

Acute denture injuries commonly occur due to wearing of a new prosthesis, which is yet to be adjusted. New dentures may cause injury to the oral mucosa resulting in pain and ulceration.

Denture Sore Mouth

This is an uncommon condition of oral mucosa, which occurs due to irritation from denture coupled with superadded candidal infections.

Clinically, the lesion presents a fiery red, smooth, swollen and painful oral mucosa, which was in direct contact with the denture base. A burning sensation due to hot and spicy food is also common.

Epulis Fissuratum

Epulis Fissuratum is a common denture injury produced by chronically ill-fitting dentures.

In these patients, ridge support becomes gradually diminished due to pressure from the artificial prosthesis, which causes resorption of the alveolar ridge.

Due to increased resorption of the ridge, the denture flanges extend deep into the sulcus and cause impingement of the soft tissue.

CLINICAL FEATURES (FIGS 12.4 AND 12.5)

- Clinically, epulis fissuratum appears as elongated rolls of tissue or large nodular masses in the mucoabial or mucobuccal fold area into which the denture flanges easily and perfectly fit.
- The lesions are painless, firm and there may be occasional ulceration.

Papillary Hyperplasia of the Palate

It is an unusual condition characterized by numerous, small, "wart-like" outgrowths on the mucosal surface of palate.

Poor oral hygiene and ill-fitting dentures, etc. are frequently associated with the development of this condition.

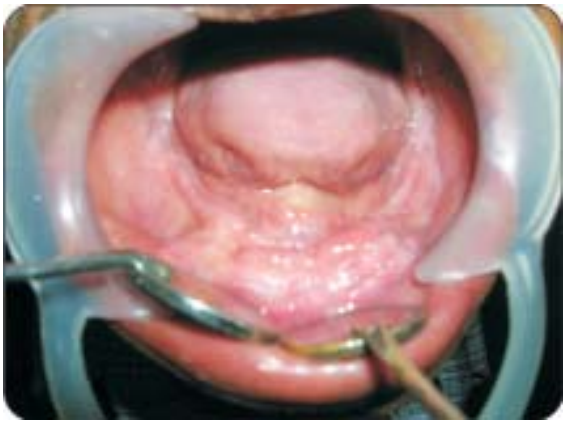

Fig. 12.4: Epulis fissuratum-I

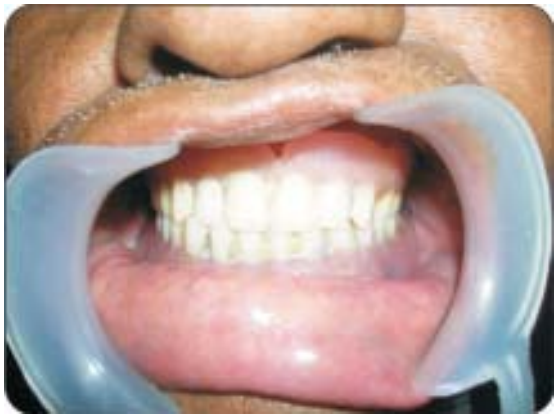

Fig. 12.5: Epulis fissuratum-II

Inflammatory hyperplasia is usually an asymptomatic condition, although secondary inflammation often occurs due to the collection of food debris between the papillary growths.

Histologically, the lesion reveals numerous, small, vertical projections, which are covered on the surface by a parakeratotic or orthokeratotic, stratified squamous epithelium. The central core of connective tissue contains blood vessels and few inflammatory cells (Fig. 12.6).

In few instances, pseudoepitheliomatous hyperplasia may be present in this lesion and sometimes it may undergo malignant transformation.

Treatment of inflammatory hyperplasia includes surgical excision of the lesion, along with correction of ill-fitting dentures and improvement of oral hygiene, etc.

ELECTRICAL BURNS IN THE MOUTH

Electrical burns of the oral and paraoral tissues are commonly seen in children usually between the ages of 2 to 4 years.

The injury occurs in the following situations:

- Due to biting on the plugged cord of an electrical appliance by the child.
- Sucking on the receptacle (female) end of an extension cord.

PATHOGENESIS

- Electrical burns are produced by an arc, which results from the electric current passing through the electrolyte rich saliva.

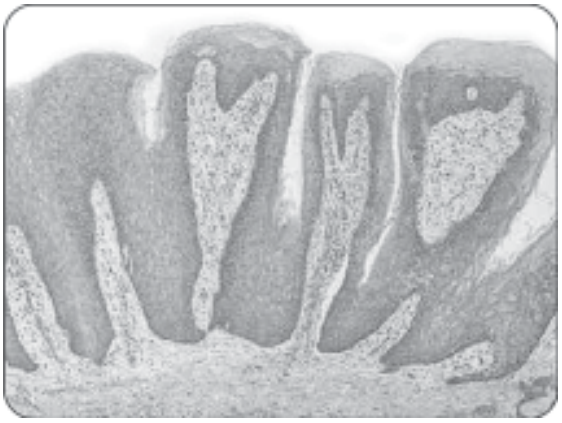

Fig. 12.6: Histology of inflammatory hyperplasia of the palate

- The arc reaches temperatures as high as 3000°C and causes deep thermal burns and local tissue destruction within moments.

CLINICAL FEATURES

- Electrical burns mostly occur in the lower lips and angle of mouth. It can also occur in the gingiva and the tongue.
- Electrical burns differ from thermal burns and produce one or more deep craters in the tissue, measuring about 1 to 3 cm in diameter with a light yellow base.
- These lesions are mostly painless and bloodless.
- Often the normal appearing tissue surrounding the crater becomes ischemic and these areas produce a peculiar "cold" sensation.
- Within next 3 to 4 weeks the base of the crater and the surrounding tissue slough out, leaving a large disfiguring defect.

Complications of electrical burns of the mouth

Anodontia	Electrical burns may cause damage to the developing tooth buds and as a result there can be anodontia involving varying numbers of teeth.
Microstomia	Electrical burns often cause damage to the growth centers of the developing jawbone and produce microstomia.
Lip deformities	Abnormal healing pattern of the lesion without timely intervention may lead to mucosal-alveolar adhesions and lip disfigurement.
Malocclusion	Damage to the growth centers of jawbone often results in failure of development of the dental arch, which leads to malocclusion.
Facial deformity	Substantial amount of current can cause damage and necrosis of the bone tissue itself, which later on sequestrates and produce severe disfigurement of the face.

TREATMENT

Cosmetic reconstruction of face and mouth.

THERMAL BURNS IN MOUTH

Thermal burns of the oral tissues occur mostly due to contact with hot foods and beverages. It can also occur rarely during dental procedures when hot instruments accidentally come in contact with oral soft tissues.

MILD BURNS

Hot foods and beverages generally cause this and the areas commonly affected are the tip of the tongue and anterior part of the palate, (since these anatomical structures come in contact with foods first).

In cases of mild thermal burn, the area shows slight erythema which resolves spontaneously in few hours time.

MODERATE BURNS

This type of burn often occurs when hot sticky foods become adhered to the palate (especially hot cheese, etc. while eating. After the injury, the area becomes erythematous with sloughing of the epithelium, and it causes pain and burning sensation for many days until the lesion heals up.

SEVERE BURN

Severe burns occur mostly during dental procedures, when an overheated instrument or material comes in direct contact with the oral soft tissues. It can occur during taking impression with an overheated hydrocolloid impression material. The gingival tissue is often damaged and it shows mucosal erythema and sloughing with intense pain.

Lip and commissural tissue may often get burnt if touched with a hot instrument (e.g. tip of the hot ball burnisher or root canal plugger, etc.). There is often severe pain in the area and it heals with scar formation.

RADIATION INJURIES

Radiation injuries occur due to the ionizing effects of electromagnetic waves or energized particles on living cells.

Radiation injuries may occur from **sun, X- ray machines and radioactive elements, etc**. As radiations (which are tremendously powerful rays of energy) pass through any living cell, they cause **damage to the cell by tearing apart the chemicals that constitute the cell.** This effect of radiation is used therapeutically in the management of head and neck cancers. Radiotherapy is the process of controlled elimination of the diseased cells by radiation. During this process some normal cells in and around the field of radiation are also damaged but often to a lesser extent.

TYPES OF THERAPEUTIC RADIATIONS

Therapeutic electromagnetic waves may be of *low energy (less than 1000 KeV or orthovoltage)* or it may be of *high energy (4 million to 25 million KeV or super voltage).*

The low-energy waves are used for the treatment of superficial skin or mucosal lesions, especially cancers, because the energy absorption in such cases mostly occur at the point of initial contact with the tissue.

When high-energy electromagnetic waves are used, the energy absorption mostly takes place in the deeper tissues and as a result the surface tissue like skin or epithelium, etc. is spared. High-energy electromagnetic waves are useful in the treatment of deep tissue neoplasms or metastatic lesions.

DOSE SELECTION

During radiotherapy treatment, the amount of cell damage depends upon the amount of energy the tissue absorbs. Generally, the amount of energy is measured as "rad" (radiation absorbed dose) or as gray (Gy). Normally, 1 rad is equivalent to the absorption of 100 ergs/g and 1 Gy equals to 100 rads.

THERAPEUTIC EFFECTS OF RADIATION

Therapeutic radiation causes injury and subsequent necrosis of the neoplastic cells either by virtue of its *direct effect* or by its *indirect effect*.

Direct Effect

Electromagnetic energy destroys the chemicals inside the cell and as a result the cell looses its ability to function or it may die.

Indirect Effect

In this case the cell necrosis occurs indirectly by means of the toxic compounds produced by the ionizing radiation, when the energy is absorbed.

The indirect process occurs through the production of free radicals that combine to form toxic substances such as H_2O_2, which damages the cell. Radiation can interrupt with cell division process.

FACTORS DETERMINING THE EFFECTIVENESS OF RADIATION

Stage of the cell cycle: Cells in the initial stages of maturation or cells which are growing rapidly, e.g. bone marrow cells or cells of the fetus, etc are very sensitive to radiation as compared to those of the more mature stages.

Mitotic index: Lesions with high index of mitotic activity are more responsive to radiotherapy than the lesions with little or no mitotic activity.

Nature of tissue: Besides the cancer cells certain normal cell, e.g. lymphoblasts, bone marrow cells, germ cells of ovaries and testes, and lining epithelial cells of the intestine are highly sensitive to radiation. Whereas the tissues like nerve, brain, endocrine glards muscles, bone and mature cartilage, etc. are relatively insensitive or resistant to radiotherapy.

X-RAY RADIATION AND ITS EFFECTS ON VARIOUS NORMAL TISSUES

Radiation (both therapeutic and diagnostic) causes mutations, it damages enzymes and sometimes interrupts with cell divisions. The fact that radiation can stop mitosis makes radiation therapy important in the treatment of cancer.

Although radiation affects virtually all tissues, certain cells are more susceptible to it than others. Persons, who work with radioactive materials or those who are working at nuclear fission reactors, or those who are receiving therapeutic radiations are most susceptible to cellular injury from radiation.

Various effects of radiation in different parts of the body, with special emphasis to the orofacial structures are discussed in the following section.

Factors determining the degrees of radiation injury

- Type of radiation
- Amount of radiation
- Part of the body treated
- Amount of normal tissue included in the zone of irradiation.

The amount of radiation different tissues can tolerate without being damaged

(Measurement is done by the unit Gray <symbol Gy> which is the SI unit of absorbed radiation dose of ionizing radiation).

- Fetus – 2 Gy
- Bone marrow – 2 Gy
- Ovaries – 2 to 3 Gy
- Lens of the eye – 5 Gy
- A child's bone – 20 Gy
- Adult's bone - 60 Gy
- A child's muscle – 20 30 Fy
- Adult's muscle – 100 Gy or more.

VARIOUS DAMAGING EFFECTS OF RADIATION ON INDIVIDUAL ORGANS OR TISSUES

Effects of Radiation on Cells

- Cells may be undamaged.
- Cells may be damaged but remain functionally viable.
- Cells may damaged and function abnormally.
- Cells are completely necrosed.

Effects of Radiation on Skin

- 2 to 3 weeks after radiation erythema appears on the skin, the initial erythema fades away quickly, but it reappears within 2 to 4 weeks.
- Very high doses of radiation cause edema, swelling and desquamation of the skin with ulcerations.
- The ectodermal components of the body, e.g. sweat glands, sebaceous glands and hair follicles, etc. are destroyed initially and the loss of *hair follicles* results in alopecia within the radiation field.

- Scarring occurs eventually with atrophy, dryness and pigmentations of skin. Increased scarring occurs due to increased connective tissue production and fibrosis.
- Telangiectasia may develop on the skin. The skin becomes rigid and less resistant to injury.
- Most of the skin reactions heal up within 4 to 6 weeks time.

Effects of Radiation on Oral Mucosa

- Initially oral mucosa becomes dry, erythematous and atrophic.
- Mucositis develops later on with necrosis, denudation, ulcerations and sloughing of the epithelium.
- Pain, discomfort in the mouth especially during meals and moreover secondary infections also commonly occur.
- The ulcer is often covered by a plaque-like yellow or pale fibrinous exudates.
- Dental procedures are often difficult to perform due to dry mouth, increased risk of secondary infections and delayed healing, etc.
- Mucositis may extend to large areas of the oral cavity, nasopharynx and esophagus, etc. and patients often complain of dryness and burning sensations in the mouth.
- Dysphasia, cough and horseness of voice are also common.
- Very often, there is loss or alteration of taste sensations due to degeneration of the taste buds (dysgeusia or hypogeusia).
- Pain and discomfort remain for about 2 weeks, and complete regeneration of the epithelium occurs in 1 month time.
- Mucosa becomes coarse and atrophic after healing, and in many cases, dysplastic changes also gradually develop.
- Use of artificial prosthesis must be stopped till complete recovery.

Effects of Radiation on Salivary Glands

- Salivary glands are extremely sensitive to the effect of radiation and they exhibit inflammatory change with painful swelling.
- Radiation causes damage to the parenchyma of the major or minor salivary glands.
- Xerostomia or dryness of mouth is the earliest and most common manifestation of radiotherapy, which occur due to glandular atrophy. However this effect is mostly a transient one.
- The saliva becomes thick and its flow is stagnant, and there is difficulty in food intake due to sore mouth.
- Increased chances of development of candidiasis along with pain and discomfort.
- Altered pH and electrolyte content of saliva along with decreased secretions of immunoglobulin.
- In few patients, xerostomia may be a permanent problem due to complete degeneration of the salivary glands.
- Often there is reduction in the buffering capacity of saliva along with fall in pH, which leads to an increased caries susceptibility of teeth.
- If radiation is continued there may be neoplastic change in the salivary gland tissue.

Effects of Radiation on TM Joint and Muscles

- Degenerative changes in the joint with subsequent fibrous ankylosis and trismus.
- Tissue regenerative capacity of both joint and the muscles are diminished.
- Muscle fibers are often damaged and replaced by fibrous tissue.
- Osteoradionecrosis of the bony component of the TMJ may sometimes occur.

Effects of Radiation on Blood Vessels

- Small vessels become thickened and distorted, which results in diminished blood supply.
- The ability of the vascular tissue to tolerate injury or trauma is greatly diminished, which results in increased susceptibility to infection and delayed wound healing.
- Vascular insufficiency due to radiation may result in some serious complication like bone necrosis.

Effects of Radiation on Teeth

- If radiation is given during the formative stage, there can be complete degeneration of the tooth buds with no tooth formation in the future.
- In other cases, there may be incomplete root formation and delayed eruption of teeth.
- The tooth may exhibit white, chalky or opaque areas on the buccal and lingual surfaces due to demineralization.

- After several months, the enamel becomes soft with loss of its translucency and it may gradually be detached from the surface, leaving some shallow groves on the tooth.
- The erupted teeth often become non-vital and brittle in nature with increased risk of fracture.
- A peculiar form of tooth destruction occurs in the cervical areas of teeth following radiation, which resembles dental caries and is often known as "radiation **caries**".
- Radiation caries may affect the cemento-enamel junction of tooth on the buccal or labial surfaces and it can lead to fracture of the tooth crown at the cervical area.
- Serious destruction of the periodontal tissue resulting in weakness of the teeth.
- Xerostomia and osteoradionecrosis may contribute greatly to the premature loss of teeth.

Effects of Radiation on Bone

- Radiation causes injury or damage to both the bone tissue as well as the metaphyseal growth cartilage.
- Effects of radiation on bone is often secondary to the damages occurred in its nutrient vessels.
- Normal balance of bone formation and bone resorption is disturbed, also there is increased risk of fracture of bone with slight trauma.
- The general bone vitality is decreased, with the occurrence of multiple areas of focal osteoporosis.
- In cases of high dose of radiation there can be complete degeneration of the osteoblast and osteocyte cells with loss of vitality of bone. Similar problems may occur if the malignant lesion receiving radiotherapy is in close proximity to the bone.
- Trauma to the affected bone (e.g. during tooth extraction) may lead to the development of "osteoradionecrosis". It is characterized by a chronic, painful infection and necrosis of the bone, accompanied by late sequestration and permanent deformity.
- Osteomyelitis sometimes occurs due to infection to the bone that is already devitalized by the direct effects of radiation.

Effects of Radiation in the Blood

- There will be decrease in certain components of blood either due to direct damaging action of radiation or due to depression of bone marrow.
- The RBC count remains normal while the platelet count falls considerably.
- There increased incidence of bleeding.

Effects of Whole Body Radiation

- Initially after receiving the radiotherapy, the patients often develop nausea, vomiting, fatigue, malaise, anorexia and diarrhea, etc.
- Abnormal mutations and genetic diseases; failure of conceptions and abnormal child birth.
- Elevation of serum and urinary amylase may be the other important features of heavy doses of radiation.
- Increased risk of cancer and the possible lesions include leukemia, carcinoma of the thyroid, breast, lung, brain, skin and stomach, etc.

Effects of Radiation in Embryo and Fetus

- Growth retardation with small head and brain.
- Poorly developed immune system and mental retardation.
- Increased incidences of developmental anomalies.
- Increased risk of childhood cancers, e.g. leukemia and solid tumors, etc.
- Genetic diseases due to the mutational change.

OSTEORADIONECROSIS

DEFINITION

Osteoradionecrosis is an acute form of osteomyelitis with formations of sequestrum due to refractory infection and necrosis of the bone. The condition occurs secondary to radiation-induced damage of the intraosseous blood vessels.

Effects of extremely high doses of ionizing radiation in the body Sievert (Sv)

Dose	Effect in the body
1 to 2 Sv	Vomiting, loss of appetite and generalized discomfort, etc. symptoms disappear within a short period.
2 to 6 Sv	Good chance of survival, provided the patient is given immediate blood transfusions and antibiotics.
6 to 10 Sv	Massive destruction of bone marrow with lack of formation of blood cells. Patients often die of infections and uncontrolled hemorrhage.
10 to 20 Sv	Patient dies of vomiting, diarrhea, infection and starvation, etc
Above 20 Sv	Massive destruction of central nervous system, cardiovascular system; patients die within a few days.

Note: Sievert (Sv) is the SI unit of absorbed radiation dose

PATHOGENESIS

Osteoradionecrosis generally occurs if the radiation dose in the body exceeds 60 Gy. Radiation therapy to the jawbone results in **intraosseous vascular damages resulting in decreased blood supply to the tissue.** The process severely compromises with the inflammatory defense of the tissue to the onslaught of secondary infections. Mandible is more often affected by osteoradionecrosis, since normally this bone has minimum vascularity. Bacterial infections initially enter the non-vital bone *via* the portals created by extractions of teeth, periodontal pockets, periapical lesions, traumatic injuries in the tissue due to surgery or wearing of prosthesis, etc. The inflammation results in acute osteomyelitis in the bone with sequestrum formation.

CLINICAL FEATURES

Age: Elderly adults.

Sex: More frequent among males.

Site: More often in mandible than maxilla.

PRESENTATION

- Ulceration, severe pain, swelling and formation of draining sinuses or fistulas on the alveolar ridge.
- Exudation of pus from the area and presence of severe foul smell.
- Malocclusion is common with development of trismus.
- Sequestration of large fragments of necrotic bone from the affected area.
- Possibilities of pathological fracture and permanent deformity in the bone.

Grades of osteoradionecrosis

Grade I	Represents osteoradionecrosis of the jaw with exposure of the alveolar bone.
Grade II	Osteoradionecrosis not responding to hyperbaric oxygen therapy and requires sequestrectomy or saucerization.
Grade III	Osteoradionecrosis with full thickness involvement of bone and/or pathological fracture.

RADIOLOGICAL FEATURES

Large areas of **'moth-eaten' radiolucency** are seen in the affected area of bone with presence of opaque sequestra.

HISTOPATHOLOGY

- The overlying soft tissue exhibits necrosis with acute inflammatory cell infiltrations.
- Absence of osteoblasts and lacunar osteocytes in the bone.
- The marrow tissue contains necrotic cells, microorganisms and inflammatory cells.

TREATMENT

Debribement of necrotic tissues should be done along with removal of the sequestrum. Administration of intravenous antibiotics and

hyperbaric oxygen therapy are essential. Maintenance of strict oral hygiene is necessary.

LASER RADIATION

Light amplification by stimulated emission of radiation or simply Laser is frequently used in different surgical procedures including those of the oral cavity.

The Laser induced hazards to the tissues occur mostly due to the intense heat that is generated at the tip of the instrument during surgery.

Following are the common Laser induced injuries, which affect the oral tissues:

- A chalky spot or a crater or a hole formation on the enamel surface.
- Charring of the dentin.
- Hemorrhagic necrosis of the pulp tissue, with acute or chronic inflammatory cell infiltrations.
- Coagulation necrosis of the odontoblast cells.
- Nonspecific ulceration on the oral epithelium with purulent inflammation.

PART II: CHEMICAL INJURIES

CONGENITAL PORPHYRIA

DEFINITION

Congenital porphyria is inherited as an autosomal recessive trait, which is responsible for the development of a defective pathway for the metabolism of hematoporphyrin and resulting in the accumulation of excessive porphyrins in the blood or urine.

PATHOGENESIS

There are many types of porphyrias but only the congenital types produce discoloration of teeth. The discoloration occurs due to the deposition of circulatory porphyrins in the teeth at the time of mineralization. Similar types of porphyria depositions also take place in the bone and the skin.

CLINICAL FEATURES

- Clinically, the teeth exhibit a 'pinkish-brown' discoloration and bright-red fluorescence under ultraviolet light (erythrodontia).
- The skin appears light brown and is extremely sensitive to sunlight.
- Hemolytic anemia develops frequently with splenomegaly.
- Bones are fragile with increased incidence of pathological fractures.
- Vesiculobullous lesions often develop on the exposed skin surfaces, which heal with scarring.
- Patients of congenital porphyria often exhibit blistering and erosions with severe scarring of the face and extremities.
- Ocular damage can lead to development of blindness.

BILIARY ATRESIA

Biliary atresia is an uncommon congenital disease of newborn infants characterized by narrowing or absence of the ductal elements of the biliary system of liver (the common bile duct between liver and small intestine is either blocked or it is absent). The condition results in elevated bilirubin levels in blood.

CLINICAL FEATURES

- Patients with biliary atresia often develop severe jaundice, clay colored stool and dark yellow-brown urine, etc.
- The liver is often enlarged and tendered, and the affected child shows poor weight gain.
- Discoloration of teeth, mainly the teeth of deciduous series is a common feature of the disease.
- The affected teeth appear dark or greenish in color, with roots of the teeth more intensely stained than the crowns.

ERYTHROBLASTOSIS FETALIS

Erythroblastosis fetalis is a hemolytic anemia of new born, which develops during intrauterine life and results from incompatible factors in the blood of the mother and the fetus.

An Rh-negative mother normally develops antibodies against the erythrocytes of an Rh-positive fetus. These antibodies when cross the placental barrier attack and destroy the fetal erythrocytes resulting in severe hemolysis.

Because of this hemolysis, large amounts of billiverdin and billirubin (blood pigments) are produced in the blood, which later on become deposited into the skin and the tooth. Billirubin may also be deposited in the brain and the condition is known as **'kernicterus'.**

Erythroblastosis induced **discolorations affect only the primary teeth** and their color varies from **green or bluish-green or yellowish gray**.

The pigments are largely confined to the dentine and in some cases **enamel hypoplasia** may also be present.

FLUOROSIS

(See enamel hypoplasia in Chapter 1).

ORAL MANIFESTATIONS OF VARIOUS METAL POISONING

Heavy metals are those, whose specific gravity is at least 5 times more than that of water. Generally they have no function nor they can be metabolized in our body, these elements can gradually accumulate in the body from environment and their toxicity develops, when their concentration goes up beyond a critical level. Systemic poisoning is often caused by a large number of metal salts, e.g. arsenic, lead, bismuth, mercury, silver and phosphorus, etc. Moreover some metals are essential for our health is small amounts, e. g. iron, zinc , etc. However, they are often toxic in higher concentrations.

The clinical manifestations of different metal poisoning

Name of the metal	Features of poisoning
Arsenic	• Gingivitis and stomatitis • Painful mucosal ulcerations, hyperpigmentations and hyperkeratosis. • Excessive salivation • Vomiting, diarrhea and neurological disturbances.
Lead	• Excessive salivary secretions • Metallic taste in the oral cavity • Swelling of the salivary glands • Development of a dark "lead-line" along the gingival margin, which occurs due to the perivascular depositions of lead-sulfide in the submucosa and basement membrane zone. • Convulsion, GI upset, anemia, neuritis and a peculiar basophilic stippling of the RBC cells.
Bismuth	• Burning sensations in the oral mucosa. • Metallic taste • A blue-black "bismuth line" on the marginal gingiva. • Blue-black pigmentation of the lips, buccal mucosa, vestibule and undersurface of the tongue, etc.
Mercury	• CNS disturbances in the form of tremors, headache, depression and insomnia, etc. • Depressed immunity as this metal is immunotoxic. • Extreme exhaustion, fever and weight loss, etc. • Excessive salivation with salivary gland swelling. • Stomatitis and glossitis. • A dark black line on the free gingival margin.
Silver	• An "**Ashen-Gray**" discoloration of the skin and oral mucosa. • Microscopy reveals a fine black, granular, deposition of silver salts in the sub mucosa.

ORAL MANIFESTATIONS OF CYTOTOXIC DRUG THERAPY

These drugs are often administered to the child suffering from leukemia or other malignant conditions. If such therapy is given at the time of development of tooth, the following dental abnormalities can be seen e.g anodontia, hypoplastic crowns, short roots of teeth and enamel defects, etc.

Important drug reactions in the mouth

Local reactions	• Chemical irritation • Disturbance of oral microflora.
Systemic reactions	• Bone marrow depression • Depressed cell mediated immunity • Lichenoid reactions • Stevens- Johnson syndrome • Fifed drug rash • Toxic epidermal necrolysis.
Miscellaneous reactions	• Gingival hyperplasia • Dry mouth • Mucosal pigmentation.

ORAL MANIFESTATIONS OF TETRACYCLINE STAINING

Tetracycline drug has got selective affinity for the calcium ions of the tooth surfaces and bone. Possibly it forms a complex substance with the calcium ions of the hydroxyapatite crystals of enamel of tooth or bone (**calcium chelation**), which becomes deposited on the tooth and the bone surfaces during mineralization of their organic matrix.

Tetracycline staining occurs frequently due to the prophylactic or therapeutic use of the drug to the pregnant mothers (in the second and third trimester) or the infants (up to the age of seven years).

CLINICAL FINDINGS (FIG. 12.7)

- Both deciduous and the permanent teeth are affected by this staining.
- The intensity and distribution of the color vary depending upon the specific form of tetracycline used and their duration of administration.

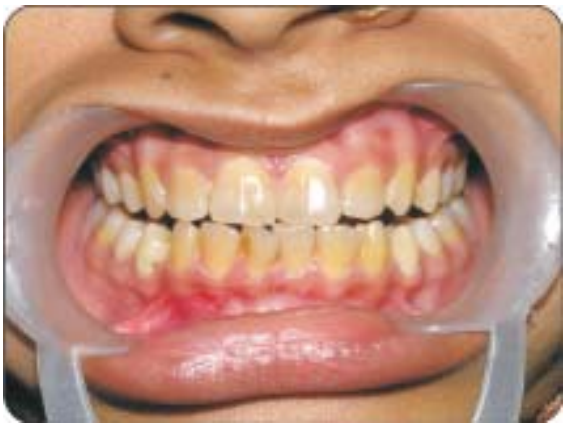

Fig. 12.7: Tetracycline staining

- The affected teeth exhibit a **yellowish or brownish-gray** discoloration.
- The **discoloration is intense at the time of eruption of teeth** and gradually the teeth become only "brownish" following exposure to light.
- The discoloration is always internal.
- The section of the tooth often produces bright yellow fluorescence under ultraviolet light.
- Chlortetracycline produces brownish-gray color while oxytetracycline tends to produce a yellowish discoloration of teeth.

ANGIONEUROTIC EDEMA

Angioneurotic edema frequently produces a rapidly developing, smooth, diffuse, edematous swelling, which often involves the face, lips, eyes, tongue and extremities.

Risk factors of angioneurotic edema

The disease may be caused by allergic reactions to the following:

- Insect bites
- Pollen
- Drug allergy
- Scales of shed animal skin
- Exposure to water or sunlight
- Foods—berries, fish, meat, eggs and milk, etc.

CLINICAL FEATURES

- The condition involves both sexes with almost equal frequency and there is no apparently detectable cause for it.

- The **edema develops very rapidly and it also subsides rapidly**, after lasting for about 24 to 36 hours.
- On rare occasions, angioneurotic edema may cause edema glottis that result in suffocation or even death.
- The disease can develop following some infections or other diseases, e.g. leukemia and lymphoma, etc.
- There is a hereditary form of angioneurotic edema.

CHEMICAL BURNS

ACETYLSALICYLIC ACID

Acetylsalicylic acid tablets are often kept over the gingiva near the root of a painful tooth or within the carious cavity of a painful decayed tooth in order to get relief from pain. Pain is sometimes relived too, with this practice but it is not because of the local effect of the drug, as believed by the patients but because of its systemic effect due to slow systemic absorption of the medicine.

When acetylsalicylic acid is put in direct contact with the oral mucosa it slowly gets dissolved in the saliva and liberates a strong acidic solution, which often causes necrosis of the mucosa.

CLINICAL FEATURES

- This type of chemical burn is often known as **"aspirin burn".**
- It produces a localized, white, friable area on the mucosa with pain.
- In severe cases, removal of the superficial white layer of the epithelium reveals a raw, erosive surface with bleeding tendency.
- Patients often complain of burning pain in the mouth.
- Upon stoppage of the practice, the lesion heals within 1 to 2 weeks.

CHEMICAL BURNS DUE TO OTHER MEDICAMENTS

Many other chemicals used in dentistry may also produce chemical burns of the facial skin and intraoral mucosal tissue. In the following section effect of some of these agents are discussed.

- **Phenol**: Used as disinfectant.
- **Silver nitrate**: Used as cauterizing agent
- **Trichloroacetic acid (TCA)**: Used as chemical cauterizing and gingival retracting agent.
- **H_2O_2**: Used as root canal medicaments.
- Bleaching agents
- Chemical burns can be caused indirectly by the **chemotherapeutic agents and barbiturates**, etc.

All these agents cause **sloughing of the mucosa in the area of contact** and produce pain, irritation and discomfort, etc.

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CHAPTER 13

Biopsy and Healing of Oral Wounds

PART I: BIOPSY

DEFINITION

Biopsy is the removal of tissue from the living organism for the purpose of microscopic examination and diagnosis.

Different types of biopsy

- **Surgical biopsy**—Incisional biopsy, excisional biopsy and punch biopsy.
- **Fine needle aspiration cytology (FNAC) and CT guided FNAC**
- **Exfoliative cytology**
- **Brush biopsy**
- **Frozen section biopsy**
- **Endoscopic biopsy**
- **Cone biopsy**
- **Core needle biopsy**
- **Suction assisted core needle biopsy**
- **Laser biopsy**

Excisional Biopsy

If a lesion is totally excised for histological evaluation, it is called "excisional biopsy", and this type of biopsy is usually done in case of small lesions. The excised tissue is then processed and histologically analyzed under microscope to determine the true nature of the tissue.

Incisional Biopsy

When only a small section of tissue is removed from a lesion for the purpose of histological evaluation, it is called "incisional biopsy". This type of biopsy is indicated in the case where the lesion is too large to excise initially without knowing the exact diagnosis, or if the lesion is of such nature that the total excision would be irrational.

Punch biopsy

Punch biopsy is useful in obtaining tissue samples from the skin and mucous membrane; it is frequently used by the dermatologists and oral pathologists. It helps in removing tissue samples from a variety of lesions, e. g. oral cancers and precancers, vesiculobullous lesions, moles and small lumps, etc.

Cone biopsy

It is a surgical biopsy and it removes the tissue which is cylindrical or cone shaped. The advantage of this technique is that it provides a large sample of tissue.

Fine Needle Aspiration Cytology (FNAC)

FNAC is done by aspirating tissue materials from inside a lesion and is commonly performed in cases of glandular or cystic lesions. This biopsy is done with a fine needle attached to a syringe; during biopsy the needle is inserted into the lesion and then vacuum is created so that tissue samples are sucked into the syringe. The sample is used to prepare a smear and seen under microscope.

CT guided FNAC

Here, the technique is same as conventional FNAC but the imaging facility attached with the instrument helps in locating the wound to be biopsied.

Core needle biopsy (core biopsy)

The technique is partly same as FNAC but here after the needle (2 mm in diameter) has been inserted into the target lesion, the needle is advanced further within the deeper cell layer to remove the core tissue. The needle has a cutting

tip that helps in removing tissue. The advantage of this technique is that it is more definitive procedure than FNAC and can be used in inaccessible lesions.

Vacuum assisted core biopsy

Here, the core biopsy syringe is attached to a suction associated with a vacuum device. Advantage of this technique is that it helps in removing multiple samples in one needle insertion.

Frozen Section Biopsy

Frozen section biopsy is performed in order to get an immediate histological report of a lesion (e.g. to determine whether a lesion is malignant or not, or to evaluate the margin of an excised cancer to ascertain that the entire lesion is removed at the time of surgery). The tissue is obtained from a lesion and the fresh tissue is quickly frozen at about -70°C in liquid nitrogen or dry ice. The frozen tissue is then sectioned in a refrigerated microtome and then stained to get a prompt diagnosis. In this type of biopsy the slides cannot be preserved for future references; hence photomicrographs of the slides are important.

Brush biopsy

This technique is used to collect cells from the surface as well as subsurface layers of a suspected lesion for microscopic examination. A round stiff bristle brush is rotated vigorously at a particular site of the lesion until bleeding starts, which ensures a sufficiently deep sample. Smear is prepared from the sample, which is scanned under microscope to detect any abnormal cells.

BIOPSY PROCEDURE

- The area of the wound from where the biopsy will be taken is cleaned first.
- The area is anesthetized:
- The most representative site of the wound is identified.
- A section of tissue from the identified site of wound (or sometimes the entire wound) is removed.

Important points to remember while performing biopsy

- Most suspected or representative site of the lesion should be chosen for biopsy.
- The wound should not be painted by any coloring agent before biopsy.
- The anesthetic solution should not be injected directly inside the lesion to avoid distortion of the tissue.
- Slough or necrotic areas to be avoided for sampling.
- Sharp instruments are to be used to avoid tissue tearing.
- A suture can be placed through the lesion for holding the tissue, which helps in controlling its movements while cutting and protects it from being swallowed by the patient or absorbed by the suction.
- Repeated cutting of the tissue during incision should be avoided.
- During biopsy, the tissue is obtained in such a way that it includes both the diseased as well as some normal tissue at the border of the wound
- If the lesion is multifocal or large, it is ideal to obtain more than one sample from different sites for making more accurate diagnosis.
- The biopsy specimen should be of sufficient thickness and depth (size of the sample should be at least 1 × 0.6 cm and the depth should be 2 mm).
- Edge of the specimen should be vertical and not beveled.
- After obtaining the tissue, it should be immediately placed on a glazed paper to avoid tissue curling.
- The sample should be labeled properly with patient's name and the clinical details of the lesion.
- The wound should be sutured and bleeding must be controlled.
- If the biopsy specimen is a calcified tissue (e.g. bone and tooth) then decalcification of the said specimen is to be done before the standard processing and sectioning. Decalcification is usually done by keeping the specimen in ethylene diamine tetra-acetic acid (EDTA) or other acid solutions.
- Biopsy should be repeated, if the diagnosis is not consistent with the clinical findings or the provisional diagnosis.

- The tissue is cleaned and put into 10 percent formalin solution for fixation.
- The biopsy site is sutured after achieving hemostasis.
- The biopsy specimen is sent to the histopathologist for diagnosis after labeling it properly.

Fixation of biopsy specimen

- Fixation of the tissue specimen is necessary immediately after biopsy to avoid autolysis; which may cause loss of microscopic details.
- 10 percent formal saline (formaldehyde solution in normal saline or a neutral pH buffer) is the routinely used fixative in biopsy.
- Small specimens are generally fixed overnight and large specimens are fixed for 24 hours; so that the fixative can penetrate and diffuse into the tissue specimen.
- Tissue specimens must be fixed before it is processed.
- The volume of the fixative should be at least 10 times to that of the tissue.
- For large specimens, proper incisions to be given to allow penetration of the fixative up to the centre of the specimen.

Before the biopsy, specimen should be properly labeled in the following manners.

- Mention the name, age and sex of the patient.
- Mention the date and time of biopsy.
- Mention the type of biopsy, the site from where it is obtained and the nature of the tissue (e.g. bone tissue or soft tissue, etc.).
- Mention the brief clinical, radiological and other relevant features of the lesion (if any).
- Mention the provisional diagnosis.

Tissue processing

- After fixation of the tissue, it is dehydrated in a series of solvents.
- It is then impregnated with paraffin wax and a wax block is prepared.
- The wax block is mounted on a microtome and ultrathin sections (4 µm) are made.
- The section is mounted on a glass microscope slide for staining.
- Hematoxylin and eosin stain is often routinely used for staining of the tissue.

Staining characteristics of various tissues with hematoxylin and eosin

Hematoxylin (basic dye) stains the tissue blue-black	Eosin (acidic dye) stains the tissue red
• Nucleus (DNA, RNA) • Ground substance of connective tissue • Reversal lines of bone.	• Cell cytoplasm • Keratin • Muscle cytoplasm • Decalcified bone • Collagen.

BIOPSY REPORT

- A negative report should not be considered final, especially if it is totally unexpected than what was thought earlier.
- Biopsy should be repeated, if there is any doubt regarding the diagnosis.
- If further investigations are required, e.g. histochemistry, immunohistochemistry, tissue culture or animal inoculation, etc. should be done.

Causes of failure of biopsy

- Specimen obtained from unrepresentative site of the lesion.
- Damaged or improperly fixed specimen.
- Specimen of insufficient depth.
- Inflammation or secondary infection may mask the exact diagnosis.
- Microscopic features are too difficult to interpret as in poorly differentiated lesions.
- Lesion with non-specific histological findings, e.g. aphthous ulcer.

EXFOLIATIVE CYTOLOGY

Exfoliative cytology is the microscopic study of cells obtained from the surface of an organ or lesion after suitable staining.

The neoplastic cells are less cohesive than the other normal cells and usually they shed on the surface of the lesion or into the secretion (e.g. the saliva). The shed neoplastic cells are obtained from the lesion by scrapping its surface and are then evaluated for possible changes like-dysplasia (indicative of their cancerous origin) or malignancy, etc.

TECHNIQUE OF EXFOLIATIVE CYTOLOGY

- First of all the surface of the lesion is cleaned by removing all the debris and mucins, etc.
- After that, gentle scrapping is done on the surface of the lesion with a metal cement spatula or a moistened tongue blade for several times.
- Thus, materials present on the surface of the lesion are adhered or collected at the border of the instrument.
- The collected material is then evenly spread over a microscopic slide and is fixed immediately with either 95 percent alcohol or equal parts of alcohol and ether.
- The slide is then air-dried and is stained by a special stain called PAP stain (papanicolaou stain).

IMPORTANT POINTS IN EXFOLIATIVE CYTOLOGY

- It is not a substitute for, but an adjunct to the conventional surgical biopsy.
- Anesthesia is not required in this technique and it is most useful for screen of cancer, detection of virally infected cells, acantholytic cells and candidal hyphae, etc.
- It is a quick, simple, painless and bloodless procedure.
- It helps to check the false-negative biopsy cases.
- Special procedures like immunohistochemistry can be performed in exfoliative cytology samples.
- The procedure is especially helpful in follow-up detection of recurrent cancer cases.
- It helps in screening a large number of lesions, which do not look like cancers clinically.
- However, it is unreliable for confirmatory diagnosis of cancers as large numbers of false negative test results are often found.

Indications of exfoliative cytology

The exfoliative cytology can be helpful for the diagnosis of the following oral lesions:

- Herpes simplex.
- Herpes zoster
- Pemphigus vulgaris
- Pemphigoid
- Squamous cell carcinoma
- Aphthous ulcer
- Candidiasis

Interpretation of findings in exfoliative cytology

The findings in exfoliative cytology smears are categorized into five classes:

Class I (normal)	The findings indicate that only normal cells are present in the smear.
Class II (atypical)	The findings indicate the presence of minor cellular atypia, but no evidence of malignancy.
Class III (intermediate)	This is an in between cytology that separates cancer from non cancer diagnosis. The cells display wider atypia that may be suggestive of cancer, but the features are not clear-cut. Biopsy is recommended for further confirmation of the diagnosis.
Class IV (suggestive of cancer)	The findings indicate that in the lesion, there is presence of few cells with malignant characteristics or many cells with borderline characteristics. Biopsy is mandatory
Class V (positive of cancer)	The cells exhibit definite features of malignancy. Biopsy is mandatory

PART II: HEALING OF ORAL WOUNDS

Factors affecting healing of oral wounds

- Age
- Type of tissue
- Location of the wound
- Mobility of the wound
- Trauma
- Local temperature
- Radiation
- Nutritional factors
- Circulatory factors
- Infections
- Hormonal factors

Individual factors affecting the healing of oral wounds are as follows:

Age: The rate of wound healing in younger individuals is faster in comparison to that of the older individuals and the reason may be due to higher rate of tissue metabolism in the former.

Type of tissue: Different types of tissue in our body exhibit a great deal of variation in their healing potential. For example, the epithelial tissue heals up at a much faster rate in comparison to the neural tissue.

Location of the wound: Wounds in an area where there is a good vascular supply heal more rapidly than those located in the relatively avascular areas.

Mobility of the wound: If the wound site is subjected to constant movements, the rate of wound healing is delayed and it may be due to repeated disruptions of the newly formed connective tissue.

The immobilized soft tissue or bony wounds usually heal at a faster pace.

Trauma: Mild trauma to the tissue may hasten its healing process, but severe trauma definitely retards the healing.

Local temperature: If the local temperature in the area is high and it is well maintained, the healing process occurs at a faster rate. But if the local temperature in the area is low, the healing process can be delayed.

Radiation: Low dose of radiation in the tissue stimulates its healing process, whereas a high dose of radiation disturbs the same.

Nutritional factors: Nutritionally deficient persons (especially with deficiency of vitamin C, proteins and minerals, etc.) usually exhibit a slower rate of wound healing.

Circulatory factors: Tissue with a very good blood supply heals at a faster rate in comparison to the tissue whose blood supply is diminished due to certain reasons, e.g. anemia, tissue dehydration or aging, etc.

Infections: A low-grade infection in the tissue may stimulate its healing process. A sterile wound on the other hand heals at a slower pace, however, severe infections in the tissue always disturb the healing process.

Hormonal factors: The trephones (wound hormones) released by proteolytic breakdown of cellular debris, accelerate the healing process. Administration of other hormones, e.g. ACTH, cortisone, etc. causes an inhibition in the growth of granulation tissue and thereby results in a delayed wound healing.

HEALING OF BIOPSY WOUND

HEALING BY FIRST INTENTION (PRIMARY HEALING)

When the cut surfaces of the biopsy wound can be approximated or closely sutured, the wound heals up by primary intention. The process occurs in the following manners:

- In the initial phase, there will be formation of blood clot, which helps to hold the parts of the wound together.
- The tissue becomes edematous and an inflammatory process starts, with the infiltration of polymorphonuclear neutrophils (PMN) and lymphocytes into the area.
- The tissue debris collected in the wound are cleared either by the process of phagocytosis or by their lysis with the help of proteolytic enzymes, liberated by the inflammatory cells.
- Once the tissue debris are cleared, granulation tissue forms that replaces the blood clot in the wound, and it usually consists of young blood capillaries, proliferating fibroblasts, PMN and other leukocytes.
- The epithelium at the edge of the wound starts to proliferate and gradually it covers the entire wound surface.
- Finally, the healing process is complete with progressive increase in the amount of dense collagen bundles and decrease in the number of inflammatory cells in the area.

HEALING BY SECONDARY INTENTION

When the opposing margins of the wound cannot be approximated together by suturing, the wound fills in from the base with the formation of a larger amount of granulation tissue, such type of healing of the open wound is known as"

healing by secondary intention" or "secondary healing". It takes place in the following ways:

- The secondary healing occurs essentially by the same process as seen in the primary healing, the only difference is that a more severe inflammatory reaction and an exuberant fibroblastic and endothelial cell proliferation occur in the later.
- In secondary healing, once the blood clot is removed, the granulation tissue fills up the entire area and the epithelium begins to grow over it, until the wound surface is completely epithelized.
- Later on, the inflammatory exudates disappear slowly and the fibroblasts produce large amounts of collagen.
- Most of the healing processes occurring due to secondary intention, result in scar formation at the healing site. However, in the oral cavity these are rare.

HEALING OF GINGIVECTOMY WOUND

EARLY HEALING PHASE

Almost immediately after the procedure there is formation of blood clot, which actually keeps the area covered. Approximately, 48 hours after gingivectomy, proliferation of fibroblast and young blood capillaries begin just beneath the blood clot. At the margin of the wound, the epithelial cells also start proliferating and approximately 72 hours after the surgery the deeper part of the blood clot is converted into a layer of young, granulation tissue. The superficial portion of the tissue is filled with PMN. The epithelium progresses to cover up the wound below the surface layer of the clot.

LATE HEALING PHASE

Organization of the clot is completed with formation of a dense connective tissue mass. The epithelium is thin but if it covers up the entire wound surface it matures gradually and there is formation of rete-pegs. There is gradual decrease in the number of inflammatory cells. Formation of the labial and lingual surface occur first and finally, within few days, there will be development of the interproximal gingiva. The later occurs by union of the labial and lingual gingiva.

HEALING OF THE EXTRACTION WOUND (FIG. 13.1)

Healing in an *extraction socket* occurs in the following steps:

- Soon after a tooth is extracted, bleeding occurs in the socket and the clot is formed.
- Within a day, the periphery of the clot shows edema and neutrophilic cell infiltrations.
- In the next 2 to 4 days, fibroblasts and endothelial cells proliferate into the surrounding bone marrow spaces and they gradually enter into the clot. This process is called "organization of the clot".
- At the same time, removal of the debris (e.g. necrotic tissue, dead cells and dead pieces of bone, etc.) from the wound also takes place, and it is done by the neutrophils, macrophages and the osteoclast cells, etc. (they cause either phagocytosis or proteolysis of the said debris).
- The clot organization process is completed usually by a week and following this, the epithelium at the periphery of the wound starts growing and it gradually covers of the entire socket area.
- Later on, the inflammatory cells decrease in number and the collagen fibers increase in the area.
- In about 10 to 15 days, immature bone or osteoids start forming at the margin of the socket. They move into the socket and gradually

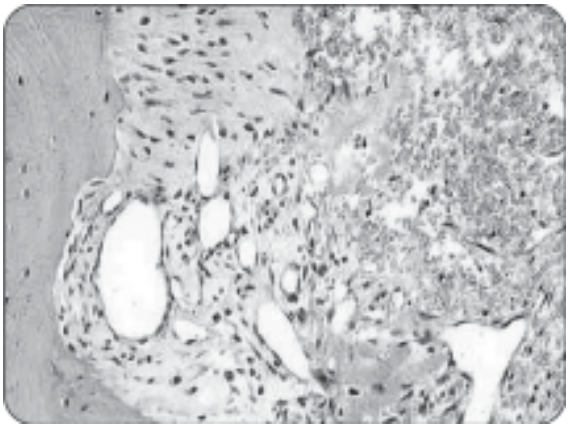

Fig. 13.1: Healing of extraction wound

fill up the entire socket by replacing the granulation tissue.
- Finally, in about 3 weeks to 6 months time, the entire socket is filled with mature bone that replaces the osteoids.

DRY SOCKET (ALVEOLAR OSTEITIS)

DEFINITION

Dry socket can be defined as the failure of appropriate healing after tooth extraction due to disruption of initial clot with eventual lack of organization by granulation tissue.

Dry socket is the most common complication of an extraction and it develops in about 5 percent cases in all extractions. However, the incidence rate is much higher in relation to impacted 3rd molars.

Possible causes of dry socket

- Traumatic extraction
- Smoking after extraction
- Excessive rinsing after tooth extraction
- Oral contraceptives use during extraction
- Foods being impacted in the socket
- Limited local blood supply
- Excessive use of vasoconstrictors in the local anesthesia
- Osteosclerotic bone disease
- Previous radiotherapy
- Pre-existing pericoronitis.

PATHOGENESIS

After a tooth is extracted blood clot forms; which stops further bleeding, protects the wound and promotes healing. Dry socket develops if the blood clot is lost from the wound and the bony wall of the socket is exposed to the air, food and fluids, etc. The loss of blood clot may be due to excessive localized fibrinolytic action or bacterial enzymes. Besides the fibrinolytic enzymes, there may be formation of kinins; which are potent pain mediators.

CLINICAL FEATURES

- Dry socket generally develops 2 to 4 days after tooth extraction and it lasts for several days.
- Maximum numbers of dry socket cases are seen in relation to the mandibular third molar teeth.
- Women suffer from the condition more often than men.
- The dry socket is usually a very painful condition; the nature of pain is intense, deep seated and throbbing type and the patient often has a foul breath.
- The pain may be continuous for weeks or months and the dead bones from the socket wall may shed as '**crumb-like**' fragments.
- Clinical examination reveals a socket devoid of clot and the bony walls of the socket are bare, whitish and visible.
- Mucosa around the dry socket is red, inflamed looking and tendered.
- Sometimes the socket may be filled with decomposing food debris and the dead bone; the bony walls of the socket may be felt as a rough area with probe.
- Local swelling and lymphadenopathy, etc. are less frequently seen.
- Sometimes the gingival tissue from the adjacent area may overgrow and fills up the socket.

RADIOLOGICAL FINDING

Radiologically, dry socket presents unhealed bony socket long time after the extraction, and sometimes there may be formation of sequestrum.

HISTOPATHOLOGY

- Histologic sections of the socket wall reveal the formation of necrotic bone, containing empty lacunae.
- There is intense inflammatory reaction in the surrounding bone.
- Dry socket is a localized osteitis and not an osteomyelitis and the condition heals very slowly.

TREATMENT

Zinc oxide eugenol pack is often given in the socket for palliative reaction.

HEALING OF THE FRACTURED JAWBONE

Once a jawbone is fractured, bleeding occurs immediately at the site and a hematoma forms,

which converted into a mass of blood clot. From this clot formation onwards, the healing is completed in three stages.

STAGE I: FORMATION OF FIBROUS CALLUS

- At this stage, inflammatory reactions take place in the bone at the periphery of the fracture site and there is proliferation of fibroblasts and endothelial cells in the bone marrow as well as in the periosteum. These cellular elements enter into the fracture site and organize the clot.
- Along with the clot organization, edema develops and inflammatory cell (e.g. neutrophils, plasma cells and lymphocytes, etc.) infiltration also gradually occur in the area.
- The necrotic cells, connective tissue and bone fragments are removed from the fracture site by phagocytosis, proteolysis and osteolysis, etc.
- Within few days, the clot is replaced by granulation tissue, which later on forms a fibrous tissue mass (fibrous callus) at the fracture site.

STAGE II: FORMATION OF PRIMARY BONE CALLUS

During this stage, the fibrous callus is gradually replaced by immature bone or osteoids at the fracture site. Generally, the primary bone callus forms in an amount which is far in excess to its requirement, and it usually extends to cover up areas beyond the fracture line in all directions.

Both the fibrous and primary bone callus binds the fractured fragments of bone together, and they appear radiolucent when a radiograph is taken.

STAGE III: FORMATION OF SECONDARY BONE CALLUS

During this stage, the mature bone replaces the primary bone callus gradually. This mature bone callus is not exuberant in amount and it usually appears radiopaque.

Later on, the secondary callus is remodeled by resorption of its excess bony tissue and finally a normal jaw outline is restored.

REPLANTATION OF TOOTH

DEFINITION

Replantation can be defined as the purposeful removal of a tooth and its almost immediate replacement with the object of obturating the canals apically while the tooth is out of its socket.

Replantation is planned to save a tooth where conventional endodontic therapy or endodontic surgery has failed. It is a system of organization, sterility and quickness.

INDICATIONS

- Difficult access in the tooth (it is true in case of lower 2nd molar).
- Anatomic limitation: Tooth apex in close proximity to the important nerves and vessels.
- Perforations in areas not accessible surgically.
- Medically compromised patients: Handicapped, geriatric and noncooperating.
- Failed previous apical surgery.
- When apical surgery can possibly create defects in other teeth.
- Deciduous teeth needed as space maintainers.
- To preserve postextraction alveolar bone for a prosthesis.
- Persistent chronic pain.
- Accidental avulsion of tooth.

CONTRAINDICATIONS

- Pre-existing moderate to severe periodontitis.
- Curved or flared roots.
- Nonrestorable tooth.
- Missing interseptal bone.

PROCEDURE OF REPLANTATION

Case selection: The ideal tooth for replantation is one that has relatively straight roots and some furcation area, because they can be more stable when replanted. A tooth with fused roots and no furcation area is not a good case for replacement, since it is difficult to stabilize such tooth in the socket. If the tooth breaks or fractures during extraction, replantation will be impossible.

Process of Extraction

- Exaction should be done under block anesthesia and there should be least amount of

trauma or compression to the periodontal ligament. Severe luxation should be avoided to protect the integrity of the cortical and interradicular bone.
- No elevators to be used during extraction to avoid damage to the periodontal ligament and the cementum.
- Beaks of the forceps should not go beyond the cementoenamel junction while holding the tooth for extraction, otherwise there will be damage of the cemental tissue.
- Extraction is done with a slow rocking movement and for the said purpose extraction of one tooth might take time as long as 20 to 30 minutes.

Postextraction Tooth Care

- Once the intact tooth is removed from the socket, it should be immediately placed into a solution, which can maintain the viability of the periodontal ligament.
- A solution called Hank's balanced salt solution (HBSS), whose composition and pH is similar to that of normal saliva can be used for this purpose.
- The socket should not be curetted and no granulation tissue should be removed from the apical region.
- If the socket is touched, there will postoperative resorption of bone.

External RCT and Apicectomy

Once the tooth is removed, apicectomy is done and root canals are filled; and the root ends are polished.

Replantation

- Once the tooth is endodontically treated (extraorally), it is placed back into the socket and the buccal and lingual cortical plates are compressed manually.
- Patient is advised to bite for few minutes on the tooth with the help of a wooden stick to stabilize it. Once the tooth is properly placed and gentle pressure is given, it often pops back into the socket with little mobility remaining. Splinting may be used in some cases.

CAUSES OF FAILURE OF REPLANTATION

Resorption: Mild resorption may result in ankylosis of the tooth and in such cases the replantation may not fail, however, in severe cases of inflammatory root resorption, the procedure may fail.

Infections: Severe chronic infection may prevent proper healing and may result in failure of the procedure.

Pain: In case of chronic uncontrolled pain the tooth should be removed.

Fracture: Fracture of the tooth or the cortical bone during replantation results in automatic failure of the procedure.

TRANSPLANTATION OF TEETH

DEFINITION

Transplantation refers to the replacement of one damaged tooth by another tooth.

Most common example of transplantation is replacement of mandibular first molar tooth by a developing mandibular third molar.

TYPES OF TRANSPLANTATION

Transplantations may be of two types:

A. *Autogenous transplantation:* When the replacing tooth is obtained from the same person.
B. *Homologous transplantation:* When the replacing tooth is collected from another person.

Once the tooth is transplanted it remains stable in the new location because it develops fresh periodontal ligament, cementum, gingiva, epithelial attachment and alveolar bone, etc. The pulp remains vital and becomes revascularized. Therefore, the transplanted tooth behaves clinically and physiologically like a normal viable tooth.

CRITERIA OF A SUCCESSFUL TRANSPLANTATION

- The transplanted tooth must develop attachment in the new socket.
- There should be development of new periodontal ligament, alveolar bone, gingiva and epithelial attachment, etc.

- The tooth should be physiologically, clinically and radiographically normal and vital.
- The transplanted tooth should perform masticatory functions as good as any other tooth in the jaw.
- It must be cosmetically acceptable.
- There should not be any periodontal or periapical lesion or any abnormal resorption.

CAUSES OF FAILURE OF TRANSPLANTATION

- Lack of generation of fresh attachment tissues in the new socket.
- Infections.
- Resorption.

HEALING AROUND OSTEO-INTEGRATED IMPLANTS

DEFINITION

Osteointegrated implants are those in which a direct, functional and structural union develops between the living bone and the surface of the implant.

CRITERIA FOR A SUCCESSFUL IMPLANT

- The material should be biocompatible.
- The surface of the implant should be rough so that it can provide a greater surface area for bone contact.
- Strict aseptic techniques should be employed to prevent any postsurgical infection.
- While drilling the bone to prepare holes for inserting the implant post, overheating must be avoided.
- Temperature above 47°C causes damage of the bone and interferes with healing.
- Plaque accumulation should be avoided around the implant margins.
- Sufficient healing period should be permitted (about three months) for proper osteointegration and during that period no load should be applied on the implant.

Healing: Once the implant is placed in the bone, first of all there is formation of a thin layer of blood clot along the surface of the implant.

The clot organizes, as there is proliferation of fibroblasts and blood capillaries from the adjacent normal connective tissue. A layer of granulation tissue forms in the process and with time, it is replaced by cancellous and compact bone and fibrous marrow.

The alveolar connective tissue comes in close contact with the implant surface and dense bundles of collagen run parallel to the long axis of the implant.

The gingival epithelium encircles around the implant as a collar and it attaches with the implant surface by a basal lamina and hemidesmosomal junction similar to that of the junctional epithelium. Although, light microscopically the implant appears to be in direct contact with the bone, electron microscopy reveals the presence of an electron dense, non- mineralized layer of tissue, which separates the two tissues.

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CHAPTER 14

Oral Aspects of Metabolic Disorders

DISTURBANCES IN MINERAL METABOLISXM

Many essential body functions require the participation of various mineral elements. These minerals could be involved in bone formation or activation of endocrine functions or maintenance of cardiovascular functions, etc. Moreover, they can also act as cofactors in various enzymatic functions. In the following section metabolic aspect of certain essential minerals will be discussed.

CALCIUM

There is about 1 to 2 kg of calcium present in average adult human body; of which about 98 percent is in the skeleton in the form of calcium phosphate salts, some amount is present in the plasma bound to albumin and rest is present in ionic form. In normal adults, the plasma concentration of calcium is about 8.8 to 10.4 mg/dl.

The concentration of calcium in plasma is critical and is subjected to tight hormonal control through parathyroid hormone. The later maintains a constant plasma calcium level either by withdrawing calcium ions from the plasma or by feeding calcium ions into the plasma by resorbing the bone.

DIETARY SOURCE

Dietary source of calcium mostly comes from milk; the other sources include dairy products, fruits, calcium rich water and green leafy vegetables, etc.

The calcium enters the plasma either via its absorption from the intestinal tract or through resorption of calcium ions from the bone mineral. The bone serves as the important storage.

Calcium leaves the plasma via secretion into the gastrointestinal tract, urinary excretion, and sweating and further redeposition into bone mineral.

Bone resorption and bone formation is a highly balanced process, being controlled by the parathormone (hormone secreted by the parathyroid glands) and thus, nearly 0.5 mg of calcium is entering and leaving the skeleton daily.

Factors affecting the absorption of calcium into the body from diet:

- Vitamin D is an important cofactor, which increases the absorption of calcium from the intestine.
- Reduction in the level of parathyroid hormone in blood causes increased calcium absorption.
- Chemicals like, citrates or oxalates and pathological conditions, e.g. sprue, etc. cause decreased calcium absorption.

Effects of decreased calcium levels in plasma

- Increased neuromuscular irritability
- Tetany—characterized by perioral muscular spasm and carpopedal spasm
- Convulsions and laryngospasms
- Defective blood coagulation
- Disturbance in normal heart rhythm
- Irregularity in normal membrane permeability
- Defective formation of bones and teeth
- Bone resorptions and increased osteoporosis
- Calcitonin helps in the incorporation of calcium into the bone.

Effects of increased calcium levels in plasma

- Anorexia, nausea, vomiting, constipation, depression and lethargy, etc.
- Depressed nerve conductivity and muscle rigor
- Coma
- Deposition of solid calcium and phosphorus stones, within the blood vessels, mucous membrane, skin and kidney, etc.

PATHOLOGIC CALCIFICATIONS

Pathologic calcification is the abnormal deposition of calcium in various tumors and organs of the body.

TYPES

- Dystrophic
- Metastatic
- Calcinosis.

Dystrophic Calcification

It is a type of pathologic calcification in which calcium salts are deposited in the dead or degenerating tissue of the body. It is not associated with increased levels of serum calcium but related to the change in the local environment, e.g. increased local tissue alkalinity, etc.

Examples of Dystrophic Calcification

- Pulp stones (Fig. 14.1)
- Calcification of the gingival tissue, tongue and buccal mucosa
- CEOT, ossifying fibroma
- CEOC
- Calcification of the tuberculous lymph nodes
- Blood vessel arteriosclerosis
- Area of faulty degenerative tissue.

Metastatic Calcification

Abnormal deposition of calcium in the tissue due to increase in the amount of serum calcium.

It occurs in hyperparathyroidism or in hypervitaminosis D. Calcification usually involves tissues, e.g. lung, kidney, G.I.tract, blood vessels and oral mucosa and jawbones.

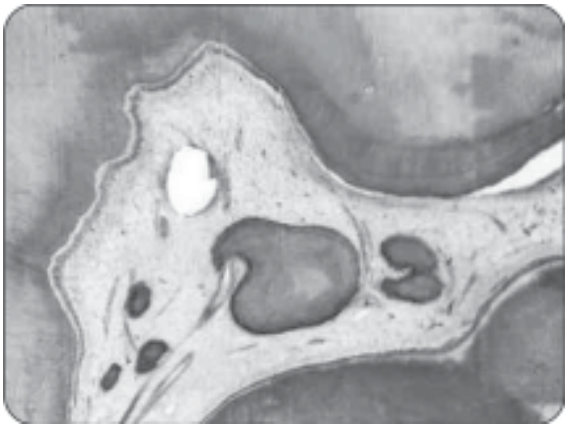


Fig. 14.1: Photomicrograph of pulp stone

Calcinosis

Abnormal deposition of calcium under or within the skin or epithelium. It is often seen in cases of scleroderma and dermatomyositis, etc.

PHOSPHORUS

Phosphorous is an essential mineral element in bone metabolism and besides being intimately related to calcium ions in the formation of bones and teeth, phosphorus always plays some other important roles in the body, which are as follows.

Functions of phosphorus in the body

- It helps in the metabolism of carbohydrates and fat by the process of phosphorylation.
- It forms phosphoproteins, nucleoproteins and nerve phosphatides, etc.
- Adenosine triphosphate (ATP) is the energy resource for various biologic functions of the body and phosphorus plays an important role in the formation of ATP.

  Normal plasma concentration of phosphorus is about 2-4 mg/dl.

HYPERPHOSPHATEMIA

Increased phosphorus levels (above 4.5 mg/dl results in hyperphosphatemia; which may cause abnormal calcification in different parts of the body. The possible causes of the condition include—renal failure with decreased excretion, hypoparathyroidism and excess phosphorus given in IV injections, etc.

HYPOPHOSPHATEMIA

Decreased phosphorus levels or hypophosphatemia occurs when the serum phosphorus level goes below 2.5 mg/dl.

Causes

- Renal failure with increased excretion
- Heavy metal poisoning
- Starvation
- Respiratory alkalosis
- Sepsis

Clinical Features

Hypophosphatemia may result in anorexia, bone pain, muscular weakness, waddling gait, defective growth in children, thrombocytopenia, decreased WBC formation, and hemolytic anemia, etc.

HYPOPHOSPHATASIA

Hypophosphatasia is a hereditary disorder characterized by the deficiency of alkaline phosphatase in the blood and in the tissues. The condition causes defective bone mineralization and there is also defective cementogenesis.

Clinical Features

- Premature loss of primary teeth.
- Enlarged pulp chambers of the primary teeth.
- Lack of cementum formation on the root surface.
- Hypoplasia of enamel.
- Inadequate mineralization of the long bones with rickets-like change.
- Premature exfoliation of permanent teeth (sometimes it is the only manifestation of the disease).

IRON

Iron deficiency is a common finding in protein energy malnutrition and it occurs due to the following causes:

- Chronic blood loss due to worm infestations
- Decreased absorption of iron
- Increased hepatic sequestration of iron

Absorption: Iron is absorbed as ferrous or ferric salts from the upper part of duodenum.

CLINICAL FEATURES

- Esophageal web in Plummer–Vinson's syndrome
- Spooning of nails
- Oral ulceration and sore tongue
- Loss of color of the facial skin
- Fissuring in the angle of the mouth

Myeloperoxidase is an iron-containing enzyme involved in antibacterial activation of neutrophilis (PMN) and it is frequently seen that iron deficiency anemia causes a decrease in the myeloperoxidase activity, which results in decreased antibacterial activity of PMN.

Hemochromotosis is a condition resulting from increased iron absorption in the body and it causes pigmentation of skin and mucosa due to excessive iron deposition. The other features of the disease include red, raw fissured tongue or the tongue may be pale in color with smooth atrophic, depapillated surface.

MAGNESIUM

Magnesium helps in phosphorilation process and it acts as a cofactor in certain enzymatic activity especially for phosphatase and cocarboxylase enzyme, etc.

Magnesium deficiency is seen in protein energy malnutrition and it may also occur due to severe loss of this mineral through vomiting and diarrhea, etc.

Deficiency of magnesium causes the following:

- CNS depression
- Anorexia
- Nausea
- Vomiting
- Corpopedal spasm.

No specific oral lesion is reported in magnesium deficiency.

ZINC

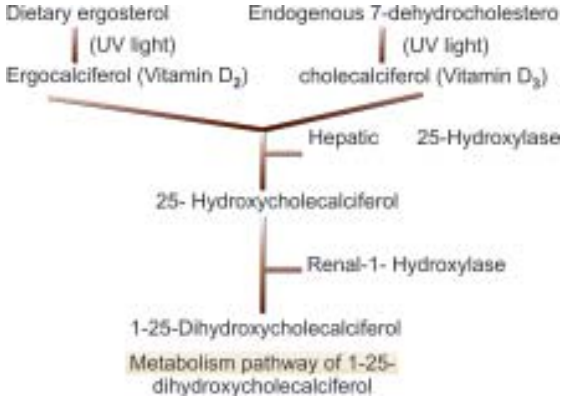
Zinc deficiency in human results in delayed wound healing, retarded bone growth and defective keratinization, etc. Deficiency of zinc occurs due to chronic intake of poor quality protein especially the vegetable proteins. According to the recent investigative reports, zinc prevents the oxidative biomembrane damage (free radical injury) of the body tissues and it has been found that increased iron concentration and decreased zinc concentration in the body increases the possibility of cancer or pre-cancer development.

DISTURBANCE IN VITAMIN METABOLISM

VITAMIN D

Although vitamin D belongs to the category of vitamins, it chemically behaves like a hormone

or prohormone in many instances. Vitamin D is fat soluble and it can be produced in the sun-exposed skin or it can be absorbed in the intestine as dietary vitamin D. The active form of vitamin D is known as 1-25 dihydroxycholecalciferol and it is metabolized in the following pathways:



Metabolism pathway of 1-25-dihydroxycholecalciferol

Functions of vitamin D

- Vitamin D helps in the absorption of calcium and phosphorus from the foods in intestine by stimulating the calcium binding proteins in the GI tract.
- It helps in calcium and phosphorous metabolism.
- It promotes the calcification or mineralization of bone, cartilage and teeth; however very high levels of vitamin D can cause bone resorptions.
- Vitamin D acts on immune system by promoting phagocytosis and by inducing immunomodulatory functions.
- It antagonistically acts against the action of parathyroid hormone.
- It increases the renal reabsorption of calcium.

DEFICIENCY OF VITAMIN D

- Rickets in children and osteomalacia in adults (both are bone softening diseases).
- Increased risk of colon and breast cancer.
- Increased risk of heart attack in men.
- Increased susceptibility to periodontal disease. multiple sclerosis and tuberculosis, etc.
- Increased risk of osteoporosis.

VITAMIN D TOXICITY

Overdose of vitamin D can cause the following problems:

- Hypercalcemia due to increased absorption of calcium.
- Can cause high blood pressure.
- Anorexia, nausea, vomiting followed by polyurea and polydipsia.
- Weakness, nervousness, pruritus (itching), renal failure and increased risk of ischemic heart disease.

OSTEOPOROSIS

Osteoporosis is a common disease characterized by gradual loss of mineral content in the bone.

ETIOLOGY

- Low intake of calcium and the minerals
- Lack of intestinal absorption of minerals
- Decreased estrogen levels in blood leading to demineralization of bone
- Increased urinary loss of calcium
- Hyperparathyroidism
- Stress
- Long-term steroid therapy
- Tetracycline and anticonvulsant therapy.

CLINICAL FEATURES

- It is frequently seen in post menopausal women.
- Males over the age of 80 years also sometimes have this problem.
- Increased incidences of spontaneous fracture of bone especially femoral neck fracture.
- Loss of lamina dura of alveolar bone with increased tooth mobility and tooth exfoliation.
- Increased incidences of jawbone fracture.
- X-ray reveals bone rarefaction and thinning of the cortex.

RICKETS

It is a hereditary disorder transmitted as X- linked dominant trait and is characterized by decreased levels of calcium and phosphorous in the body in childhood; coupled with decreased renal reabsorption and increased renal excretion of the mineral.

CLINICAL FEATURES (FIGS 14.1A AND B)

- Wide fontanels of skull and frontal bossing.
- Decrease in the body length.
- Bowing of legs as the bones are soft and weak.

Fig. 14.1A: Familial rickets

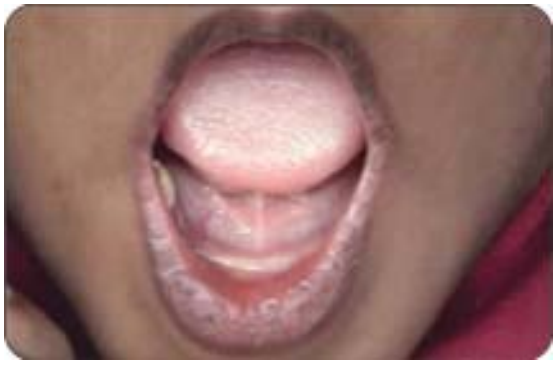


Fig. 14.1B: Lack of tooth development in rickets

- Increased incidence of bone fracture.
- Muscular weakness.

Oral manifestations of rickets

- Formation of globular hypocalcified dentin.
- Wide band of predentin formation.
- Large pulp horns, which may be extending up to the dentinoenamel junction.
- No increase in the caries susceptibility.
- Periapical lesions in multiple teeth.
- Delayed eruption of teeth.
- Abnormal cementum formation.
- Loss of lamina-dura of alveolar bone.

VITAMIN A

Vitamin A is a fat-soluble vitamin, which is derived from the carotenes (plant pigments). It is commonly found in the fish oils, butter and eggs, etc. The transformation of carotenes into vitamin A and its absorption takes place in the small intestine.

FUNCTIONS

- Vitamin A helps in the maintenance of the structure and function of specialized epithelium.
- It produces photosensitive pigments in the eye.
- It prevents the growth of epithelial malignant tumors.
- It maintains the normal skeletal growth.
- Maintenance of lysosomal stability and synthesis of glycoprotein.

Effects of vitamin A deficiency

- Night blindness and impaired vision.
- Bitot's spot—a gray, triangular, elevated spot in the conjunctiva.
- Xerophthalmia (dry conjunctiva).
- Corneal ulceration.
- Follicular keratosis of the skin.
- Squamous metaplasia of the columnar epithelium and gingivitis.
- Decreased salivary secretions due to metaplasia of the secretory epithelium of salivary glands.
- Hyperkeratosis of the oral mucosa, etc.

EFFECTS OF HYPERVITAMINOSIS A (EXCESS VITAMIN A IN THE BODY)

- Among children: Cortical thickening of bone, retarded bone growth, hemorrhage and bulging of the fontanels.
- Among adults: Fatigue, anorexia, bone pain, skin pigmentations and alopecia, etc.

VITAMIN B COMPLEX

THIAMINE (B_1)

Thiamine plays an important role in carbohydrate metabolism and its deficiency produces "beriberi". The oral manifestations of beriberi include edema of the tongue, loss of its papillae and glossodynia.

NIACIN (NICOTINIC ACID)

Niacin plays an important role in the intracellular oxidation process and its deficiency causes pellagra.

Clinical Features of Niacin Deficiency

- The disease pellagra is summarized by **4Ds—dementia, dermatitis, diarrhea and death**.
- In addition to this, there can be disturbed gastrointestinal and neurological functions.
- Nasolabial seborrhea, malar pigmentations
- The oral mucous membrane in pellagra presents generalized stomatitis with burning sensation, swelling, redness, pain and ulceration, etc.
- The tongue becomes red, enlarged and depapillated, with a "bald" surface. The tongue can also be thickly coated with a grayish pigmentation of the surface.
- Deep ulcers on the tongue may be seen in severe cases.
- Gingival margins are often red, swollen and ulcerated.
- Painful lips and angular chelitis often develop.
- Dermatitis involving the exposed parts of the body, especially around the neck above the cloths margin (Casal necklace).

RIBOFLAVIN (B_2)

The riboflavin deficiency mostly occurs due to malabsorption syndrome and it has profound **impact in the oral tissues.**

Clinical Features of Riboflavin Deficiency

- The disease causes reddening, inflammation and depapillation of the tongue.
- Tongue is often sore and it also sometimes become ulcerated.
- **Magenta glossitis** is a peculiar form of glossitis, which occurs due to riboflavin deficiency. In this disease the tongue is magenta in color and its surface appears granular or 'pebbly' due to flattening and mushrooming of the papillae.
- **Angular cheilitis**—The lips show reddening with fissures, painful cracks, dry scaling and maceration at the corner of the mouth (Fig. 14.1C).
- Lip lesions may extend into the oral mucosa and give rise to white patchy lesions.
- Oral mucosa in general looks red and shiny; the gingiva is not affected in riboflavin deficiency.

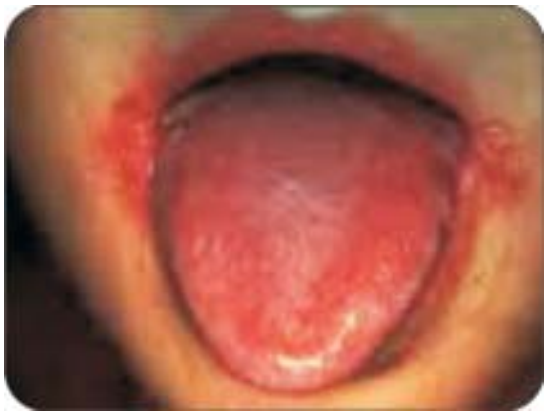


Fig. 14.1C: Angular cheilitis in riboflavin deficiency

FOLIC ACID

If folic acid is given during pregnancy, it can reduce the risk of neurological defects in the child and moreover, it can also reduce the risk development of orofacial clefts.

Causes of Folic Acid Deficiency

- Malnutrition
- Pregnancy
- Malabsorption
- Drug treatment with phenytoin.

Deficiency of folic acid causes the following:

- Loss of filliform and fungiform papilla of tongue; which results in a smooth, shiny appearance.
- Defective keratinization and increased susceptibility to infection in the oral mucosa.
- Gingivitis and oral ulceration.
- Atrophy of the tongue papillae with glossitis.

VITAMIN C (ASCORBIC ACID)

Vitamin C or ascorbic acid is a water soluble vitamin and it plays very important role in the synthesis of collagen fibers. The collagen fibers form the ground substance of all the connective tissues, i.e. connective tissue proper, bone, cartilage and blood vessels, etc.

Humans don't have the ability to synthesize their own vitamin C and must obtain through diet. Vitamin C is available in fresh foods, however, heating or drying of fruits cause loss of considerable amount this vitamin.

Functions of vitamin C

- Synthesis of collagen.
- Helps in the synthesis of neurotransmitter norepinephrine.
- Synthesis of carnitine, a molecule that helps in transport of fat to mitochondria to produce energy.
- Metabolism of cholesterol.
- Highly effective antioxidant.
- Decreases the risk of cardiac diseases, strokes and cancer, etc.
- Decreases the oxidative stress and thereby reduce the risk of diabetes mellitus.

DEFICIENCY OF VITAMIN C

Deficiency of Vitamin C leads to **scurvy** and other related disorders; these diseases manifest with the following symptoms:

- **Petechiae** and **ecchymosis** in the oral mucous membrane (Fig. 14.1D).
- Fatigue due to defective fat metabolism.
- Bruising, premature loss of hair, joint pain and swelling.
- Intrabony hemorrhage causes hematoma formation, which becomes calcified in the future.
- **Poor collagen synthesis causes weak attachment between bone and periosteum**; which often leads to detachment of periosteum from bone, resulting in severe pain, bleeding and swelling, etc.
- **Hyperemia, edema and enlargement of the gingiva, with an increased bleeding tendency.**
- Mild to marked **loosening of teeth** and sometimes **premature exfoliations of teeth.**

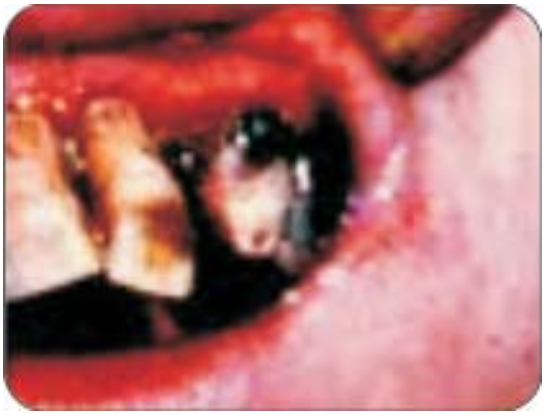


Fig. 14.1D: Oral lesions of scurvy

- Pain, swelling and bleeding in the mouth with bad breath and difficulty in taking food.
- **Retardation of wound healing.**
- Defective function of odontoblast and osteoblast cells.
- Disturbed bone growth in children due to defective collagen synthesis and osteoid matrix formations.
- Follicular hyperkeratosis—a skin condition characterized by excessive synthesis of keratin in the hair follicles; which results in rough, cone-shaped, elevated papules in the skin.
- Hematoma formations in the skin due to increased capillary fragility.
- Swelling of the legs due to unsupported, dilated and fragile blood vessels; because of poor ground substances owing to lack of collagen synthesis.

VITAMIN K

Vitamin is **essential for synthesis of prothrombin (clotting factor-II)** and it also helps in synthesis of other clotting factors, e.g. factor VIII, IX and X. Most of vitamin K is synthesized by intestinal microflora in humans and some amount of it can be available from natural fruits.

Deficiency of vitamin K causes decreased prothrombin levels in blood with increased tendency for hemorrhage and bruising. There can also be increased bleeding after tooth extraction and following minor surgical procedures, etc.

DISTURBANCES IN PROTEIN METABOLISM

AMYLOIDOSIS

Amyloids are abnormal fibrillar proteins, which have a peculiar homogenous, translucent appearance and a characteristic staining property.

Amyloidosis is a pathological condition characterized by the extracellular deposition of amyloids within the tissue.

TYPES

Amyloidosis is of two types:

Primary (idiopathic) type: Arising as a result of derangement of immunoglobulin synthesis and

consists of fragments of IgG molecules in the tissues.

Secondary (reactive) type: Occurs as a complication of many diseases, especially the chronic destructive inflammatory lesions like rheumatoid arthritis and few malignant conditions.

CLINICAL FEATURES

- Oral amyloidosis is commonly seen among patients suffering from multiple myeloma or monoclonal gammopathy, etc. and the disease occurs due to overproduction of immunoglobulin light chains.
- Smooth surfaced, waxy papules or plaques may be found on the lips, eyelids and neck, etc.
- Localized amyloidosis in the oral cavity commonly produces **macroglossia** and **gingival swelling,** etc. and the swelling is usually firm and indurated.
- There can be presence of hemorrhagic bullae on the surface of the lesion, which ruptures to produce shallow ulcer.
- The tongue lesion may present a lobulated growth, which sometimes may be so massive that it will prevent the closure of mouth.
- The surface of the lesion appears **pale or purplish** and the lateral border of the tongue often shows indentations of teeth.
- **Petechiae and ecchymosis** can be present in other parts of the oral mucous membrane in amyloidosis.
- Systemic amyloidosis may cause **claudication** (severe cramp-like pain, mostly occurs in legs) of jaw muscles due to infiltration of amyloids into blood vessels.
- Reactive amyloidosis occurs secondary to rheumatoid arthritis or chronic infections like tuberculosis, sarcoidosis or osteomyelitis, etc.
- Amyloids can also be found in large amounts in Pindborg's tumor.
- Amyloidosis of the salivary glands may produce xerostomia with dryness of mouth and hoarseness of voice.

HISTOPATHOLOGY

- Microscopically amyloids appear as weakly eosinophilic, homogenous, amorphus hyaline materials, which often show a perivascular distribution.
- Amyloids are generally deposited extracellularly within the submucous connective tissue.
- Congo red is the special stain used for the detection of amyloids in the tissue and it produces a typical 'apple-green' birefringence, when viewed with polarized light.
- Crystal violet stain exhibits red colored amyloid materials in the tissue.

TREATMENT

By surgical excision. Prognosis can be poor in some cases due to cardiac, hepatic or renal failures.

PORPHYRIA

Porphyria refers to an inborn error of porphyrin metabolism and it is characterized by the overproduction of uroporphyrin and other related substances. The condition may also results from certain infections.

Porphyria is commonly of two types:

A. Erythropoietic porphyria.
B. Hepatic porphyria.

CLINICAL FEATURES

- The erythropoietic porphyria is characterized by red urine, photophobia, hairy face and reddish or brownish colored teeth.
- The tooth discoloration is due to deposition of porphyrins in enamel, dentin and cementum, etc.
- The discoloration is more intense in deciduous teeth with both enamel and dentin is affected; discoloration is less severe in permanent teeth.
- The discolored areas or zones of teeth exhibit a red fluorescence when exposed to Wood's UV light.
- The disease sometimes produces vesiculobullous skin lesions.

Porphyria does not require any treatment, only veneering of discolored teeth is done to improve esthetics.

DISTURBANCES IN CARBOHYDRATE METABOLISM

HURLER'S SYNDROME

Hurler's syndrome is a disturbance of carbohydrate metabolism and is characterized by

elevated mucopolysaccharide levels in urine. The disease is sometimes fatal in nature and it commonly affects children.

CLINICAL MANIFESTATIONS

- Mental retardation
- Dwarfism with large head and prominent foreheads
- Hypertelorism
- Puffy eyelids and corneal clouding
- Hepatosplenomegaly.

ORAL MANIFESTATIONS

- Deformed face with broad saddle-nose
- Short and broad mandible
- Coarse and thick lips
- Lack of tooth eruption or delayed eruption
- Large tongue, open mouth
- Microdontia, diastema formation
- Gingival hyperplasia.

RADIOGRAPHIC FEATURES

Radiolucencies around the crowns of unerupted teeth in the jaw due to mucopolysaccharide deposition are common findings in this disease. Localized bone destruction in the jaw.

HISTOPATHOLOGY

- Abnormal deposition of intracellular mucopolysaccharides in different vital organs, e.g. liver, spleen, heart and nervous system, etc.
- Presence of 'hunter's cells' in the tissue, these cells are large with crescent shaped nuclei and metachromatically staining cytoplasms.

TREATMENT

No treatment is possible, death often occurs from cardiac or lung involvement.

DISTURBANCE IN LIPID METABOLISM

The diseases, which occur due to the disturbance in lipid metabolism, are classified into two broad groups:

A. **Histiocytosis 'X'**
B. **Lipid reticuloendotheliosis**

The histiocytosis X group includes three diseases, namely:

A. Hand-Schuller-Christian disease
B. Eosinophilic granuloma.
C. Letterer-Siwe disease.

The lipid reticuloendotheliosis also includes two diseases and these are:

A. Gaucher's disease
B. Niemann-Pick disease.

HAND-SCHULLER-CHRISTIAN DISEASE

Hand- Schuller- Christian disease occurs among young children and it primarily causes replacement of the normal bone marrow cells by proliferating macrophages.

CLINICAL FEATURES

- Unilateral or bilateral exophthalmos
- Diabetes insipidus
- Skin rashes
- Hepatosplenomegaly
- Otitis media
- Facial asymmetry
- Ulceration and necrosis of oral mucous membrane
- Loosening and premature exfoliation of teeth
- Halitosis
- Delayed wound healing.

RADIOGRAPHIC FEATURES

Presence of multiple, punched-out radiolucent areas in the skull bone. Diffuse radiolucency of the jaw, with destruction of alveolar bone and displacement of teeth.

HISTOPATHOLOGY

Microscopically the lesion reveals, multiple, large, vacuolated foam cells and small non-vacuolated cells. Both types of cells are histiocytic in nature.

Treatment is done by surgery, chemotherapy and occasionally by radiotherapy.

Some patients may undergo spontaneous remission.

EOSINOPHILIC GRANULOMA

Eosinophilic granuloma is a chronic, localized form of bone disorder, which commonly occurs in the second and third decade of life.

CLINICAL FEATURES (FIGS 14.2 TO 14.4)

- Fever, malaise, headache and anorexia.
- Localized pain, swelling and tenderness in the jawbones (Fig. 14.2).
- Gingival soft tissue swelling (sometimes), halitosis and mobility of teeth.

RADIOGRAPHIC FINDINGS

Radiographs present single or multiple areas of bone destruction and the teeth in the X-rays appear as "hanging-in-the air" like condition. Often there is increased possibility of pathological fractures of the bone (Fig. 14.5).

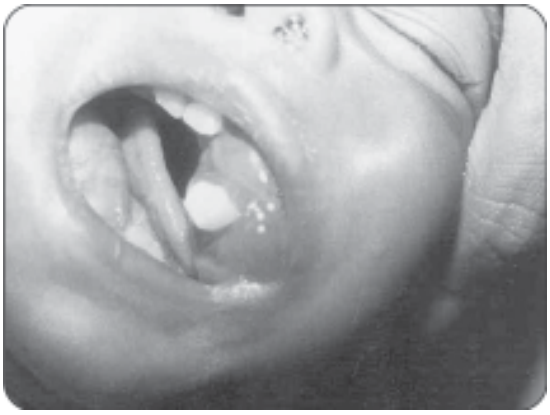


Fig. 14.2: Eosinophilic granuloma of maxilla

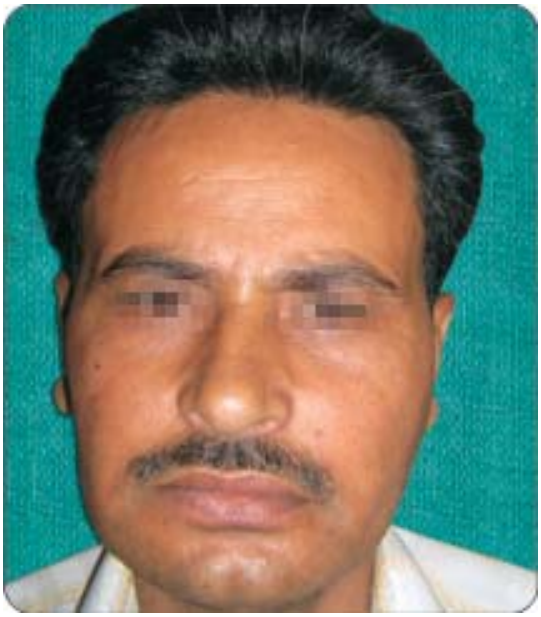


Fig. 14.3: Eosinolhilic granuloma-I

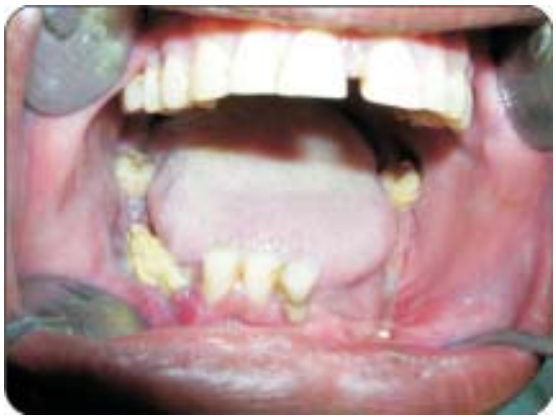


Fig. 14.4: Eosinophilic granuloma-II

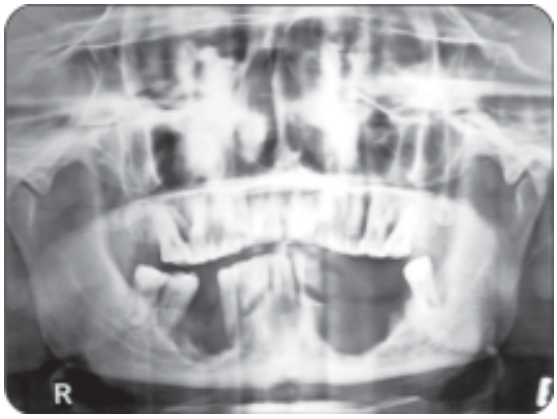


Fig. 14.5: Radiograph of eosinophilic granuloma

HISTOPATHOLOGY

Microscopically, eosinophilic granuloma shows numerous proliferating histiocytes in diffuse sheets, within which many eosinophils are dispersed. Individual cells club together to form multinucleated giant cells (Figs 14.6 and 14.7).

TREATMENT

Surgical curettage and radiotherapy. Prognosis is good.

LETTERER-SIWE DISEASE

Letterer-Siwe disease is the most fatal form of histiocytosis X and it usually occurs before the age of two years.

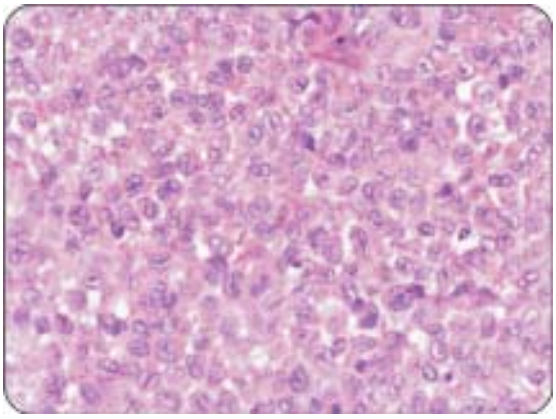


Fig. 14.6: Photomicrograph of eosinophilic granuloma

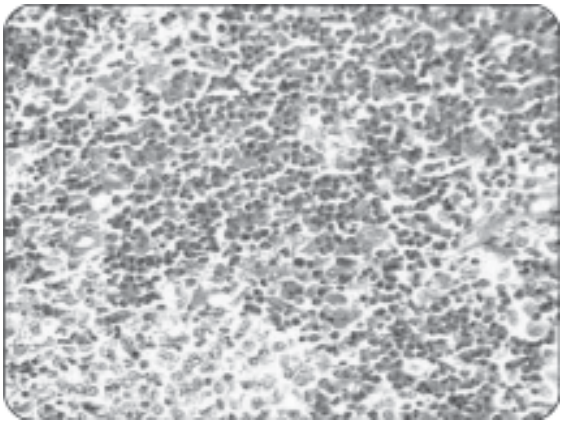


Fig. 14.7: Photomicrograph of histiocytosis-X

CLINICAL FEATURES

- The disease primarily affects the viscera, like spleen, liver, lung, lymph nodes, bone marrow and skin, etc.
- Hepatosplenomegaly and lymphadenopathy.
- Fever, malaise and irritability.
- Petechiae or ecchymosis of skin and mucous membrane.
- Anemia, mucosal ulcerations and gingival hyperplasia.
- Loosening and premature exfoliation of teeth.
- Radiographs reveal diffuse areas of bone destruction in the jaws.

HISTOPATHOLOGY

The lesion microscopically shows marked proliferations of nonlipidized histiocytes.

TREATMENT

No specific treatment is possible. Prognosis is grave.

GAUCHER'S DISEASE

Gaucher's disease is characterized by the deposition of kerasin (a lipid) in the reticular cells of liver, spleen, bone marrow and lymph nodes.

It can occur at any age and females are affected more often than males.

Skin pigmentation, gingival bleeding, hepatosplenomegaly and ecchymosis, etc. are the common clinical manifestations of the disease. Patients may also suffer from CNS disorders and increased incidences of pneumonia, etc.

Microscopically, large foam cells with "crumpled silk" cytoplasm (Gaucher's cells) are found in the lesion.

NIEMANN-PICK DISEASE

Niemann-Pick disease is characterized by the accumulation of sphingomyelins (a lipid) in the cells of the reticuloendothelial system. It is a fatal disease and occurs most commonly among infants. Destructive jaw lesions, mental retardation and blindness, etc. are the usual manifestations of this disease.

DISTURBANCE IN HORMONE METABOLISM

HYPOPITUITARISM

Hypopituitarism in infancy leads to dwarfism, in which the patients usually have a much shorter but well-proportioned body.

CAUSES

The disease occurs due to reduced synthesis of growth hormone because of the following reasons:

- Tumor of pituitary, e.g. craniopharyngioma
- Hypophyseal fibrosis
- Supracellar cyst
- Destruction of pituitary gland by trauma.

Decreased tissue response to growth hormone can also give the features similar to hypopituitarism despite having normal growth hormone level.

CLINICAL FEATURES

- Short stature of the body.
- Sparse hair on the head and other hairy regions.

- Atrophy of all organs of the body.
- Wrinkled atrophic skin and childish face.
- Hypogonadism, impotence and amenorrhea.
- Extreme weight loss.
- Coma and death in several cases.

Oral manifestations of hypopituitarism

- Small face in comparison to the skull
- Delayed exfoliation of deciduous teeth
- Delayed completion of tooth roots
- Delayed eruption of permanent teeth
- Crowing of teeth
- Underdevelopment of maxilla and mandible
- Smaller crown size of the teeth and smaller root length
- Lack of development of third molars

DIAGNOSIS

- Hypoglycemia
- Decreased serum growth hormone levels
- Skull X-rays reveal tumor in sellar region
- CT-scans and MRI to detect tumors in the brain.

PITUITARY INSUFFICIENCY IN ADULTS

CLINICAL FEATURES

- Easy fatiguability and weakness.
- Hypotension.
- Lack of resistance to cold.
- Irregular menstrual cycle in females.
- Lack of development of secondary sexual characteristics.
- Failure of lactation.
- Dry and wrinkled skin.

TREATMENT

Administration of corticosteroids, estrogens, androgens and thyroxin, etc.

DIABETES INSIPIDUS

DEFINITION

Diabetes insipidus is a disorder of water metabolism caused by the deficiency of vasopressin, the antidiuretic hormone (ADH) secreted by the posterior pituitary.

ETIOLOGY

- *Idiopathic*
- *Secondary causes:* Head trauma, neoplasm, surgical ablation or irradiation of pituitary gland.

CLINICAL FEATURES

- **Marked polyurea**—Daily output of 5 to 25 liters of urine.
- Polydipsia (increased thrust) —4 to 40 liters of fluid required daily.
- Patients have a craving for cold water.
- Dehydration, headache, fatigue and irritability.
- Xerostomia (dry mouth) is the most significant oral manifestation.
- There can be noninflammatory swelling of the salivary glands (sialosis), which particularly involves the parotids.

DIAGNOSIS

- Increase in plasma osmolarity
- Low specific gravity of urine (1.001-1.005)
- Fluid deprivation test: Fluid intake is restricted for 8 to12 hours and even after that if there is no increase in the specific gravity or osmolality of urine, the case should be diagnosed as diabetes insipidus.

TREATMENT

- Administration of vasopressin.
- Administration of chlorpropamide to reduce urine volume and to potentiate the action of vasopressin.
- Detection and treatment of cranial lesion, if any.

HYPERPITUITARISM

Hyperpituitarism or increased production of growth hormone from the anterior pituitary leads to gigantism in infants (before the fusion of bone epiphyses). Hyperpituitarism causes acromegaly in adults (after the fusion of bone epiphyses).

CAUSES

- Hypersecretion of growth hormone due to functional pituitary adenoma.

- Increased function of anterior pituitary, which regulates the secretion of growth hormone.

PITUITARY GIGANTISM

The following features characterize gigantism clinically:

- Generalized symmetric overgrowth of the body.
- Extreme body height (above 7 feets) with long extremities.
- Genital underdevelopment, excessive perspiration.
- Headache, lassitude, joint and muscle pain.
- Defective vision.
- A large number of cases occur as part of Albright's syndrome.

Oral manifestations of gigantism

- Enlarged maxilla and mandible with severe growth of the facial soft tissues.
- Marked increase in the vertical dimension of face.
- Large size of teeth (true generalized macrodontia) and early eruption of teeth.
- Root length is generally greater than normal.
- Macroglossia and hypercementosis of teeth, etc.

ACROMEGALY

The disease occurs due to hypersecretion of growth hormone in adults after the closure of epiphyseal end plates.

CLINICAL FEATURES

The patients with acromegaly do not have a gigantic body but they often develop the following general features:

- Thick bones with larger hands and feet; which often have a 'spade-like' appearance.
- Enlarged skull with increased intracranial pressure.
- Patients often suffer from hypertension, cardiac problems and peripheral neuropathy, etc.
- Increased intracranial pressure often causes headache, photophobia and visual disturbances, etc.
- Patients also exhibit hepatomegaly and cardiomegaly.
- Osteoporosis, arthralgia, excessive sweating and myalgia.
- Bowing of the legs and barrel shaped chest.

Oral manifestations of acromegaly

Some interesting changes take place in the oro-facial region of the patient suffering from acromegaly and these changes are as follows:

- Overproduction of growth hormone in adults causes activation of condylar growth center in mandible with abnormal increase in the size of the bone.
- Large mandible often leads to gross skeletal deformity with development of class III malocclusion (prognathism) and anterior open bite.
- Macroglossia with indentations of teeth on the lateral border of tongue.
- Thick lips, which often produce a Negroid appearance to the patient.
- Proclination of teeth with diastema formation due to abnormal growth of jaws after the eruption of teeth.
- Hypercementosis in tooth.
- Increase in the thickness of the jaw bones (like other bones) due to subperiosteal new bone deposition.
- Hypertrophy of tissues of soft palate, which often causes disturbance in sleep.
- Large nose, ears and prominent eyebrows.
- Increased incidences of periodontitis.
- Poor fitting of old prosthesis due to large size of the jaw (especially lower).
- Enlargement of maxillary air sinuses.
- A typical coarse facial features due to abnormal soft tissue growth.

DIAGNOSIS

- Increased serum inorganic phosphorous level.
- Glycosuria and hypercalcinuria.
- T_4 level is normal or low.
- X-ray of skull reveals large sella.
- Serum growth hormone level is increased.

TREATMENT

Surgery or radiotherapy to the pituitary tumor.

HYPOTHYROIDISM

Hypothyroidism (decreased levels of thyroid hormone in the body) usually causes decreased metabolic rate in the body, which often results in the retardation of *growth, differentiation* and *function* of the entire body systems.

During childhood, hypothyroidism produces a disease called **cretinism** and it produces another disease **myxedema** among adults.

CAUSES

- Decreased secretion of TSH (necessary for secretion of thyroid hormone) by pituitary gland.
- Atrophy or damage to the thyroid gland.
- Congenital absence of thyroid gland.

CRETINISM

It is clinically manifested by the following features:

- Neonatal jaundice, horse-cry, constipation and teething problems.
- A short, poorly developed and mentally retarded child.
- Delayed development of speech and walking capability.
- Larger size of the skull and generalized non-pitting edema.
- Coarse dry skin and sparse brittle hair
- Brittleness of the fingernails.
- Hypotension, protuberant abdomen with umbilical hernia.
- Retraction of the bridge of the nose with flaring.
- Atrophy of the sweat glands.

Oral manifestations of cretinism

- Delayed eruption and exfoliation of deciduous teeth.
- Broad flat face due to defective growth of the skull and facial bones.
- Macroglossia with protruding tongue and thick lips.
- Dull expressionless face with dry coarse skin.
- Constant drooling of saliva from the mouth.
- Malocclusion and underdevelopment of mandible.

MYXEDEMA

Myxedema commonly produces the following features:

GENERAL SYMPTOMS

- It frequently develops among the middle-aged males.
- Patients often suffer from weakness, weight gain, fatigue, lethargy, low blood pressure and mental retardation, etc.
- Dry coarse skin with loss of hair, swelling of the face and extremities.
- Cold intolerance, husky voice, decreased sweating and anorexia.
- Loss of memory, hearing impairment, arthralgia, muscle cramps and paresthesia.
- The lethargic stage may progress to coma.

Oral manifestations of myxedema

- Dull expressionless face with periorbital puffiness and loss of hair.
- The tongue, lips and eyelids, etc. are edematous (nonpitting) and swollen.
- The large tongue often interferes with speech.
- Underdevelopment of maxilla and mandible.

DIAGNOSIS

- Reduction in serum T_3 and T_4 levels
- Elevation of serum TSH level
- Increased BMR.

TREATMENT

Administration of thyroid preparations.

HYPERTHYROIDISM

Hyperthyroidism is the disease, which is caused by excessive production of thyroid hormone in the body.

CAUSES

- Hyperplasia of thyroid gland with increased function (goiter).
- Increased secretion of thyroid hormone due to benign tumor in the gland.
- Increased TSH secretion due to pituitary overfunction.

CLINICAL FEATURES

Clinically, the disease produces the following features:

- The disease mostly occurs in 3rd and 4th decade of life.
- A definite female predilection is often noticed.
- Hypertension, weight loss and exhaustion.
- Excitability, anxiety and irritability.
- Weight loss (despite increased appetite), palpitations (tachycardia) and anorexia.
- Widened pulse pressure (increased systolic and decreased diastolic pressure).
- Increased risk of cardiovascular disease.
- Emotional instability with easy tearing, photophobia, warm smooth skin.
- Nervousness, muscle weakness, tremors.
- Exophthalmos, hyperdefecations.
- Osteoporosis, excessive sweating.

Oral manifestations of hyperthyroidism

- Early exfoliation of deciduous teeth.
- Premature eruption of permanent teeth.
- Alveolar bone atrophy.
- Increased susceptibility to oral infections.
- Difficulty in undergoing dental extractions or other dental surgical procedures because of the cardiac abnormality.

DIAGNOSIS

- Increased BMR.
- Elevated serum protein bound iodine concentration.
- Decreased urinary excretion of iodine.

TREATMENT

- Administration of antithyroid drugs.
- Surgery or radiotherapy to the thyroid gland tumor, if any.

HYPERPARATHYROIDISM

In the human body, there are four parathyroid glands present, and these glands release the hormone called the parathormone. The primary function of parathormone is to maintain the normal calcium and phosphorus levels in blood.

Whenever there is a decrease in the calcium or phosphorus levels in blood, the parathormone cause erosion of bone from the skeleton in order to liberate free calcium or phosphorus ions to make up the deficit. Parathormone also increases the blood phosphorus levels by inhibiting its urinary excretion.

Excessive concentration of parathormore in the blood is known as hyperparathyroidism, and it is of two types: (i) **primary hyperparathyroidism**, and (ii) **secondary hyperparathyroidism**.

- The primary hyperparathyroidism occurs due to excessive parathormore production in the body. It occurs as a result of adenoma, hyperplasia or functional carcinoma of the parathyroid glands.
- Secondary hyperparathyroidism occurs as a result of hyperplasia of the gland secondary to some disease, like end-stage of renal disease, osteomalacia and multiple myeloma, etc.

The clinicopathological manifestations of both types of hyperparathyroidism are almost same.

CLINICAL MANIFESTATIONS (FIG. 14.8)

- The disease occurs more commonly among the middle-aged females (postmenopausal).
- The early symptoms include fatigue, weakness, anorexia, polyurea, thirst, and constipation, etc.
- Depression, insomniance, loss of memory of recent events.
- Increased incandesce of peptic ulcers and itching sensations in the skin.

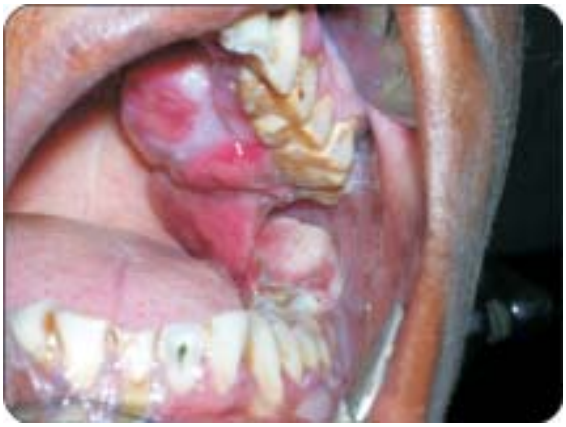


Fig. 14.8: Hyperparathyroidism

- Hypertension and CVS due to renal damage.
- Vomiting, stone formation in the kidneys (due to increased excretion of calcium) and joint stiffness.
- In severe cases, headache, bone pain, pathological fractures and coma, etc. may occur
- The common oral manifestations are loosening and mobility of teeth, and fracture of the jawbones, etc.
- Smelling of the jaw with development of brown tumor

RADIOLOGICAL FEATURES (FIG. 14.9)

- Generalized osteoporosis with thinning of the bony trabeculae.
- Loss of lamina dura around the roots of teeth is an early manifestation of the disease followed by thinning of bony trabaculae in the jaws.
- In severe cases of hyperparathyroidism, radiographs reveal **multiple, well-defined, unilocular or multilocular radiolucent areas** in the jawbones, which often resemble cysts or tumors (osteitis fibrosa cystica).
- Similar osteoclastic lesions can also be seen in other bones, e.g. pelvic bones, ribs and clavicles, etc.
- Thinning of the cortical plates and increased resorptions of medullary bone.
- Decrease in the trabecular density and blurring of normal trabecular pattern often produce a typical '**ground-glass**' appearance in the jawbone.
- Lateral skull radiograph reveals a "**salt and pepper**" effect.

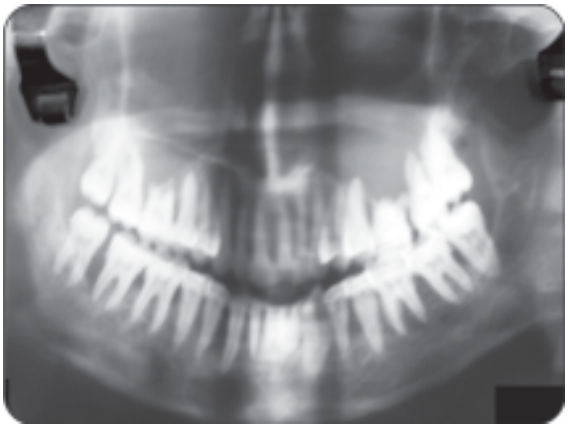


Fig. 14.9: Radiograph of hyperparathyroidism

- Long standing lesions can cause severe cortical expansion of bone.
- Subperiosteal resorption of bone in fingers and resorption of the terminal phalanges.

HISTOPATHOLOGY (FIGS 14.10 AND 14.11)

- Microscopy reveals osteoclastic resorptions of many bony trabeculae, as well as formation of new bones by the osteoblast cells.
- Proliferation of extremely vascular granulation tissue characterized by large number of blood capillaries and endothelium-lined spaces within the bone.
- There are some areas of excessive hemorrhage and hemosiderin pigmentations within the tissue.
- The gross tissue specimen often has a reddish-brown appearance due to the blood pigments and hence the lesion is often referred to as the *"brown tumor or brown nodules".*

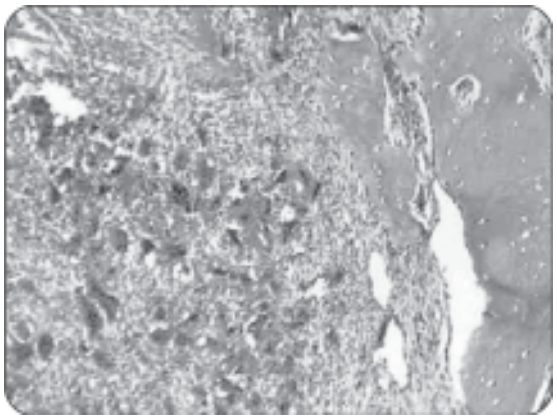


Fig. 14.10: Photomicrograph of hyperparathyroidism-I

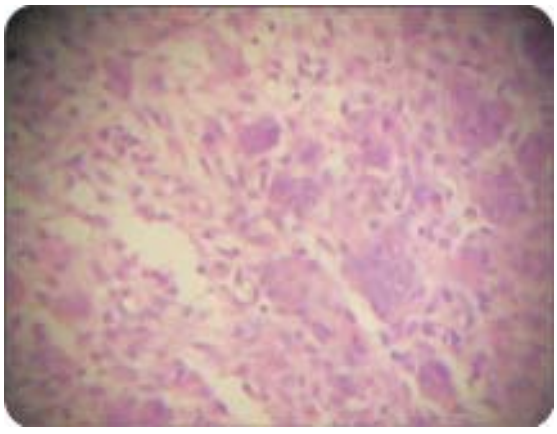


Fig. 14.11: Photomicrograph of hyperparathyroidism-II

- Multiple multinuclead osteoclast type of **giant cells** are often found in the tumor.
- In some cases, bone marrow is replaced by cellular fibrous connective tissue.
- Histologically, the tissue looks very similar to giant cell granuloma. However, multiple bone involvement, which is commonly seen in heperparathyroidism, is not seen in giant cell granulomas. Moreover, parathormone assay helps in differentiating these two lesions accurately.

Laboratory investigations of hyperparathyroidism

- Serum calcium level may be as high as 15 to 17 mg/dl (normal is 9 – 12 mg/dl).
- Serum alkaline phosphatase and urinary hydroxy proline levels are not elevated unless the condition is extremely severe.
- Serum phosphate level may be as low as 2.5 mg/dl.
- USG, CT-scan, etc. are done to detect the tumor in the gland.
- Urinary calcium and phosphate levels are elevated.
- Serum parathormone level is elevated (could be detected by immunoassay).

TREATMENT

Excision of the parathyroid tumor, administration of vitamin D and dietary phosphate supplements (Fig. 14.12).

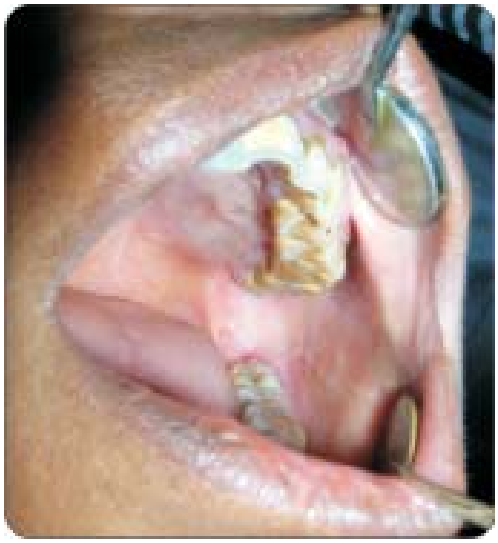


Fig. 14.12: Hyperparathyroidism after treatment

HYPOPARATHYROIDISM

Hypoparathyroidism refers to the deficiency of parathyroid hormone levels in the body and it is a much more rare entity as compared to hyperparathyroidism.

CAUSES

- If parathyroid gland is mistakenly removed during surgical intervention of the thyroid.
- Autoimmune damage of the parathyroid gland.
- Rare diseases like DiGeorge syndrome or endocrine candidiasis syndrome.

CLINICAL FEATURES

- Hypocalcemia follows the loss of parathyroid hormone.
- Increased neuromuscular excitability if the calcium level falls below 7 to 8 mg/dl.
- Tetany with carpopedal spasm occurs if serum calcium level falls below 5 to 6 mg/dl.

LABORATORY DIAGNOSIS

- Decreased level of parathormone in blood as seen in radioimmunoassay.
- Decreased serum calcium concentration.
- Decreased serum phosphate level.
- Normal renal functions initially.

TREATMENT

Administration of vitamin D precursor (ergocalciferol).

Oral manifestations of hypoparathyroidism

- **Chvostek's sign** is an important finding associated with hypocalcemia, which is characterized by twitching of the upper lip when the facial nerve is tapped just below the zygomatic process.
- Aplasia or hypoplasia of teeth with failure of eruption.
- Short roots of teeth but thick lamina dura.
- Incompletely mineralized dentin.
- Enamel hypoplasia (pitting type) and short roots of teeth.
- Chronic persistent candidiasis in young people.

ADRENAL HORMONES

The adrenal gland is made up of two parts—cortex and medulla. The adrenal cortex liberates three hormones:

- **Mineralocorticoids**, e.g. aldosterone.
- **Glucocorticoids**, e.g. cortisol.
- **Sex hormones**, e.g. adrenal androgens.

The adrenal medulla produces two hormones—**epinephrine and nor-epinephrine**.

FUNCTION OF MINERALOCORTICOIDS

These hormones are concerned with sodium and water retentions and potassium excretions in the body.

FUNCTION OF GLUCOCORTICOIDS (STEROIDS)

- To antagonize the action of insulin (promotes gluconeogenesis, which provides glucose).
- Increases breakdown of protein.
- Increases breakdown of fatty acids.
- Suppresses inflammation, inhibits scar formation.
- Blocks allergic reactions.
- Decreases the number of circulating eosinophils and leukocytes.
- Decreases size of the lymphatic tissue.
- Exerts a permissive action on functioning of CNS.
- Inhibits release of adrenocorticotropins.

Indications of steroid therapy

Hormone disorder:	Addison's disease
Rheumatic condition:	Rheumatoid arthritis Acute rheumatic fever
Blood disorders:	ITP (Idiopathic thrombocytopenic purpura) Leukemia Hemolytic anemia
Allergic conditions:	Bronchial asthma, allergic rhinitis
Dermatologic conditions:	Drug rashes, giant hives, lichen planus, atopic dermatitis
Ocular diseases:	Conjunctivitis, uveitis.
Collagen diseases:	Lupus erythematosus, periarteritis nodosa
GI problems:	Ulcerative colitis
Organ transplant recipients:	As an immunosuppressive drug
Neurological problems:	Cerebral edema
Miscellaneous conditions:	Gout, multiple sclerosis, etc.

Common side effects of long-term steroid therapy

- Suppression of adrenocortical function with risk of circulatory failure.
- Suppressed inflammatory response.
- Immunosuppression.
- Increased susceptibility to opportunistic infections.
- Depressed protein metabolism.
- Impaired wound healing.
- Moon face.
- Raised blood sugar.
- Sodium and water retention.
- Mood change.

INDICATIONS OF GLUCOCORTICOIDS

- Status asthmaticus.
- Acute adrenal insufficiently.
- Anaphylactic reaction (only after adrenaline has been given).

Steroid Crisis

The steroid hormone plays an essential role in maintaining life because it performs important metabolic activity of the body. It provides the capacity to resist all types of noxious stimuli and environmental changes. The secretion of steroid hormone is controlled by the pituitary hormone called the adrenocorticotropic hormone (ACTH).

If a patient takes steroid (cortisol) from outside sources for a longer duration of time, the function of the adrenal cortex becomes diminished in the body. Such exogenous steroid-dependent person if stops taking the drug abruptly, he or she may go into severe shock when exposed to some kind of stress or strain.

Such type of condition is known as "steroid crisis" and it occurs due to the lack of steroid production by the adrenal cortex during emer-

gency. For such reason, in steroid-dependent persons, the therapy should not be stopped abruptly; rather the therapy should be ended by gradually tapering the dose of steroid.

MINERALOCORTICOIDS

ALDOSTERONE

It is a steroid hormone of mineralocorticoid group produced by the outer section (zona glomerulosa) of the adrenal cortex in the adrenal gland. It acts on the kidney nephrons to conserve Na ion and secrete K ions in order to increase blood pressure. Aldosterone is decreased in Addison's disease and it is increased in Conn syndrome.

Aldosteronism: It is an abnormality of electrolyte balance in the body caused by excessive secretion of aldosterone.

Primary hyperaldosteronism: Occurs due to over secretion of aldosterone by an adrenal adenoma; characterized by hypokalemia, alkalosis, muscular weakness, polyuria (multiple urination), polydipsia (excessive thirst) and hypertension, etc.

Secondary hyperaldosteronism: Occurs due to extra-adrenal stimulation of aldosterone; usually associated with nephritic syndrome, cirrhosis liver, heart failure and malignant hypertension, etc.

Conn's syndrome: When hyperproduction of aldosterone (primary hyperaldosteronism) occurs due to a solitary benign aldosterone-secreting adenoma of the adrenal gland, the condition is known as Conn's syndrome. It is characterized by overproduction of aldosterone by the adrenal glands and the condition clinically presents muscle weakness and cramps, headache, metabolic alkalosis and hypokalemia, etc.

CAUSES OF ACUTE ADRENOCORTICAL INSUFFICIENCY

- Surgical removal of adrenal gland.
- Destruction of adrenal gland due to injury or infection.

CLINICAL FEATURES

- Headache
- Nausea
- Vomiting
- Abdominal pain
- Low blood pressure.

TREATMENT

Administration of glucocorticoids, mineralocorticoids and anabolic steroids.

WATERHOUSE–FRIDERICHSEN SYNDROME

Waterhouse-Friderichsen Syndrome occurs as a result of acute adrenocortical insufficiency, in association with infection by *Meningococci, Streptococci, Pneumococci*, etc.

The disease is often characterized by rapidly fulminating septicemia, purpura and death within 48 to 72 hours.

CHRONIC ADRENOCORTICAL INSUFFICIENCY (ADDISON'S DISEASE)

Addison's disease is a debilitating and potentially fatal condition, which occurs due to chronic insufficiency of the adrenocortical hormone; as a result of destruction of adrenal cortex.

The clinical manifestatiation includes:

- Postural hypotension, weakness, anorexia, etc.
- Fatigue, irritability, weight loss, nausea, vomiting and diarrhea, etc.
- Brown hyperpigmentations of skin including orofacial region (this is called **bronzing hyperpigmentations** and it occurs due to increased level of beta-lipoprotein or increased ACTH, both cause stimulations to the melanocytes to produce more melanin in the skin or mucosa).
- Small and feeble pulse.
- Brown, gray or black bronzing hyperpigmentations also occurs in the oral cavity and involves the labial and buccal mucosa, floor of the mouth and ventral surface of tongue, etc.
- Chronic mucocutaneous candidiasis.

HYPERFUNCTION OF ADRENOCORTICAL HORMONE (CUSHING'S SYNDROME)

Cushing's syndrome results from over activity of the adrenal glands with consequent hypersecretion of gluccocorticoids.

Clinical features of Cushing's syndrome

- Persistent hyperglycemia (**steroid diabetes**).
- Weakness due to muscle wasting.
- **Increased capillary fragility** resulting in ecchymosis, easy bruisability and hematoma formations following veinpuncture.
- **Severe osteoporosis** leads to pathological bone fracture under low impact trauma. The bones commonly affected include mandible, maxilla and alveolar bone, etc.
- Potassium depletion leading to hypokalemia, arrhythmias, muscle weakness and renal disorder
- Sodium and water retention which causes hypertension and edema.
- Abnormal fat deposition in the orofacial region produces a puffy and bilateral edematous swelling of the face **("moon facies")**.
- Development of abnormal fat pad on the neck **(buffalo-hump).**
- Generalized obesity and **lowered resistance to stress** cause an increased risk of circulatory collapse.
- **Decreased immunity** with increased susceptibility to infection (especially opportunistic infections).
- Due to **suppression of inflammatory response**, people with Cushing's syndrome show few signs of inflammation and also demonstrate poor wound healing. This includes healing of extraction socket and jaw fracture wounds.
- Increased production of androgens causes virilism in women.
- Oligomenorrhea and variable degrees of facial hirsutism.
- Mental changes include memory loss, poor concentration and depression (steroid psychosis).
- Occasional chloasma like pigmentations of face and pressure points.

CAUSES

- Administration of high dose of ACTH or increased ACTH production in a pituitary tumor.
- Administration of high dose of corticosteroids.
- Adrenocortical hyperplasia with over production of glucocorticoids.
- Adenoma or carcinoma of the adrenal cortex.
- Ectopic ACTH syndrome.

DIAGNOSIS

- Increased levels of urinary 17–hydroxy–corticosteroids.
- Increased plasma cortisol levels.
- Glycosuria not controlled by insulin.
- Albuminuria.
- Adrenal tumor can be detected by MRI.

TREATMENT

Surgical removal of the gland tumor or radiotherapy.

PANCREATIC HORMONE (INSULIN)

DIABETES MELLITUS

Diabetes mellitus is metabolic disorder characterized by glucose intolerance, and it is caused by an imbalance between insulin supply and insulin demand in the body.

Insulin is a hormone which is secreted by the '**beta cells of the islets of Langerhan's**" of pancreas. This hormone maintains the balance between high and low glucose levels in blood.

TYPES

There are two main types of diabetes mellitus:

A. Insulin-dependent diabetes mellitus (IDDM)

B. Noninsulin-dependent diabetes mellitus (NIDDM).

Diabetes exhibits hyperglycemia due to lack of insulin or reduced effectiveness of insulin. The disease affects the metabolism of carbohydrates, proteins, fat, water and electrolytes.

CLINICAL MANIFESTATIONS

- There are four cardinal signs of diabetes mellitus: (i) polyuria, (ii) polydypsia, (iii) polyphagia, (iv) weight loss.
- Besides these, patients may also have symptoms, like tiredness, nocturia, increased susceptibility to infection, etc.
- Many patients develop myopia, paresthesia of the limbs, pain in the limbs and impotence, etc.

Oral manifestations diabetes mellitus

- Pronounced hyperplasia of the attached gingiva
- Severe rapidly destructive, periodontitis and periodontal abscess formations (diabetes increases the progression of periodontal disease by altering the tissue response to local irritants)
- Pain and inflammation of gingiva, with frequent bleeding
- Dry mouth due to polyuria and dehydration
- Delayed wound healing is one of the most common and important manifestations of the disease
- Diabetic sialosis (symmetrical, painless, recurrent swelling of the salivary glands, particularly parotids) and sialorrhea (excessive secretion of saliva) may also occur
- Increased caries susceptibility in poorly controlled diabetes with higher DMFT caries index
- Increased tendency for oral infections by hemolytic *Streptococci* and *Staphylococci*
- Unusually prolonged oral candidiasis, especially erythematous candidiasis with central papillary atrophy of tongue
- Burning mouth syndrome due to dry and damaged mucosa
- Occasional presence of erosive lichen planus-like lesions in the mouth
- Increased prevalence of "dry socket" after tooth extraction
- Loss of taste sensation or altered taste sensations (dysgeusia)
- Increased incidence of enamel hypoplasia
- Atypical dental pain
- Benign migratory glossitis and mucomycosis may occur in IDDM cases

- In some cases, the disease may be completely asymptomatic and the patients are not aware of the disease at all.

DIAGNOSIS

- Blood sugar estimation—fasting, postprandial and random.
- Glucose tolerance test (GTT)—if sugar concentration in venous blood is above 130 mg/dl, diabetes is confirmed.
- Urinary glucose estimations—if the level is above 10 to 20 mg/dl, diabetes should be suspected.
- Detection of ketone bodies in urine.

TREATMENT

- Diet control.
- Administration of oral hypoglycemic drugs.
- Insulin therapy whenever necessary.

Complications of diabetes mellitus

- Diabetic ketoacidosis
- Diabetic neuropathy
- Diabetic nephropathy
- Diabetic retinopathy
- Vascular disorders
- Ischemic heart disease
- Increased susceptibility to infection
- Hypoglycemic coma and death
- Increased risk of hypoglycemic shock following dental extractions especially in case of delay in taking normal diet.
- Oral lichenoid reactions
- Sialadenosis.

PROGERIA

Progeria is a disease of unknown etiology and it is characterized by dwarfism and premature senility.

The affected infants exhibit alopecia, skin pigmentation, atrophic skin, high-pitched voice, smaller mandible, muscular atrophy and joint deformity, etc.

The patients usually have an above normal IQ and they resemble a "**wizened little old person**".

Delayed eruption of teeth and excessive secondary dentin formation are the common oral findings.

IMBALANCE OF SEX HORMONES

Imbalance of sex hormones in the body and their related changes in the oral tissue take place during

puberty, menstruation, pregnancy and menopause. Puberty is usually associated with hyperplastic gingivitis and gingival bleeding. Pregnancy is associated with gingivitis and pregnancy tumor. Transitory gingivitis and cyclical oral ulcerations may occur during menstruation, while desquamative gingivitis, dry mouth and glossodynia occur commonly during menopause.

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CHAPTER 15

Diseases of Bone

PAGET'S DISEASE OF BONE (OSTEITIS DEFORMANS)

DEFINITION

Paget's disease is a relatively uncommon bony disorder characterized by excessive, uncoordinated phases of bone resorption and subsequent deposition of new bone in the same area. The disease finally results in severe distortion and weakening of the affected bone. Paget's disease was first reported in the year 1877 by Sir James Paget.

ETIOLOGY

The disease is a focal alteration in the morphology and histopathology of bone which exhibits disorganized formation and remodeling of osseous structures, unrelated to the functional requirements.

The exact etiology of the diseases is not known, although several factors have been implicated, which probably trigger the disease, these factors include the following:

- Genetic abnormality
- Inflammatory reaction to the bone
- Circulatory disturbances
- Defective connective tissue metabolism
- Slow viral infections (especially paramyxovirus)
- Autoimmune disorders
- Endocrine abnormality.

CLINICAL FEATURES

Incidence: The incidence rate is about 2.5 percent of all persons over 40 years of age.

Age: The disease can occur at any age but usually most of the patients are in their fifth, sixth and seventh decade of life.

Sex: Males are slightly more commonly affected than females (3:2).

Sites: Paget's disease has a predilection for the weight bearing areas of the body, especially the vertibral column and femur, etc. The skull, pelvis and sternum, etc. are also commonly involved. Among the jawbones, maxilla is affected twice as often as mandible.

NATURAL HISTORY OF THE DISEASE

The natural history of paget's disease can be divided into three progressive and overlaping phases:

A. Initial predominantly osteolytic phase.
B. An active stage of mixed osteolysis and osteogenesis.
C. Predominantly osteoblastic or sclerotic final phase.

PRESENTATION (FIGS 15.1 AND 15.2)

- Most of the patients complain initially of a deep and aching bone pain, with bilaterally symmetrical swelling of the involved bone (Fig. 15.1).

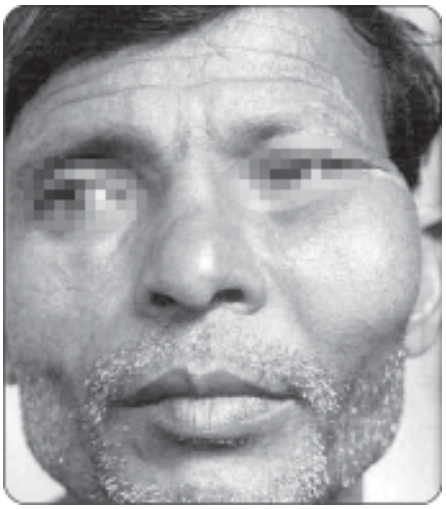

Fig. 15.1: Paget's disease of bone causing swelling of the maxilla

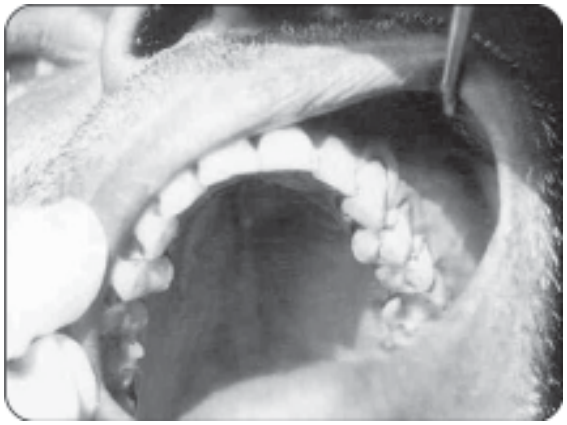

Fig. 15.2: Intraoral view of the same patient showing expansion of the maxillary bone

- The pain can be sometimes so severe that the patient is unable to move the affected organ. Many cases however are asymptomatic and the bony abnormality is detected only during routine radiographic examinations.
- More deformity in the bone is usually observed in the **stress bearing areas,** e.g. spine, femur, sacrum and pelvis, etc.
- The disease in the weight bearing areas of the body may cause severe bowing deformity and thereby results in a typical **'monkey-like stance'**. Moreover, these patients often have a characteristic **waddling gait.**
- In Paget's disease, involvement of the facial bone is referred to as "**leontiasis ossea**" and patients often have a **grotesque appearance of the face** due to severe bony deformity.
- The patients may develop **headache**, **deafness**, **blindness** and **facial paralysis**, etc. which occur **due to the narrowing of the skull foramina** and subsequent **compression of the cranial nerves** passing through them (both sensory and motor disturbances are seen).
- Progressive **enlargement of the skull**, bowing of the legs with thickening and curvature of the spine are commonly seen.
- Increased localized temperature of the skin in the affected areas of bone is often noticed.
- Due to the gradual enlargement of the skull, patients often feel **difficulty in wearing their old hats.**

RADIOLOGICAL FEATURES

The radiographic findings of Paget's disease of bone are highly variable depending upon the stage of the disease.

Oral manifestations of Paget's disease

- Denture-wearing people often complain of tightness of their old dentures with poor fit due to progressive enlargement of the jawbones, especially the alveolar ridge.
- Facial paralysis due to compression of the nerve as a result of obliteration of the cranial foramina.
- Maxillary bone is affected by the disease more often than the mandibular bone.
- Diastema, loosening of teeth and difficulty in lip closure is common and all the teeth in the jaw are vital.
- Movements and migration of teeth with concomitant development of malocclusion is a common problem in dentulous patients.
- Flattening of palate, retroclination of incisors and palatoversion of posterior teeth often occurs.
- Moreover, the disease may cause necrosis of the gingiva and the underlying alveolar bone; due to excessive internal pressure in the jaw.
- Gross **hypercementosis of teeth** is a characteristic finding of Paget's disease and the teeth are often fused with the jaw bone.
- Extraction can be difficult in these patients because of fusion of tooth with the jaws, post-extraction hemorrhage and chances of development of osteomyelitis, etc.
- Maxillary lesions often cross the midline and involve both quadrants of the jaw.
- **Pathological fractures** in the affected bones may occur, since these bones are very weak despite their gross thickening.
- Osteogenic sarcoma develops in about 10 percent cases of pre-existing Paget's disease of bone.
- Besides osteosarcoma, giant cell tumors can also develop from the pre-existing Paget's disease of bone.

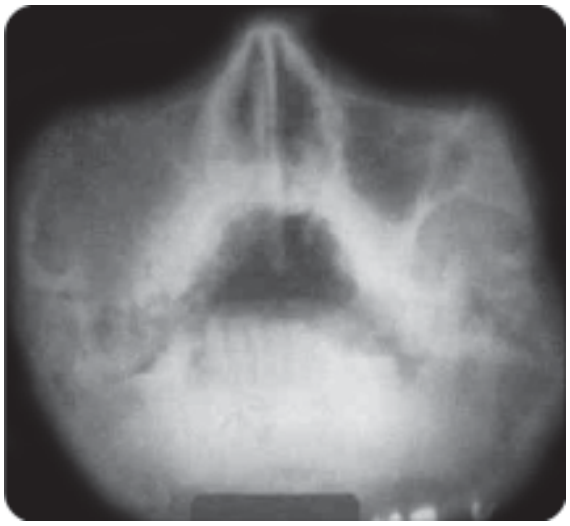

Fig. 15.3: Radiograph shows cotton-wool appearance of maxillary bone in Paget's disease

- Initially, there is presence of only radiolucent areas in the affected bone due to decreased density.
- In the next stage, radiographs of the involved bone reveal haphazard arrangement of newly formed bony trabaculae within the radiolucent area, which often produces a patchy radiopaque pattern called **"cotton-wool"** appearance (Fig. 15.3).
- The lesions become more and more radiopaque due to increased osteosclerosis with loss of normal trabaculations in the later phases of the disease.
- Lateral skull projection reveals a large, prognathic, pagetoid mandible. The maxillary lesions often extend to the sinuses and cause decreased airspace or obliteration.
- **Hypercementosis** of the tooth, which involves the entire dentition.
- Loss of lamina dura and ankylosis with obliteration of the periodontal ligament space.
- Root resorptions are also commonly observed.
- Monostotic form (involving only a single bone) of Paget's disease of mandible presents a typical "**black beard**" image on bone scan.

HISTOPATHOLOGY (FIG. 15.4)

- Rapid, irregular and exaggerated bone resorption and subsequent bone deposition are the hallmark features of Paget's disease.
- In the initial stage of the disease, random osteoclastic bone resorption occurs, and the bone is replaced by a highly vascularized cellular connective tissue.
- The osteoclasts are usually larger and may even contain over one hundred nuclei.

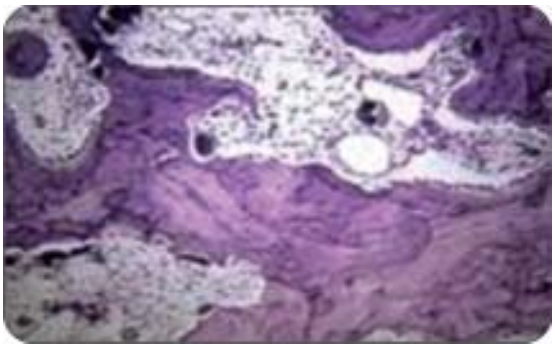

Fig. 15.4: Photomicrograph of Paget's disease of bone

Key points of Paget's disease

- Paget's disease is a bony disorder characterized by repeated resorption and deposition with severe weakening and deformity of the affected bone.
- The disease mostly affects older individuals, who complains of deep and aching pain, with swelling of the involved bone.
- Progressive enlargement of skull causes difficulty in wearing old hats and enlargement of alveolar ridge makes it difficult to wear dentures.
- Patients may have headache, deafness, blindness and facial paralysis, etc. due to the narrowing of the skull foramina.
- Flattening of palate, retroclination of incisors and palatoversion of posterior teeth, diestema and malocclusion often occurs.
- Radiograph reveals a typical **"cotton-wool"** appearance in the bone and hypercementosis of the teeth.
- Histologically, the bone exhibits rapid resorption and subsequent bone deposition with the presence of multiple reversal and resting lines.
- Laboratory investigation shows markedly raised serum alkaline phosphatase level.
- Paget's disease increases the tendency for pathological fracture of the affected bone as well as increases the risk of development of osteosarcoma.

- In the later stage, deposition of new lamellar or oven bone within the connective tissue by the osteoblast cells occur and the fatty, hemopoetic bone marrow is replaced by a fibrous stroma (fibrosis of bone marrow).
- The newly formed bone may again be resorbed by the osteoclast cells and thus causing loss of normal architecture of the bone.
- This bone resorption and bone deposition alternate rapidly and these changes in the bony activity are often marked by prominent basophilic "**reversal and resting lines**" (these lines indicate the junction between alternating areas of bone resorptions and bone formations).
- The irregular pattern of such lines often characteristically produces a "**jigsaw-puzzle**" or "**mosaic pattern**" in the bone.
- The affected bone becomes thick, sclerosed and the medullary cavity becomes obliterated.
- Chronic inflammatory cells and many dilated blood capillaries are present within the bone.

LABORATORY FINDINGS

- During the osteoblastic phase of the disease, the serum alkaline phosphatase level may be markedly elevated up to 250 Bondansky units (normal 1.5–5 units).
- There may be an increased urinary calcium hydroxyproline level during the osteolytic phase of the disease.
- Bone scan may be helpful in determining the exact extent of the disease.
- Although considerable amount of loss of bone minerals occurs due to resorption, the serum calcium and phosphorus levels however are always normal or near normal.

DIFFERENTIAL DIAGNOSIS

- Acromegaly
- Fibrous dysplasia of bone
- Florid osseous dysplasia
- Hyperparathyroidism
- Osteopetrosis
- Cementifying or ossifying fibromas
- Osteosarcoma
- Metastatic carcinoma
- Sclerosing osteomyelitis.

TREATMENT

Only symptomatic treatments can be done (e.g. administration of analgesics to relieve pain).

Recent investigators believe that administration of "calcitonin" may suppress the bone resorption and deposition rates in this disease.

Surgery may be required in cases of severe bony deformities and in cases of pathological fractures of the affected bone.

Unfortunately few cases of Paget's disease of bone may transform into osteosarcoma.

FIBROUS DYSPLASIA OF BONE

DEFINITION

Fibrous dysplasia is an idiopathic condition, in which an area of normal bone is gradually replaced by abnormal fibrous connective tissue, which then again undergoes osseous metaplasia and eventually the normal bone is transformed into a abnormal dense lamellar bone.

TYPES

Fibrous dysplasia is broadly divided into two types.

Monostotic fibrous dysplasia: When a single bone is involved by the disease in a localized area. This type accounts for about 80 to 85 percent of all cases. Jaw bones are frequently affected in this type.

Polyostotic fibrous dysplasia: When multiple number of bones (more than two) are involved by the disease.

The polyostotic fibrous dysplasia of bone has two subtypes:

Jaffey's type: In which several bones of the skeleton are affected in association with café-au-lait skin pigmentations.

Polyostotic fibrous dysplasia in association with Albright syndrome: The condition is characterized by fibrous dysplasia of multiple bones, café-au-lait skin pigmentation and endocrine disturbances.

ETIOLOGY

The exact etiology of the disease is not known, however it is believed to be a non-neoplastic self-limiting condition caused by some genetic abnormality. Some investigators believe that fibrous dysplasia could be a developmental disorder.

Previously it was considered by many people that the disease may be initiated by several predisposing factors which are as follows:

- Liver damage
- Infections
- Glandular dysfunctions
- Neurofibromatosis
- Lipoid granulomatosis
- Trauma
- Abnormal osteoclastic maturation of bone forming mesenchyme.

However, the role of any of these factors in the pathogenesis of fibrous dysplasia of bone has not been fully substantiated.

CLINICAL FEATURES

Age: Fibrous dysplasia usually occurs in the first and second decade of life. Abnormal bony growth continues upto late teens or early twenties.

Sex: The polyostotic type of the disease occurs 2 to 3 times more commonly among females, however in monostotic type, males and females are almost equally affected.

Sites: The polyostotic fibrous dysplasia commonly involves the skull, facial bones, clavicles, pelvic bones and long bones, etc.

The monostotic fibrous dysplasia frequently involves the jaw bones, Maxilla is usually more commonly affected than mandible.

The mandibular lesions are often truly monostotic in most cases, whereas the maxillary lesions are frequently associated with other bones, e. g. frontal, zygomatic and sphenoid, etc.

CLINICAL PRESENTATION (FIGS 15.5 TO 15.7)

- The **monostotic type of fibrous dysplasia** is more common (80-85%) than the polyostotic type.

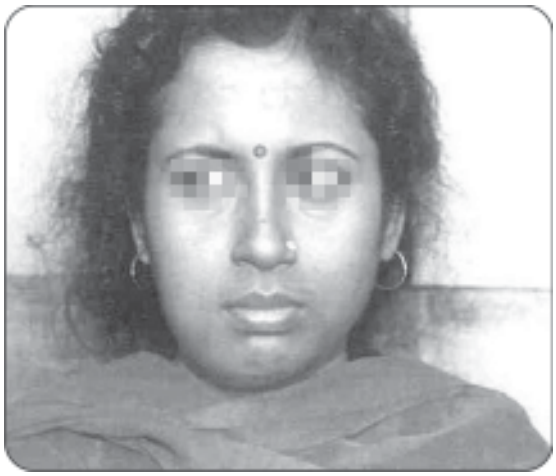

Fig. 15.5: Fibrous dysplasia of bone involving the right side of mandible

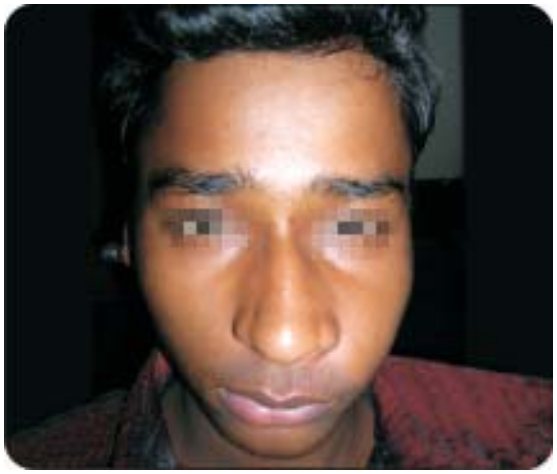

Fig. 15.6: Fibrous dysplasia-I

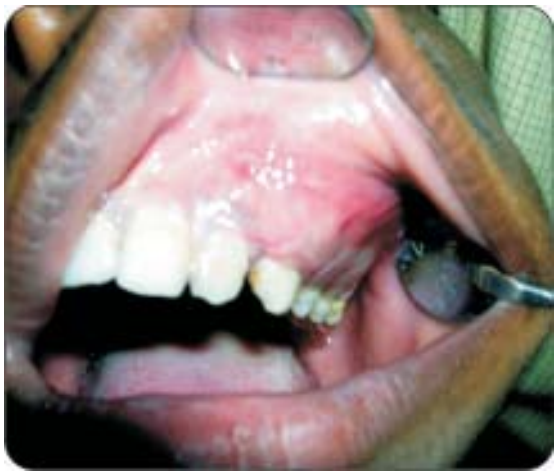

Fig. 15.7: Fibrous dysplasia-II

- It causes a slow enlarging, painless, smooth, rounded, unilateral localized swelling of the jaw (Fig. 15.5).
- Gradually increasing facial asymmetry with marked swelling of the cheek may be the first sign of fibrous dysplasia in a child, the disease eventually causes huge deformity of the orofacial region (Fig. 15.6).
- Expansion and gradual distortion of the cortical plates, displacement of teeth, disturbances in tooth eruption (many teeth may even fail to erupt), etc. are commonly observed.
- The teeth may be drifted, rotated or misaligned in the jaw due to the growing bony mass and in many patients severe malocclusion often develops.
- The monostotic form of the disease never transforms into polyostotic form with time.
- Although the process is slow enlarging some lesions may be very aggressive, however, palpation in the affected area does not elicit pain.
- The maxillary lesions may sometime extend into the maxillary air-sinus and occasionally into the orbital floor, the later often results in exophthalmos, proptosis and nasal obstructions, etc. Moreover, maxillary lesions may also exhibit obliteration of the canine fossa.
- Mandibular lesions mostly concentrate near the molar-premolar area and if lower border of the mandible is involved, there is often presence of a bulging and an increase in the depth of the jaw.
- Larger lesions may sometimes become traumatized and ulcerated due to impingement by the teeth during chewing.
- The **polyostotic type of fibrous dysplasia** causes gross swelling and deformity in multiple numbers of bones, with pain and sometimes pathological fractures.
- The polyostotic fibrous dysplasia with multiple bone involvement and skin "**café-au-lait**" pigmentation but without any endocrine disturbances is known as **Jaffe-Lichtenstein syndrome**.
- The "**café-au-lait**" skin pigmentations are characterized by **light-brown** pigmented areas over the skin, which has a typical **jagged periphery**. These are seen in those areas, which overlie the affected bones , e.g. neck, buttock back, trunk, thigh and sacral areas. However these are rarely seen in the oral mucosa.
- The café-au-lait pigmentations are also seen in Von-Recklinghausen's disease, where they have a characteristic 'smooth border' rather than a 'jagged border'.
- Polyostotic fibrous dysplasia of bone with "café-au-lait" skin pigmentations and multiple endocrinopathies like precocious puberty in females, pituitary adenoma, acromegaly, goiter, Cushing syndrome, hyperparathyroidism and hyperthyroidism, etc. constitute the syndrome called **McCune-Albright's syndrome.**
- The **precocious puberty** in Albright's syndrome occurs in young women and it consists of **premature vaginal bleeding** in the first few months of life, **breast development and axillary and pubic hair growth, etc.** at the age of about 2 to 3 years**.**
- The bony changes in fibrous dysplasia usually occur during the period of active skeletal growth and it ceases during adult life (at the time of skeletal maturation).
- On rare occasions, fibrous dysplasia lesions may undergo malignant transformation and develop fibrosarcomas.

RADIOLOGICAL FEATURES (FIGS 15.8 TO 15.10)

- In the initial stages, both forms of the disease produce **unilocular or multilocular radiolucent areas in the bone** containing faint bony trab aculae (Fig. 15.8).
- The disease often produces expansion and distortion of cortical plates of bone with displacement of teeth.
- Sometimes 'egg-cell' crackling of the expanded cortex of the affected bone may be seen.
- Later on, as the lesion matures, **a classical "ground glass" or "orange peel" or "pebbled" appearance of bone** is observed in radiographs and ground glass type is the most common radiographic appearance of fibrous dysplasia.

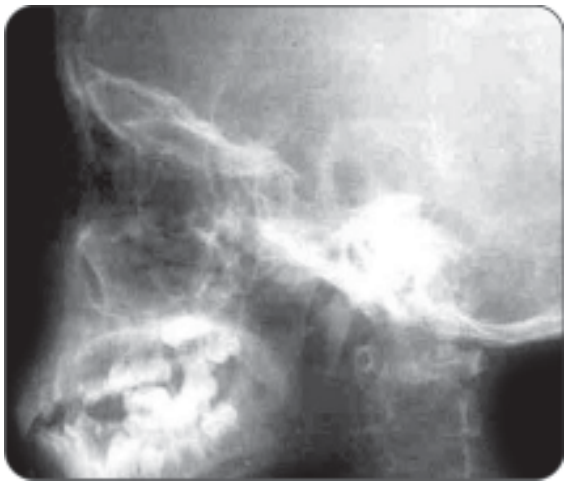

Fig. 15.8: X-ray shows diffuse radiolucency in mandible (Right side)

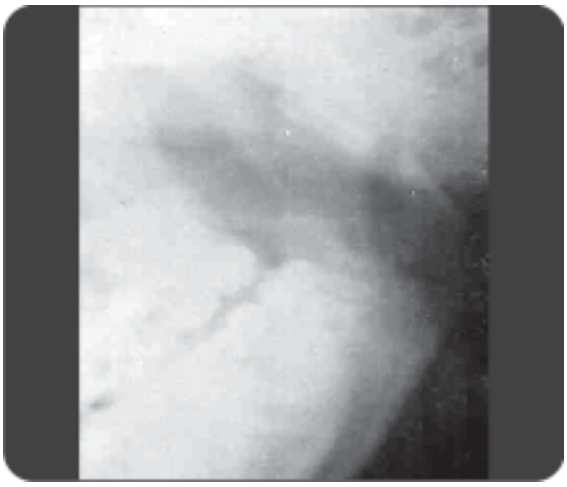

Fig. 15.9: X-ray shows diffuse radiolucency in mandible with multiple radiopacities

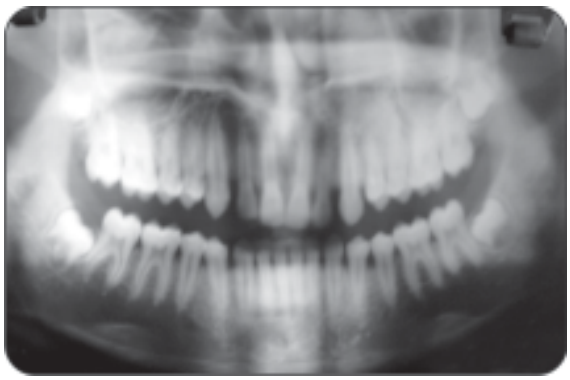

Fig. 15.10: Radiographic view of fibrous dysplasia

- The margin of the lesion is not well-demarcated and it gradually **blends imperceptibly with the adjacent normal bone.**
- Mandibular lesions exhibit expansion of both buccal and lingual cortical plates with bulging distortion of the lower borders.
- The inferior alveolar canal is often displaced superiorly from its normal position due to the expanding bony lesion.
- Both erupted and unerupted teeth are randomly distributed within the lesion.
- Fibrous dysplasia often radiographically exhibits narrowing of the periodontal ligament space and an ill-defined lamina dura.
- Maxillary lesions present obliteration of the maxillary sinus with superior displacement of the sinus floor.
- Involvement of multiple skull bones, e. g. occipital, frontal and sphenoid, etc. by the disease along with the maxillary bone often characteristically produces **increased density of the base of the skull.**

Key points of fibrous dysplasia of bones

- Fibrous dysplasia is a fibro-osseous disorder, in which an area of normal bone is gradually replaced by abnormal fibrous connective tissue.
- The disease occurs in two main forms- monostotic (when a single bone is affected) and polyostotic (when multiple bones are affected).
- The disease causes progressive, painless, smooth, swelling of the jaw with facial asymmetry.
- Polyostotic fibrous dysplasia may be associated with McCune-Albright's syndrome, which presents multiple bone swelling, 'café-au-lait' skin pigmentations and precocious puberty, etc.
- On radiographs the disease produces a classical, "ground glass" appearance of bone.
- Histologically, fibrous dysplasia exhibits a highly cellular, well-vascularized fibrillar connective tissue that replaces the normal bone.
- Multiple irregular, trabeculae of immature bone are found within the fibrous tissue, typically produce a "**Chinese letter**" pattern.

LABORATORY FINDINGS

- The serum calcium, phosphorus and alkaline phosphatase levels are within normal limits.
- Occasionally, there may be elevated serum alkaline phosphatase levels in polyostotic form of the disease.
- BMR may be moderately high.

- Premature secretion of pituitary follicle stimulating hormone may occur in some cases.

HISTOPATHOLOGY (FIG. 15.11)

- Histologically fibrous dysplasia reveals the presence of a highly cellular, proliferating, well-vascularized fibrillar connective tissue that replaces the normal bone.
- Within the fibrous tissue stroma, multiple spindle-shaped, fibroblast cells of uniform size, are arranged in a "**whorled pattern**" and moreover, the collagen fiber bundles completely lack their orientation.
- Multiple coarse, irregular, trabeculae of immature bone are distributed within the fibrous tissue and they typically produce a "**Chinese letter**" pattern. These bony trabeculae are formed due to **osseous metaplasia** of the connective tissue stroma.
- These bony trabeculae are evenly spaced, uniformly distributed and are separated from one another, the trabeculae are not bordered by osteoblast cells as seen in the normal bone, instead there may be few osteoblast cells scattered throughout the bone trabeculae.
- Spheroidal areas of calcification resembling cementum may be present within the lesion and occasionally there may be presence of foci of giant cells in the lesion.
- In jaw lesions the bony trabeculae may be thicker and blunter than that of the long bone lesions.
- Osteoblastic and osteoclastic activity may be present in relation to some trabeculae of bone.
- At the margin, the **lesion gradually blends with the surrounding normal bone** (this feature particularly distinguishes fibrous dysplasia from ossifying fibroma of bone, since the later lesion is well-demarcated from the surrounding bone by a capsule).
- With increase in the age of the lesion, the amount of cellularity within the fibrous tissue decreases and the amount of bone tissue increases. This feature is more commonly evident in the jaw lesions rather than the long bone lesions.
- Progressive remodeling of the woven bone to lamellar bone is also commonly observed as the lesion matures.
- Occasionally, fibrous dysplasia of bone may be associated with the development of aneurysmal bone cyst.

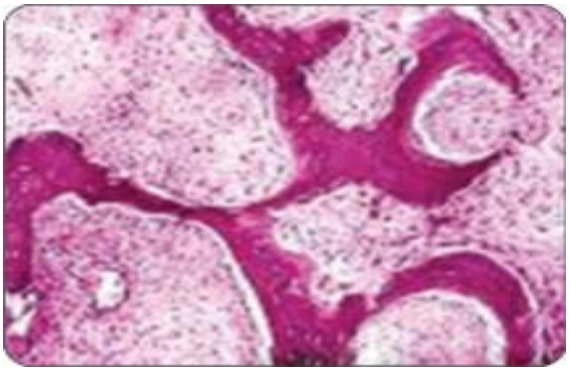

Fig. 15.11: Photomicrograph of fibrous dysplasia of bone

DIFFERENTIAL DIAGNOSIS

- Ossifying fibroma
- Cementifying fibroma
- Paget's disease of bone
- Garre's osteomyelitis
- Hyperparathyroidism.

TREATMENT

Fibrous dysplasia is a self-limiting disease and the growth usually ceases after puberty, with spontaneous bone remodeling. However, surgical recontouring of bone may be needed in larger lesions for cosmetic or functional reasons. Fibrosarcoma may develop from these lesions, especially, following radiotherapy.

CHERUBISM

DEFINITION

Cherubism is a rare benign hereditary condition, being inherited as an autosomal dominant trait, which affects only the jawbones. The disease is characterized by "**bilaterally symmetrical enlargement**" of mandible or sometimes the maxilla.

The entity Cherubism was first reported by Jones in the year 1933.

PATHOGENESIS

Cherubism is a hereditary disease, however, according to many investigators it can occur as a result of the following reasons:

- Anomalous development of bone
- Latent hyperparathyroidism
- Hormone dependent neoplasm.
- Trauma
- Disturbance in the development of bone forming mesenchyme.

CLINICAL FEATURES

Age: The disease commonly affects the young individuals, usually at the age between 1 to 5 years.

Sex: More common among males than females.

PRESENTATION

- The disease follows a familial pattern and several members of the same family may be affected. Some non-familial cases are also reported, which occur due to new mutations.
- At birth the appearance of the patient is absolutely normal. However, between the age of 1 and 5 years **a bilateral, painless, symmetric swelling** develops in mandible or sometimes in maxilla in severe cases (Fig. 15.12).
- In cherubism, symmetrical mandibular swelling (which starts at the angle region on both sides) along with excessive cheek fullness often give rise to a typical appearance of "**chubby face**" to the child.
- Since most little children naturally have a somewhat chubby face, the parents may not appreciate the abnormality unless the mandibular swelling becomes substantial.
- When the maxillary swelling is very extensive, pressure on the floor of the orbit may result in an upward turn of pupils of the patient's eyes and thus revealing a rim of white sclera below the iris; this phenomenon is often referred to as the "**heavenward look**".
  This so called heavenward look often gives patient an '**angelic appearance**'.
- Moreover, the severe maxillary swelling in cherubism may cause stretching of the facial skin and retraction of the lower eye-lids.
- Patients with cherubism commonly exhibit increased cheek fullness, expansion and widening of the alveolar ridge, flattening of the palatal vault (Fig. 15.13).
- On rare occasions there can be destruction of the infraorbital ridge.
- Non-inflammatory submandibular lymphadenopathy also develops in cherubism, which occurs due to reactive hyperplasia.
- Premature exfoliation of deciduous teeth, extensive diastema formation and delayed eruption of permanent teeth, etc. are often associated with the disease.
- Cherubism can also exhibit rotation or transposition teeth and occasional resorption of roots of teeth in the affected zone of the jawbone.
- The teeth are often irregularly arranged in the jaw or they may be displaced. Moreover, hypodontia of the permanent teeth is common in cherubism.
- In addition to facial deformity, random malalignment of teeth in the arch results in malocclusion.

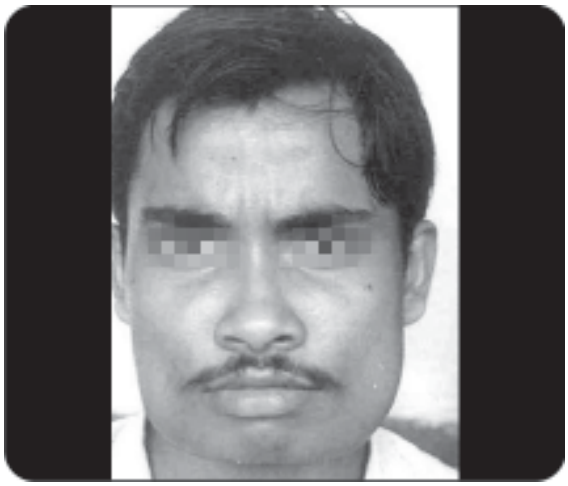

Fig. 15.12: Cherubism producing bilateral mandibular swelling

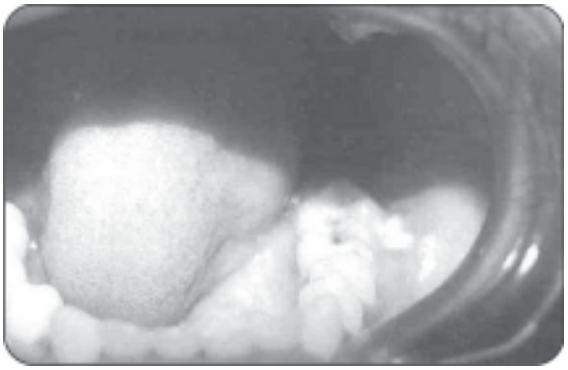

Fig. 15.13: Severe bony expansion in cherubism

Key points of cherubism

- Cherubism is a rare benign hereditary condition of the jaws, characterized by "bilaterally symmetrical enlargement" of mandible or sometimes the maxilla.
- The disease occurs at a very young age and because of the large swelling of the facial bone the affected child typically has a "chubby face".
- Moreover the patient often has a so called "heavenward look" because of the upward turn of the pupil of the eye, this also gives an 'angelic appearance to the patient.
- Massive jaw swelling in cherubism can cause gross facial deformity and malocclusion; which lead to masticatory, swallowing, speech and even breathing difficulties.
- Radiograph in cherubism presents multiple cyst-like spaces in the jaw and sometimes multiple unerupted, teeth may look like just 'floating' within these cysts.
- Histologically the disease presents a highly cellular and vascular connective tissue stroma, containing numerous proliferating fibroblasts and variable numbers of multinucleated giant cells.
- The disease is self limiting and thus, no treatment is required.

- In severe cases of cherubism, the jaw swelling can be so massive that the patients may have masticatory, swallowing, speech and even breathing difficulties.
- Compression of the cranial nerves may cause visual and auditory disturbances in Cherubism.
- Cherubism has been reported to occur in conjunction with Noonan syndrome, which is characterized by congenital heart disease, chest deformity, mental retardation, facial bone anomalies, webbed neck, gingival fibromatosis, blood coagulation disorder and obstructive sleep apnea, etc.
- The disease is at its peak during the age of 5 to 6 years, the bony growth usually becomes static shortly after puberty and then it slowly regresses.

RADIOLOGICAL FEATURES

- In cherubism, the involved jaw bone radiographically shows well-defined, multilocular, "**cyst-like**" **radiolucent areas or cavities** on both sides of mandible (Fig. 15.14).

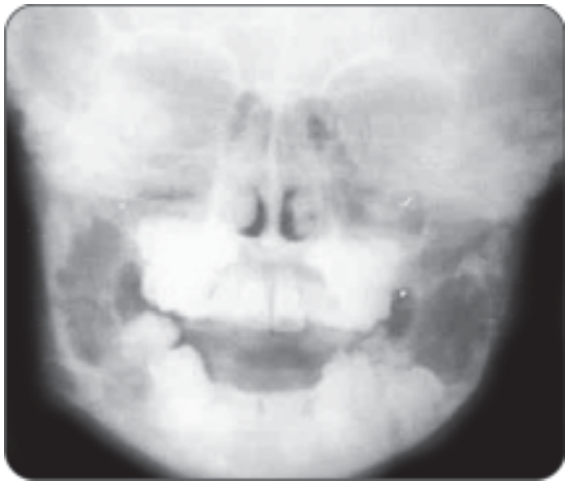

Fig. 15.14: Cherubism radiographically showing multicystic radiolucency in mandible

- The small radiolucent areas often coalesce together to from larger lesions defects in the bone.
- The initial destruction of bone starts at the angle of the mandible, which can be detected by X-rays even before the clinical manifestations of the disease start to appear.
- Cherubism in later stages causes severe bilateral expansion of the jaw with thinning of the cortical plates.
- In few cases, there may be presence of the classic '**ground glass**' appearance in cherubism.
- Radiographs also reveal displacement of the inferior alveolar canal or obliteration of the maxillary antrum in few cases.
- Sometimes, multiple unerupted and displaced teeth appear to be floating within the cyst-like spaces and the condition is often referred to as **'floating tooth syndrome'**.
- Cortical perforations rarely occur and maxillary lesions often extend to the sinus.
- The radiographic changes in cherubism are often more overwhelming and extensive than the actual clinical swelling produced by the disease.
- Interestingly, lateral skull radiographs often reveal exposure of the posterior part of the hard palate due to forward displacement of the permanent teeth.

Grading system in cherubism

According to Ramon and Engelberg, cherubism lesions can be divided into the following grades depending upon the extent and severity of the disease process.	
Grade I	Cherubism involving ascending ramus of mandible on both sides.
Grade II	Cherubism involving ascending ramus bilaterally along with both maxillary tuberosities.
Grade III	Massive involvement of whole maxilla and mandible except the condylar processes.
Grade IV	Same as grade III with involvement of floor of orbits causing orbital compression.

- Moreover, the radiographic defects in the bone may persist even after the disease had clinically subsided.

HISTOPATHOLOGY

- Microscopic section from the lesion presents a highly cellular and vascular connective tissue stroma, which is often arranged in a "**whorled pattern**".
- Numerous proliferating fibroblasts and variable numbers of **multinucleated giant cells** are also found within the stroma.
- Giant cells are relatively smaller in size and they often aggregate around the thin walled blood capillaries.
- The number of giant cells gets fewer and fewer as there is more and more spontaneous repair of the bony defect.
- A distinctive feature of the disease is the presence of an "**eosinophilic perivascular cuffing**" of collagen fibers, which often surrounds the blood capillaries.
- Varying amounts of metaplastic bony tissues are found within the stroma.
- Within the connective tissue extravassated blood and deposits of hemosiderin pigments are sometimes seen.
- Lymph nodes exhibit reactive hyperplasia, fibrosis and chronic inflammatory cell infiltration.
- In older lesions, the number of giant cells decrease and the connective tissue becomes more fibrous.

LABORATORY INVESTIGATIONS

Serum alkaline phosphates levels are raised during the osteoblastic phase (phase of repair) of the disease.

CT scans can be used to determine the extent to which the disease has involved the jaw.

DIFFERENTIAL DIAGNOSIS

- Fibrous dysplasia of bone
- Hyperparathyroidism
- Caffey's disease
- Central giant cell granuloma
- Aneurysmal bone cyst
- Gorlin-Goltz syndrome.

TREATMENT

No treatment is required since cherubism is a self-limiting disease and with skeletal maturation the disease regresses spontaneously after puberty.

OSTEOGENESIS IMPERFECTA

Osteogenesis imperfecta is a genetically transmitted disease of bone characterized by defective matrix formation and lack of mineralization, which results in an increased bone fragility.

PATHOGENESIS

The disease osteogenesis imperfecta occurs due to failure of the fetal collagen (procollagen) to transform into mature collagen (type I) through cross linking of adjacent molecules at the time of formation of bone. These results in defective bone matrix formation along with failure of bone mineralization, leading to increased fragility of the bone tissue. In osteogenesis imperfecta the bones grow to their normal length but are often thin with lack of usual cortex formation as may be seen in a normal compact bone.

CLINICAL FEATURES (FIG. 15.15)

There are at least four types of osteogenesis imperfecta, two of them are inherited as

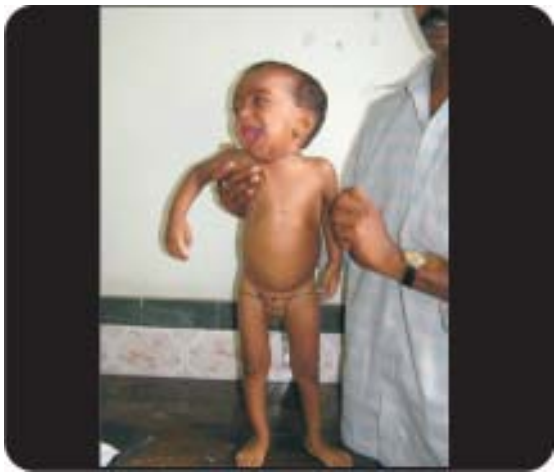

Fig. 15.15: Osteogenesis imperfecta

autosomal recessive trait, while the other two are inherited as autosmal dominant traits.

Interestingly, the recessive variants of the disease are more severe in nature in comparison to the dominant variants.

General clinical manifestations of osteogenesis imperfecta include the following:

- Bowing deformity of the bone with multiple fractures due to increased fragility.
- Blue sclera with defective teeth in the form of 'bulbous crowns, dentinogenesis imperfecta and blue or brown translucency (**opalescent teeth**)'.
- Loss of hearing due to obliteration of the cranial foramen with compression of nerve.
- Hypermobility of the joints.
- Increased incidence of Class-III malocclusion due to maxillary hypoplasia.
- Excessive bruising tendency.

TYPES OF OSTEOGENESIS IMPERFECTA

- Neonatal lethal type
- Severe non-lethal type
- Moderate and deforming type
- Mild and non-deforming type.

Neonatal Lethal Type

This type of osteogenesis imperfacta is the most severe from of the disease (10%) and it is characterized by multiple fractures of bone *in utero* or during parturition and the child seldom survives.

Severe Non-lethal Type

In this from of osteogenesis imperfecta, the disease is not evident until the late childhood and the patient shows fractures of bone with minimum trauma. Sometimes the fractures may occur at birth and the patients often have generalized bony deformity. Although the fractured bone heals up rapidly, considerable skeletal deformity and a dwarfed stature often develop.

Moderate and Deforming Type

Patients in this type are less severely affected then the other two types already mentioned. This type of osteogenesis imperfecta may be associated with dentinogenesis imperfacta (more in relation to deciduous teeth) and blue sclera in about 25 to 50 percent cases.

These patients may also exhibit deafness, defective heart valves, joint dislocations, abnormal muscular conduction, abnormal shape of the skull, etc.

The **sclera appears blue** because it is so thin that the pigmented choroids become visible through it.

Mild Non-deforming Type

This type of the disease occurs in nearly 60 percent cases and the patients are clinically normal, although they have an increased tendency for bone fracture due to trauma. These patients also have blue sclera and the associated dentinogenesis imperfecta in about 25 percent cases.

Oral manifestations of osteogenesis imperfecta

- Large head size.
- Frontal bossing.
- Maxillary hypoplasia.
- Bulbous crowns of teeth with dentinogenesis imperfecta and blue or brown translucence (opalescent teeth).
- Class III malocclusion with anterior and posterior cross bite.
- Severe attrition of deciduous teeth.
- Multiple impacted permanent teeth.
- Excessive bruising tendency.
- Increased incidences of development of osteitis and osteomyelitis following extraction of teeth.

RADIOLOGICAL FEATURES

Radiographically, osteogenesis imperfecta reveals the following features:

- Shortened and deformed extremities with large areas of cyst-like radiolucencies.
- The midshaft areas are narrowed with bulbous metaphyseal–epiphyseal zones.
- Multiple fractures or healed areas of previous fractures are often present in the bone.
- The teeth exhibit features of dentinogenesis imperfecta with bulbous crowns, obliteration of pulp chamber and short roots.
- Radiolucent or mixed 'radiolucent-radiopaque' lesions are found in the mandible with extreme thinning of the cortex.
- '**Warmin bones**' in the skull characterized by multiple small sutural bones in the skull arranged in a mosaic pattern.

HISTOPATHOLOGY

- Severe form of osteogenesis imperfacta histologically reveals thinning of the cortex, which is composed of immature woven bone.
- Bony trabeculae are short, thin, and fragile and they are widely spaced and disorganized.
- Bony tissue displays increased number of osteoblasts with severely reduced bone matrix
- The immature woven bones do not transform into mature lamellar bones.

PATHOGENESIS

The disease develops due to failure of the fetal collagen to transform into mature collage through cross-linking of adjacent molecules. This results in a defective bone matrix formation with increased fragility.

TREATMENT

No treatment is possible to alter the course of the disease. Some improvements in the condition occur automatically after puberty. Care should be taken during extraction of tooth, so that alveolar bone is not fractured.

CLEIDOCRANIAL DYSPLASIA

DEFINITION

Cleidocranial dysplasia is a rare genetic disorder characterized by abnormal growth of the bones in clavicles, skull and the face with a tendency for failure of tooth eruption.

ORIGIN

The disease may be hereditary in nature with autosomal dominant trait or it may occur as a result of spontaneous mutations.

CLINICAL FEATURES

- There may be complete absence or hypoplasia of one or both clavicles with hypermobility of the shoulder joints and it is the most important feature of cleidocranial dysplasia.
- The disease affects both sexes equally.
- Interestingly, the **patient can move their opposing shoulders medially up to the midline** due to partial or complete absence of the clavicles and weakness of the muscles attached to them.
- Frontal and parietal skull plates are elongated (**bossing**), although the other bones of the skull are normal.

Key points of cleidocranial dysplasia

- Cleidocranial dysplasia is a rare genetic disorder characterized by abnormal growth of clavicles, skull and the face with a tendency for failure of tooth eruption.
- Due to abnormal development of clavicles, patient can often move their opposing shoulders medially up to the midline.
- Patients also have short stature, big head, frontal bossing, delayed closure of fontanels, etc.
- Oral manifestations of the disease include hypoplasia of the jaws and multiple impacted or unerupted supernumerary teeth.
- Radiograph reveals partial or complete loss of clavicles, warmin bone in the skull with open fontanels and multiple impacted teeth in the jaw.

- Patients often have short stature, big head, long neck and narrow shoulders, etc.
- Delayed closures of the fontanels, underdeveloped paranasal sinuses, ocular hypertelorism

and photophobia, etc. are the other important features of the disease.

ORAL MANIFESTATIONS

- Entire mid-face is underdeveloped with retrusion maxilla and decreased lower facial height.
- Nose is flat, broad based and lacks the bridge.
- Although, the mandible is of normal size, it appears elongated because of the hypoplastic maxilla.
- High and narrow arched palate is almost always seen with increased incidences of cleft palate.
- In the oral cavity multiple embedded and impacted permanent teeth are often present.
- Large numbers impacted supernumerary teeth are also found in the jaws, which exhibit defective crowns and abnormal root patterns.
- Patients of cleidocranial dysplasia often exhibit multiple retained deciduous teeth with delayed eruption of permanent teeth.
- Roots of the teeth are often thin and short, moreover there may be absence of cellular cementum on the roots.
- Development of partial or complete anodontia may be seen in few cases.
- Cystic lesions (especially dentigerous cysts) may develop in the jaws, mostly in association with the impacted or embedded teeth.
- **Cleidocranial dysostosis** is another condition, which is almost similar to the cleidocranial dysplasia and the only difference between them is the presence of normal clavicles in the former.

RADIOGRAPHIC FEATURES

- Tortuous suture lines in the skull bones (warmin bones) with open fontanels and open sutures.
- Partial or complete loss of clavicles.
- Multiple unerupted and impacted teeth in the jaws, some of which are deciduous and some are supernumerary teeth.
- Roots of the teeth are thin and lack cellular cementum deposition.
- Maxillary sinus is small and rudimentary.
- Ascending ramus of the mandible is narrow.
- There may be hypoplasia of the alveolar process.

HISTOPATHOLOGY

The permanent teeth have no cellular cementum.

DIFFERENTIAL DIAGNOSIS

- Craniofacial dysostosis
- Cleidocranial dysostosis.

TREATMENT

No treatment is possible.

OSTEOPETROSIS (MARBLE BONE DISEASE)

DEFINITION

Osteopetrosis is an uncommon hereditary disorder of bone characterized by abnormal increase in the bone density due to absence of physiologic bone resorption. The disease occurs due to reduced osteoclastic activity in the bone, which results in increased solidification, extremely high density along with increased fragility of the affected bone.

TYPES

- ***Autosomal dominant***—benign type (Adult osteopetrosis).
- ***Autosomal recessive***—malignant type (Infantile osteopetrosis).

PATHOGENESIS

The pathogenesis involves genetic defects characterized by loss of normal balance between bone formation and bone resorption in the skeleton. In this disease the bone deposition by the osteoblast cells is normal, however the bone resorption and remodeling by the osteoclast cells is completely lacking; this often results in the formation of hypermineralized, inelastic, solid bones with profound tendency for fracture. The medullary cavities of bone are obliterated due to uninterrupted bone depositions and the epiphyseal end plates of bone often appear club-shaped. There is also lack of resorption of the calcified cartilages during the endochondral growth.

CLINICAL FEATURES

- In osteopetrosis, the abnormalities in the bone often results in altered sutures, compression of cranial nerves and frequent fractures, etc.
- Decreased bone marrow hemopoetic functions with increased tendency for the development of severe osteomyelitis of the jaws are also common.
- The infants suffering from malignant version of this disease generally have osteopetrosis at birth or in the early childhood and they rarely survive longer.
- Most of the patients develop anemia, thrombocytopenia and leucopenia, etc. which occur due to decreased hemopoiesis because of lack of marrow (as the medullary space is often completely obliterated by abnormal bone deposition).
- Patients often have broad face, hypertelorism and snub nose, etc.
- Loss of function of bone marrow results in compensatory extramedullary hemopoiesis within the liver and spleen, which often results in hepatosplenomegaly.
- Patients often suffer from deafness, blindness, pain and facial paralysis, etc. due to narrowing of the cranial foramina and the resultant compression of nerves.
- Enlarged cranium, frequent bone pain and prominent frontal bossing, etc. are also frequently seen.
- Long bones are often shortened and are extremely fragile.
- Severe cases of osteopetrosis results in breathing and hearing difficulties due to oversized facial bones and mastoid process.
- The teeth often have defective enamel and short roots. Their eruption process can be delayed.
- There can be increased incidence of dental caries and many of the teeth in the dental arch can be ankylosed.
- Increased bone density and fragility may cause frequent fractures of jawbone and subsequent osteomyelitis following tooth extractions, these occur due to decreased blood supply to the bone along with increased susceptibility to infections.
- Decreased bone marrow activity often leads to leucopenia and thrombocytopenia, which can cause spontaneous hematoma formations and multiple infections in the bone (especially odontogenic infections).
- Osteomyelitis frequently develops following tooth extraction.

RADIOLOGY

In osteopetrosis, radiographs often show the classical feature of "**bone within the bone appearance**". It results from increased thickening of the cortex and obliteration of the medullary spaces of bone. Radiographs of the jawbone exhibit increased radiodensity of the bone, which is almost equal to that of the tooth.

The cartilaginous portions of the rib also exhibit an uncharacteristic increase in the opacity.

Cranial bones appear thickened and sinus cavities are reduced in size.

DIFFERENTIAL DIAGNOSIS

- Endosteal hyperostosis
- Van-Buchem disease
- Sclerosteosis

HISTOPATHOLOGY (FIG. 15.16)

Microscopy shows a very dense and sclerotic bone with little compensatory remodeling.

The medullary cavities are small and they contain very little amount of marrow tissue and large amounts of amorphous bone.

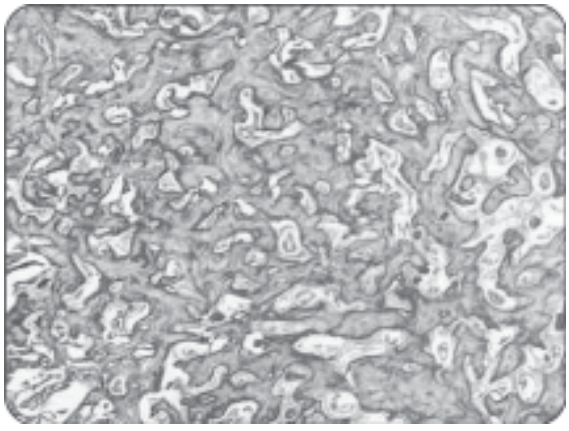

Fig. 15.16: Photomicrograph of osteopetrosis

In the bone marrow, osteoblasts are present in normal numbers, but the osteoclasts are almost absent.

In some cases, normal number of osteoclast cells may be present in the bone, but these cells are not functionally viable.

TREATMENT

No treatment except bone marrow transplantations. Supportive therapies like repeated blood transfusions and antibiotics are essential for the survival of the patient.

PIERRE ROBIN SYNDROME

Pierre Robin syndrome is a hereditary disorder, characterized by the following features:

- Development of mandibular micrognathia, which results in a characteristic "**bird facies**" of the patients.
- 'U' shaped cleft palate and glossoptosis (dropping of the tongue).
- Micrognathia in this disease often leads to the downward and backward displacement of tongue, which often results in breathing trouble.
- Patients often have malocclusion of the teeth in association with multiple missing teeth or sometimes many supernumerary teeth.
- Absence of temporomandibular joint, mongolism, congenital heart defects, hydrocephaly, microcephaly and mental retardation, etc. are the other important features of the disease.
- Difficulty often occurs in terms of feeding and maintenance of airway during infancy.
- Psychological trauma is often associated with this syndrome due to abnormal appearance and speech difficulty.

GARDNER SYNDROME

It is a hereditary disorder characterized by colorectal polyps in association with various other lesions involving the skin, eyes, teeth and the skeletal system, etc.

CLINICAL FEATURES

- Multiple intestinal (colorectal) polyps, multiple osteomas of the skin, paranasal sinuses and jaws (preferably mandible).
- Jaw lesions of osteoma cause facial deformity and difficulty in mouth opening.
- Multiple supernumerary teeth, impacted teeth and odontomas frequently develop in the jaw.
- Patients may have desmoid tumors of the soft tissue and dermoid cysts of the skin.
- Pigmented lesion in the ocular fundus is an important clinical finding of Gardner syndrome.
- The intestinal polyps may undergo malignant transformation and develop invasive adenocarcinomas. Patients also have an increased tendency for developing thyroid cancer.

TREATMENT

Prophylactic colonectomy, surgical removal of osteomas and the dermoid cysts.

MARFAN'S SYNDROME

DEFINITION

Marfan's syndrome is a hereditary disease transmitted or inherited as autosomal dominant trait and is characterized by defective organization of collagen.

CLINICAL FEATURES (FIGS 15.17 AND 15.18)

- The classic clinical finding in this disease is the presence of abnormally long, thin extremities and spidery fingers (Fig. 15.18).
- Patients are usually very tall and slim, and they often have muscle hypotonia.
- The patients often show hyperextensibility of joints, with recurrent habitual dislocations,

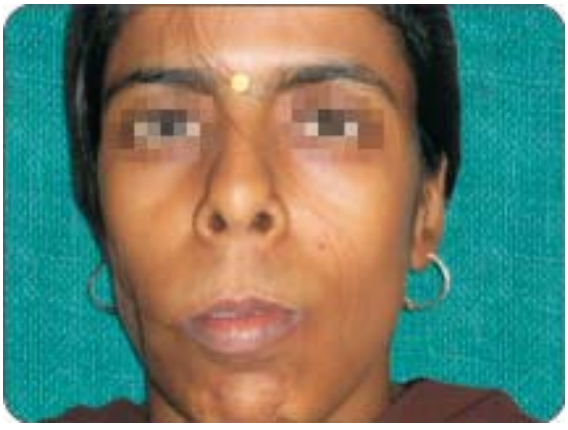

Fig. 15.17: Marfan's syndrome-I

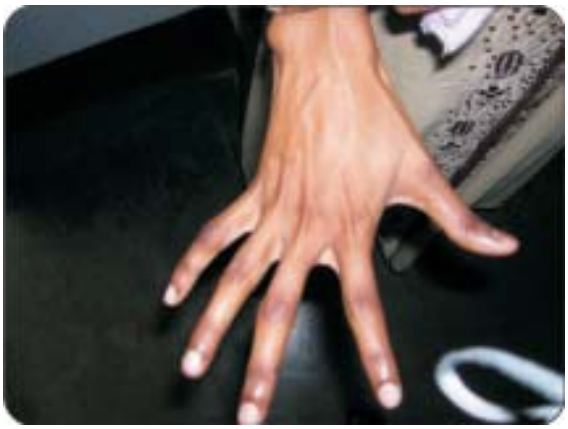

Fig. 15.18: Marfan's syndrome-II

frontal bossing, large external ears and shrunken eyes, etc.

- Many of the patients also develop kyphosis, scoliosis and flat foot, etc.
- Cardiac abnormalities like aortic aneurysm, aortic regurgitation and valvular defects, etc. are also commonly associated with this disease.

ORAL MANIFESTATIONS (FIG. 15.19)

- Patients often have a long and narrow face, bifid uvula, cleft palate and high palatal vault.
- Malocclusion of teeth, temporomandibular joint (TMJ) dysarthrosis.
- Increased chances of development of multicystic lesions in the jawbone.

DIFFERENTIAL DIAGNOSIS

- Sickle cell anemia
- Klinefelter's syndrome
- Homocystinuria.

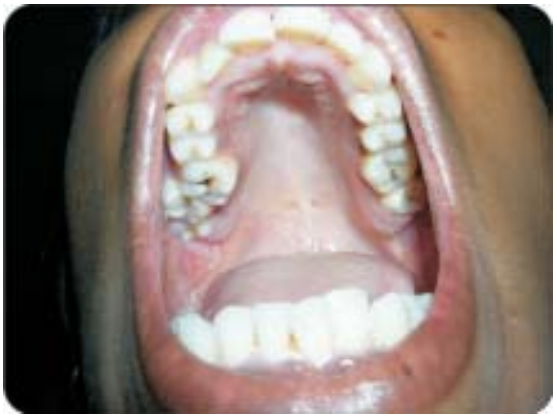

Fig. 15.19: Marfan's syndrome-III

DIAGNOSIS

By determination of upper and lower segment ratio and the metacarpal index.

TREATMENT

No treatment.

DOWN SYNDROME (TRISOMY 21)

Down syndrome is the most common chromosomal abnormality to occur in man. There are many forms of the disease but the most common one is trisomy 21 (about 94%), which is caused by the chromosomal non-disjunction, thereby resulting in an extra chromosome with the chromosome pair of 21.

The down syndrome of trisomy 21 type involves almost all organs of the body and it affects the child more often, if the maternal age is above 45 years.

CLINICAL FEATURES (FIGS 15.20 AND 15.21)

- Patients with Down syndrome present a variety of defects like–short stature, flat face, depressed nasal bridge and small slanting eyes with epicanthral folds (features of **typical mongoloid facies**) (Fig. 15.20).
- Mental retardation, large anterior fontanel, open cranial sutures, small ears and sexual underdevelopment, etc. are often present.

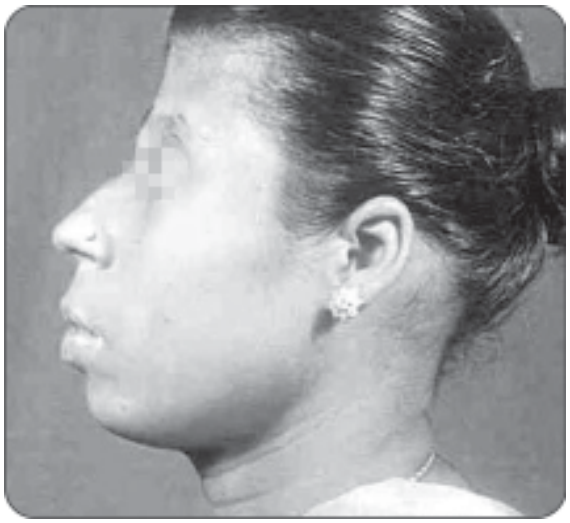

Fig. 15.20: Typical facial profile of Down syndrome

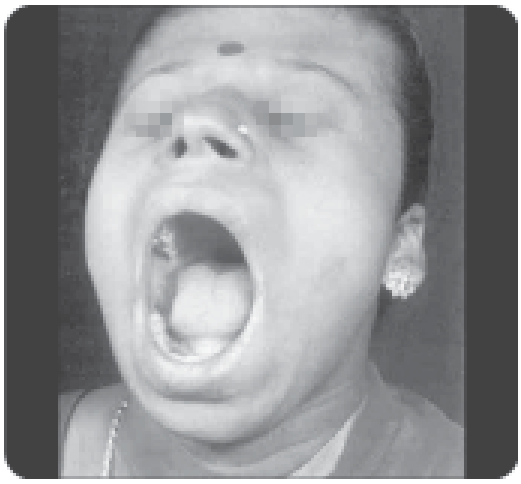

Fig. 15.21: Intraoral picture of Down syndrome showing no remarkable abnormality

Oral manifestations of Down syndrome

- Short head, small and open mouth with protrution of tongue due to macroglossia.
- High-arched palate, hypoplastic maxilla.
- Mandibular prognathism with class III malocclusion, delayed eruption of teeth.
- There may be presence of cleft lip or palate with difficulty in speech.
- Tongue is generally large (macroglossia), it is pebbly and fissured (scrotal tongue).
- Lips are often thick, everted, dry and fissured with presence of angular cheilitis.
- Malocclusion, partial anodontia and microdontia with short roots of teeth.
- Malformed teeth, taurodontism, supernumerary teeth and enamel hypoplasia, etc. are frequently seen.
- Low caries activity.
- These patients may have an increased tendency to develop acute necrotizing ulcerative gingivitis (ANUG) and juvenile periodontitis.
- Gross plaque accumulations.
- Bruxism.
- Poor muscle tone.
- Increased susceptibility to infection.

- Patients often have broad and short hands with small feet and digits, protuberant abdomen and delayed puberty, etc.
- These patients often have heart anomalies (40 percent cases), moreover they come in the higher risk category for development of leukemia and Alzheimer-like dementia in later life.
- The iris shows brushfield spots.

TREATMENT

No treatment is required.

INFANTILE CORTICAL HYPEROSTOSIS (CAFFEY'S DISEASE)

DEFINITION

Caffey's disease is a perplexing anomaly of unknown etiology and it is characterized by an abnormal enlargement of bone in children, along with other systemic complications.

TYPES

Two types—familial and sporadic, the familial type arises usually earlier than the sporadic type and some lesions can be present even at birth.

CLINICAL FEATURES

- Most of the patients are below 6 months of age and in few cases it may even develop in the intrauterine life.
- Patients often exhibit rapidly developing, bilaterally symmetrical mandibular swelling, which disappears in 3 to 12 months. However, the disease should not be confused with cherubism, which also presents bilateral mandibular swelling.
- There may be presence of few deep-seated, tendered, soft tissue swellings.
- The patients are often highly irritable and are unable to take food, and they may also have fever, leukocytosis, raised ESR and elevated serum alkaline phosphatase levels, etc.
- Dysphagia, pseudoparalysis, anemia and leukocytosis often occur.
- Soft tissue swellings usually develop in those areas of the body from where hyperostosis of the bone occurs in future.

Oral manifestations

- Frequent mandibular bone involvement with deformity and facial swelling.
- Soft tissue or muscle swelling of the face.
- Difficulty in swallowing.
- Refusal of food by the child.
- Malocclusion of teeth.

RADIOGRAPHIC FEATURES

Radiographically, the disease exhibits abnormal thickening of mandibular cortical bone and bulging of its lower border due to subperiosteal new bone formation. The sub-periosteal new bone formation with cortical thickening is often known as **periosteal cloaking.**

HISTOPATHOLOGY

Microscopy reveals edema and thickening of the periosteum, with apposition of many thin bony trabeculae parallel to one another.

DIFFERENTIAL DIAGNOSIS

- Osteomyelitis
- Osteoma
- Abnormally healed fractured bone
- Cherubism
- Osteopetrosis.

TREATMENT

No surgical intervention is required and prognosis is good. Steroids may be given to eliminate the symptoms.

MANDIBULOFACIAL DYSOSTOSIS (TREACHER-COLLINS SYNDROME)

Mandibulofacial dysostosis is rare hereditary or familial disease characterized by defects in the structures derived from 1st and 2nd branchial arches. The disease often shows multiple closely related defects of the head and face area.

CLINICAL FEATURES

Malformation of the external ear (distorted pinna) with absence of external auditory canal, there is occasional deformity in the middle and internal ear.

Antimongoloid palpebral fissures with coloboma of the outer portion of the lower eye lids.

Marked hypoplasia of the mandibular body and zygoma with narrow face and depressed cheek.

All these facial changes give the patient a typical **"bird-face"** or **"fish-face"** like appearance.

Patients often have a down turned mouth with presence of lateral facial clefts.

Important oral manifestations of this disease include crowding and malocclusion of teeth, high arched palate and occasional clefts, etc.

Atypical hair growth in the form of 'tongue shaped" hairline.

Parotid hypoplasia.

Narrowing of larynx and trachea combined with mandibular hypoplasia often causes respiratory and speech difficulties in children.

RADIOGRAPHIC CHANGES

Radiographs reveal partial or complete agenesis of mandible and malar bones with small paranasal sinuses.

TREATMENT

No treatment is required.

ACHONDROPLASIA

DEFINITION

Achondroplasia is the hereditary defect of endochondral ossification.

CLINICAL FEATURES

- Patients with achondroplasia often exhibit dwarfism, short and muscular extremities, bowed legs and large head, etc.
- The limbs are extremely short in relation to the trunk and head. Dwarfism in achondroplasia occurs due to failure of normal cartilage proliferation at the epiphysis, which results in failure of longitudinal growth of the long bones.
- The short-limbed dwarfs of achondroplasia traditionally become circus clowns.
- The insufficient growth at the base of the skull causes retrusive mid-face development with a concave profile.
- Oral manifestations of this disease include short maxilla, depressed nasal bridge, relative mandibular prognathism and malocclusion, etc.

RADIOLOGICAL FINDING

Radiographs reveal long bones, which are shorter than normal with thickening of the ends. Maxillary retrusion is also seen.

Typical radiological features of some bony lesions

• Paget's disease of bone	Cotton-wool appearance.
• Fibrous dysplasia of bone	'Ground glass' appearance.
• Ameloblastoma	'Soap bubble' or 'honey comb' appearance.
• Cherubism	Multiple cyst-like radiolucency often occurs in mandible bilaterally.
• Osteogenesis imperfecta	Deformity of bone, narrow mid shaft and bulbous metaphyseal and epiphyseal ends and multiple fractures.
• Osteopetrosis	'Bone within the bone' appearance.
• Infantile cortical hyperostosis	Abnormal thickening of mandibular bony cortex with bulging of the lower border.
• Osteosarcoma	Sun-ray or sun-burst appearance.
• Myxoma	Tennis racket appearance.
• Multiple myeloma	Multiple 'punched-out' radiolucency.
• Carcinoma	'Moth-eaten' appearance.
• Carcinoma of maxillary antrum	'Clouding' of the antrum.
• Pindborg's tumor	'Driven-snow' appearance.
• Thalassemia	'Hair on end' or 'crew cut' appearance of skull bone.
• Garre's osteomyelitis	'Onion skin' appearance and 'duplication of cortex' of bone.
• Cleidocranial dysplasia	'Warmin bone' and multiple unerupted or impacted teeth.
• Dentigerous cyst	Well-defined unilocular radiolucency enclosing the crown of an impacted tooth.
• Radicular cyst	Well-defined radiolucency at the root apex of a non-vital tooth.
• Nasopalatine duct cyst	A 'heart shaped' radiolucency in the anterior palate.
• Globulomaxillary cyst	'Inverted pear' shaped radiolucency.
• Hyperparathyroidism	Multiple cyst-like radiolucency of bone, 'salt and pepper' effect on lateral skull radiograph.
• Osteoarthritis of TM joints	Osteophytic lipping and occasional 'Ely's cyst'.
• Peripheral giant cell granuloma	'Peripheral cuffing' of bone.
• Central giant cell granuloma	'Soap-bubble' type multilocular or 'drop- shaped' unilocular radiolucency.
• Compound odontome	Multiple miniature tooth-like structures projecting from a single focus.
• Cementoblastoma	A large radiopaque mass associated with a tooth root surrounded by a thin zone of radiolucency.

HISTOPATHOLOGY

Microscopically, the affected bone reveals retardation of endochondral growth and non-replacement of the cartilage by the normal bone.

TREATMENT

No treatment is possible. Malocclusion can be corrected with orthodontic treatment.

MASSIVE OSTEOLYSIS (VANISHING BONE DISEASE)

DEFINITION

It is an uncommon and unusual disease characterized by sudden, spontaneous and massive resorption of bones leading to their complete disappearance and subsequent replacement by fibrous tissue.

CLINICAL FEATURES

Age: Teen age and young adults.

Sex: Commonly affected bones by the disease are clavicle, scapula, humerus, ribs and sacrum, etc.

Among the jawbones, mandible is more frequently affected than maxilla.

- The disease is spontaneous and asymptomatic, and it progresses rapidly.

  Some patients have past history of trauma in the bone of the affected area.
- Sometimes, there may be pain in the jawbone and mobility of teeth, in the absence of any underlying cause.
- Pathological fractures occur following minor trauma, as the bone is severally weekend by the disease.
- Among the jawbones, mandible is frequently affected.
- Involvement of the jaw bones leads to pain, displacement of teeth and facial asymmetry. Besides pathological fracture, sometimes the entire jaw can be destroyed.

RADIOGRAPHIC FEATURES

Initially the disease produces small, localized, and ill-defined osteoporotic foci in the bone, which coalesce to form massive zones of osteolysis. The borders of the lesion are ill-defined and non-corticated. Moreover there is no signs reossification in the osteolytic areas of bone.

HISTOPATHOLOGY

- In the earlier stages of the disease normal bony trabaculae exhibit foci of resorption.
- Bone is completely resorbed within a short span of time and is replaced by a fibrovascular connective tissue with some evidence of chronic inflammatory cell infiltration.
- The fibrous tissue replacing the bone contains many thin walled, dialated vascular spaces.

DIFFERENTIAL DIAGNOSIS

- Hyperparathyroidism
- Cherubism
- Histiocytosis–X
- Malignancy (predominantly metastatic)
- Osteolytic phase of osteosarcoma.

TREATMENT

Radiation therapy may prevent the progression of the disease, otherwise there is no successful treatment.

Typical radiological features features of some any lesion.

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CHAPTER 16

Diseases of Temporomandibular Joint

DEVELOPMENTAL DISORDERS

HYPOPLASIA OF THE MANDIBULAR CONDYLE

Condylar hypoplasia is characterized by reduction in the size of condylar process.

ETIOLOGY

- Heredity
- Birth injury
- Infections to the adjoining structures
- Developmental anomalies, e.g. Treacher Collin's syndrome, hemifacial microstomia, etc.

CLINICAL FEATURES

- Underdevelopment of ramus.
- Deviation of mandible to the affected side during mouth opening.
- Antigonial notch is deeper on the involved side.
- Midline shift of dentition towards the affected side.
- Masticatory insufficiency
- Cosmetically poor appearance of the face

TREATMENT

Genioplasty or osteotomy.

HYPERPLASIA OF THE MANDIBULAR CONDYLE

Condylar hyperplasia is a rare defect, which is often characterized by a unilateral enlargement of the mandibular condyle with facial asymmetry.

ETIOLOGY

The condition develops probably due to some localized proliferative reactions in the jawbone, which are as follows:

- Osteomyelitis
- Middle ear infection
- Infection in the infratemporal fossa
- Overactivity of the condylar cartilage
- Gigantism
- Acromegaly
- Paget's disease, etc.

CLINICAL FEATURES

The clinical features of condylar hyperplasia include deviation of chin to the opposite side during mouth opening, cross bite, excessive vertical lengthening of the ramus and occasional pain in the TMJ, etc.

DIFFERENTIAL DIAGNOSIS

Osteochondroma.

TREATMENT

The condition is treated by surgical recontouring of the condyle.

TRAUMATIC DISORDERS

LUXATION AND SUBLUXATION

Luxation or dislocation of TMJ occurs when the head of the condyle moves anteriorly over the articular eminence into such a position from where it cannot return back to its original position by itself.

When the condyle is completely dislocated, it is called **luxation**, while the partial dislocation of the same is called **subluxation**.

ETIOLOGY

Luxation or subluxation occurs mostly due to:

- Trauma to the TMJ.
- Wide mouth opening for an extended period of time (e.g. dental procedures, etc.).

CLINICAL FEATURES

The patients usually complain of "sudden locking" of the jaw with inability to close the mouth. In the initial phases, the problem happens rarely, but later on, patients may have such situation quite frequently, thereby, making eating and talking very difficult.

TREATMENT

In case of luxation or subluxation, the dislocated condyle is to be guided into its normal position by giving inferior and posterior pressure while holding the mandible firmly in the molar region.

Patients should be advised not to open the mouth too widely. In recurrent cases, flattening of the articular eminence is done.

ANKYLOSIS OF TEMPOROMANDIBULAR JOINT

Ankylosis of the TMJ is characterized by lack of movement of the condylar head within the glenoid fossa, due to fusion of the opposing components of the joint with obliteration of the joint space. It results in the limitation of mouth opening.

ETIOLOGY

A large number of factors can cause the development of TMJ ankylosis and important among them are as follows:

CLINICAL FEATURES

Age: Ankylosis usually occurs in children below the age of 10 years.

Sex: Both sexes are almost equally affected.

TYPES OF ANKYLOSIS

False ankylosis: False ankylosis is extra-articular and it occurs due to fibrous or bony union

Etiology of ankylosis of TMJ

Trauma	• Birth injury due to forceps delivery. • Intracapsular fracture with bleeding. • Accidental trauma to the mandible that pushes the head of the condyle into the glenoid fossa. • Lack of early mobilization after TMJ fracture. • Malunion of the condylar fractures. • Radiotherapy to the TMJ.
Infections	• Otitis media. • Mastoiditis. • Congenital syphilis. • Osteomyelitis. • Pyogenic arthritis of TMJ from hematogenous infections.
Systemic juvenile arthritis	• Psoriatic arthritis. • Osteoarthritis. • Rheumatoid arthritis.
Neoplasms	• Chondroma. • Osteochondroma. • Osteoma. • Metastatic tumors.
Miscellaneous	• Congenital developmental defect in the joint. • Synovial chondromatosis.

between the coronoid process and maxilla or zygoma. Here the joint itself is not deformed or damaged.

True ankylosis: True ankylosis is intra-articular and it is again of two types:

True bony ankylosis: When the TMJ space is completely obliterated by the deposition of bone following destruction and subsequent fusion of temporal fossa, meniscus and head of the condyle, the condition is called a true bony ankylosis and in such cases complete loss of mouth opening results.

True fibrous ankylosis: Intra-articular fibrous ankylosis occurs, if the TMJ space is obliterated by the deposition of a fibrous tissue mass (e.g. scar). In such cases, limited degrees of mouth opening are possible. Fibrous ankylosis occurs due to hemorrhage in the joint space due to trauma with subsequent fibrosis (hemarthosis).

PRESENTATION

- Mostly seen in young people and both sexes are equally affected.
- Difficulty in mouth opening is the chief complain in TMJ ankylosis, patients can open the mouth partly in case of fibrous ankylosis, but in case of bony ankylosis complete lack of mouth opening is seen (Fig. 16.1).
- Microstomia with severe malocclusion (Fig. 16.2).
- Difficulty in taking food and difficulty in speech.

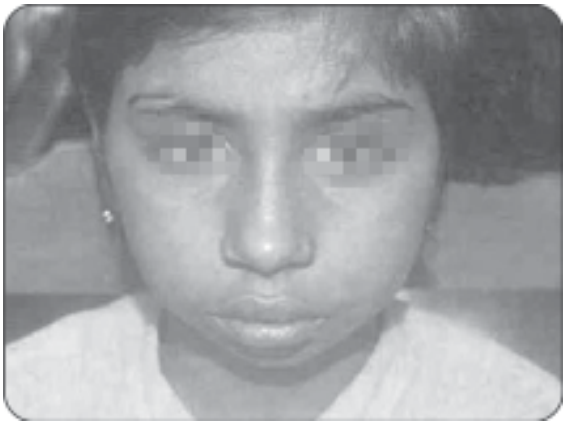

Fig. 16.2: Ankylosis of TM joint causing microstomia

- Maximum numbers of ankylosis cases are of unilateral type, patients exhibit displacement of chin (backwards and laterally) towards the involved side on attempted mouth opening.
- Ankylosis causes retrusion of mandible with increased over jet of teeth.
- Bilateral ankylosis in the younger age causes microstomia and receding chin.
- Occasionally, the patient may complain of pain and tenderness in the TMJ area.

RADIOLOGICAL FEATURES

In case of bony ankylosis, radiograph shows the loss of normal architecture of TMJ and obliteration of the joint space due to deposition of bone. In case of false ankylosis the TMJ appears normal (Fig. 16.3).

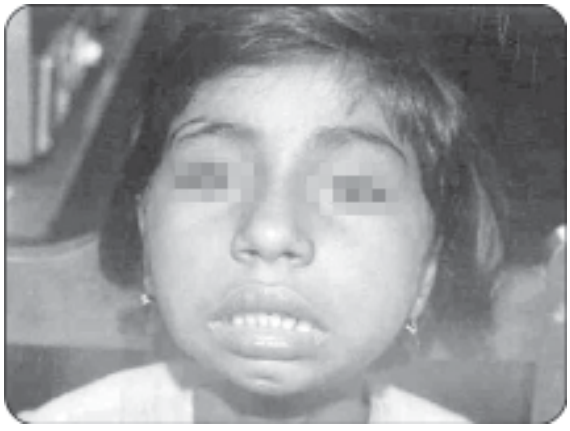

Fig. 16.1: Ankylosis of TM joint with complete lack of mouth opening

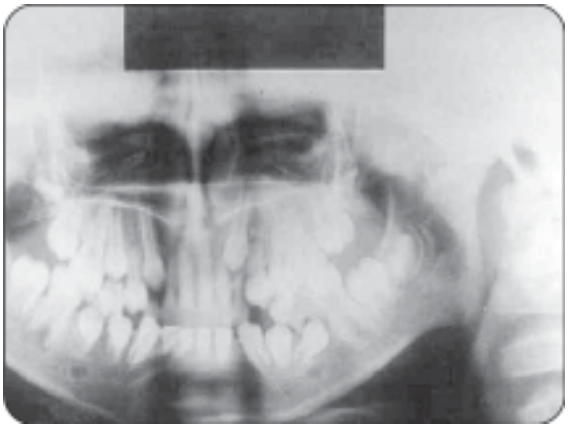

Fig. 16.3: Ankylosis of TM joint showing obliteration of the joint space

HISTOPATHOLOGY

Microscopically the ankylosed joint shows destruction of the component parts of TMJ, e.g. head of the condyle, meniscus and the fossa, etc. The joint space is completely filled up with either fibrous tissue or by bone.

TREATMENT

TMJ ankylosis is treated by surgical correction of the joint (arthroplasty). Moreover to eliminate further possibility of ankylosis or recurrence, a gap is constantly maintained between the head of the condyle and the glenoid fossa, by placing some non-absorbing material, e.g. tendon sheath, in the joint space. This procedure is known as "gap arthroplasty".

Costochondral grafting is done sometimes in young patients to facilitate the growth of mandible.

INFLAMMATORY DISORDERS

ANKYLOSING SPONDYLITIS

Ankylosing spondylitis is a chronic inflammatory disease of the connective tissue, which primarily affects the axial skeleton and the central joints including the TMJ.

ETIOLOGY

- Exactly not known.
- Trauma and rheumatoid arthritis could cause this disease.

CLINICAL FEATURES

- Stiffness resulting from immobility of the joint during sleep.
- Stiffness is relieved by heat and exercise. It is more common in men and there may be some facial asymmetry.

RADIOGRAPHIC FEATURES

Flattening of the condyle with presence of osteophytes, bony erosion and sclerosis.

TREATMENT

Intra-articular injections of corticosteroids.

OSTEOARTHRITIS

Osteoarthritis is a degenerative and destructive disease of the weight-bearing joints, although TMJ is not a weight-bearing joint, osteoarthritis can still occur in it due to the ageing process or trauma.

CLINICAL FEATURES

Clinically, osteoarthritis presents the following features:

- Clicking sounds in the joint while opening and closing movements of the jaw.
- Limitation of movements of the joint.
- Sometimes there may be deep ache or pain in the joint.
- Muscles of mastication are often tendered due to strain caused by non-use or restricted use of the painful joint.

RADIOGRAPHIC FEATURES

Radiograph shows "**osteophytic lipping**" or protruberance on the articular disc with flattening of the articular surfaces of the joint.

In few cases, subarticular radiolucent areas (Ely's cysts) can be seen.

Narrowing of the joint space due to abnormal ossifications.

OTHER INVESTIGATIONS

- CT scanning
- Arthroscopy
- MRI.

HISTOPATHOLOGY

- Osteoarthritis histologically shows **vertical and horizontal cracks on the articular cartilage**. In more chronic cases these cracks may even extend up to the underlying bone.
- The cartilage also becomes less elastic with decrease in the number of chondrocytes.
- Degeneration of chondrocytes, localized destruction of cartilage and eubernation of bone, etc. are also seen.
- Large degenerating spaces or sub-chondral cysts may develop beneath the articular cartilage.

- In few cases, localized areas of repair produce multiple elevations on the disk surface and the condition is known as **"lipping"**.
- The bone beneath the joint cartilage shows reduced osteoblastic or osteoclastic activity with fatty degeneration of the marrow.

TREATMENT

There is no satisfactory treatment for osteoarthritis, however condylectomy should be considered in very severe cases.

RHEUMATOID ARTHRITIS

Rheumatoid arthritis is a systemic disease that usually affects many joints including the TMJ and the disease is characterized by progressive inflammatory destruction of the joint structures.

ETIOLOGY

Detection of increased serum IgG, rheumatoid factor and antinuclear antibodies, etc. indicate that an "autoimmune mechanism" probably initiates the disease. The autoimmune reaction brings about inflammatory change in the synovial membrane of the joint with subsequent fibroblastic proliferations. The inflammatory process also generates collagenese and other enzymes, which cause destruction of the joint cartilage and the underlying bone.

CLINICAL FEATURES

- The disease usually occurs in the third and forth decade of life and females are more commonly affected.
- During the acute phase of the disease, patient may suffer from fever, malaise, fatiguability, weight loss, anemia and raised ESR, etc.
- The TMJ is involved mostly bilaterally along with other joints.
- It becomes swollen, tendered and stiff.
- The **maximum feeling of stiffness is experienced in the early mornings** and it diminishes gradually as the day progresses.
- There may be occasional presence of pain, crepitations and tenderness in the joint, resulting in restricted jaw movements.
- Clicking sounds in the joint may develop in chronic cases, where structural alterations have taken place in the meniscus and the articular cartilage.
- There may be presence of salivary gland swelling and dryness of mouth.
- On rare occasions, rheumatoid arthritis patients may develop secondary Sjogren's syndrome.
- In cases of rheumatoid arthritis in children (Still's disease), restricted jaw movements may cause mandibular underdevelopment with concomitant occurrence of class II division I malocclusion.
- Ankylosis of the TMJ may develop on rare occasions due to rheumatoid arthritis.

RADIOLOGY

Radiograph shows irregularity of the condylar as well as the articular surfaces, with flattening of condyle and widening of TMJ space.

HISTOPATHOLOGY

- Microscopy reveals edema, exudation and other inflammatory changes within the synovial membrane of the joint.
- The articular surface is ultimately destroyed and is replaced by the granulation tissue.
- Chronic inflammatory cell infiltration by lymphocytes, macrophages and neutrophils is often seen in the damaged tissue of the joint.
- There can be development of fibrous or even bony ankylosis of the joint in some cases.

TREATMENT

Systemic steroid therapy and antibiotics.

ACUTE TRAUMATIC ARTHRITIS

Acute traumatic arthritis occurs due to trauma to the mandible, which results in inflammatory changes within the TM joint space. It may also occur due to hemarthrosis, in case blood vessel is torn inside the joint.

CLINICAL FEATURES

- Pain and tenderness in the joint.
- Inability to close the mouth completely.
- Pain increases while opening and closing the mouth.

TREATMENT

Giving adequate rest to the joint and application of heat. Mobilization of the joint after ten days.

MYOFACIAL PAIN DYSFUNCTION (MPD) SYNDROME

Myofacial pain dysfunction syndrome is a disease complex that disturbs the entire masticatory apparatus and is characterized by pain and limitation of movement of the TMJ.

ETIOLOGY

- The disease occurs due to defective neuromascular coordinations coupled with emotional stress, which eventually results in masticatory muscle spasm and fatigue.
- The condition is further aggravated by occlusal disharmonies like defective restoration, lack of posterior occlusion due to loss of molar teeth and faulty dentures, etc.
- Habitual grinding of teeth (bruxism) can also initiate the disease.
- Anxiety, stress and personality disorders can play a major role in the initiation of the disease.
- Minor injury to the TMJ caused by violent yawning, laughing and strenous dental treatment of long durations.

CLINICAL FEATURES

- More than 80 percent of the patients are females and they are usually aged between 20 and 30 years.
- The pain in this disease is dull in nature and it is usually present unilaterally in the preauricular area or in the ear.
- In many cases, the pain radiates to the angle of mandible or temporal region.
- The intensity of pain varies at different times of the day.

LABORATORY INVESTIGATIONS

- Complete blood count (CBC) to rule out any systemic infection.
- ESR, Rheumatoid factor (RF) and Antinuclear antibody (ANA) are done to rule out possible diagnosis of rheumatoid arthritis.
- Serum uric acid should be checked to rule out the underlying disease 'gout'

DIFFERENTIAL DIAGNOSIS

- Referred pain from the nearby teeth.
- Organic disease in the TMJ, e.g. inflammation with fluid accumulation in the joint space.
- Trigeminal or glossopharyngeal neuralgia.
- Migraine.

TREATMENT

The disease is self-limiting and does not progress to any permanent disability or damage. Conservative treatment is often done by administering analgesics, muscle relaxants and tranquilizers, etc. Besides this, correction of occlusal disharmonies, psychological counseling and warm compress, etc. are also done.

NEOPLASIA OF TEMPORO-MANDIBULAR JOINT

Both benign and malignant neoplasms can develop from the TMJ, but their incidence is usually rare.

Clinically four positive features and two negative features of MPD

Positive features	*Negative features*
• Pain in the TMJ and adjacent areas. • Muscle tenderness. • Limitation of movements and deviation of the jaw. • Clicking sounds in the TMJ during opening and closing of the mouth.	• Absence of any clinical, radiological and biochemical evidence of organic change in the joint. • Absence of tenderness in the joint, when palpated through the external auditory meatus.

Common neoplasms of TMJ	
Benign neoplasms	*Malignant neoplasms*
• Osteochondroma • Osteoma • Chondroma • Fibromyxoma • Giant cell lesions • Chondromatosis	• Chondrosarcoma • Primary intrinsic malignant neoplasms • Synovial sarcoma • Fibrosarcoma

SITE OF ORIGIN

Neoplasms of TMJ can occur from any structural components of the joint like head of condyle, articular fossa, disc or the capsule, etc.

CLINICAL FEATURES

Neoplasms of TMJ can cause the following problems:

- TMJ dysfunctions
- Facial asymmetry
- Malocclusion
- Prognathic deviation of mandible to the opposite side.
- Pain and swelling.

TOMOGRAPHY

Malignant neoplasms can cause destruction of the joint structures, which could be easily detected by tomography.

TREATMENT

It depends upon the specific nature of the lesion.

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CHAPTER 17

Oral Aspects of Hematological Disorders

PERNICIOUS ANEMIA

DEFINITION

Pernicious anemia refers to the anemia characterized by impaired RBC maturation secondary to insufficient vitamin B_{12} due to defective intrinsic factor required for its absorption through intestinal wall.

Pernicious anemia is a type of chronic, progressive, megaloblastic anemia of adults and is caused by deficiency of an intrinsic factor in the stomach.

Vitamin B_{12} and folic acid act as essential co-factors for the maturation of RBC within the bone marrow. Although folic acid deficiency can be ameliorated by dietary supplements, the **vitamin B_{12} deficiency cannot be rectified in pernicious anemia by dietary supplements**, as there is lack of a transport protein (**intrinsic factor)** in the intestine which is essential for its absorption.

CLINICAL FEATURES

There are four major cardinal features of pernicious anemia:

A. Abnormally large red blood cells.
B. Hypochlorhydria.
C. Neurologic and gastrointestinal symptoms.
D. A fatal outcome, unless the patient receives lifelong injections of vitamin B_{12}.

CLINICAL PRESENTATION

- Generalized weakness, fatigue, palpitations, nausea, vomiting, anorexia, diarrhea, dyspnea, headache, feeling of faint and weight loss, etc.
- The above mentioned features develop due to reduced oxygen carrying capacity of blood.
- Patients often have a smooth, dry and yellow skin.
- Neurological manifestations include tingling sensations in the hands and feet, paresthesia and numbness of the extremities due to peripheral nerve degeneration.
- Stiffness, difficulty in movement, depression and irritability, etc. are also common.
- Diminished vibratory and positional sense.

ORAL MANIFESTATION

- Glossitis, glossodynia (painful tongue), loss of taste sensation and glossopyrosis (itching and burning tongue), etc. are the hallmark features of pernicious anemia.
- Tongue lesions may develop even before the fall of blood hemoglobin level.
- The **tongue often appears "beefy red" in color** with areas of patchy ulcerations on the dorsum and lateral borders.
- Sometimes, atrophy and inflammation of the filiform papillae produces a "**bald**" appearance of the tongue and the condition is often known as **'Hunter's glossitis'**.
- Initially, the tongue is fissured or lobulated and it eventually becomes smooth, flabby and atrophic.
- Burning sensations may also develop in the lips, buccal mucosa and other mucosal sites.
- Few patients have inflammation and macular lesions in the entire oral mucosa, which cause burning sensation, dysphagia and difficulty in denture wearing.
- Focal areas of atrophy, erythema and sometimes hyperpigmentation may occur in the oral mucosa.
- There may be pallor in the oral mucosa with purpuric spots and occasional aphthous-like ulcerations.
- There is increased susceptibility to oral infections in pernicious anemia.

HISTOPATHOLOGY

- Histologically oral epithelial cells in pernicious anemia reveal enlarged, hyperchromatic nuclei with prominent nucleoli and serrated nuclear membranes.
- Often there is marked atrophy of the epithelium with loss of rete pegs and intra or subepithelial chronic inflammatory cell infiltration.
- Cellular atypia is sometimes present with increased nuclear-cytoplasmic ratio and prominent nucleoli.

DIAGNOSTIC ASSESSMENT

- Total RBC count is reduced to less than 3 million per mm^3 of blood, elevated mean cell volume (MCV) and mean cell hemoglobin concentration (MCHC).
- Decreased WBC count and mean cell hemoglobin (MCH).
- If MCV is less than 96 fl (RBC is large), it frequently indicates pernicious anemia.
- Peripheral blood smear shows oval, macrocytic and hyperchromic red blood cells.
- Bone marrow contains large number of megaloblasts.
- Unconjugated bilirubin is elevated due to increased hemolysis.
- Serum lactate dehydrogenase (an enzyme liberated from damaged tissue) level is extremely high.
- **Schilling's test** detects the absence of intrinsic factor in the stomach.
- Gastric secretion analysis reveals the presence of higher level of free hydrochloric acid.

TREATMENT

Intramuscular injections of vit B_{12}.

IRON DEFICIENCY ANEMIA

Iron deficiency anemia is a chronic, microcytic, hypochromic type of anemia, which occurs either due to inadequate absorption or excessive loss of iron from the body.

It is the most common form of anemia and the erythrocytes besides being hypochromic and microcytic, are also severely decreased in number.

CAUSES

- Inadequate absorption of iron in the body.
- Excessive loss of blood.
- Increased demand for RBC.
- Decrease intake of iron in the body.

CLINICAL MANIFESTATION

- Fatigue, easy tiring, lightheadedness and lack of energy.
- Plapitations, dizziness and sensitivity to cold.
- Lemon-tinted palor of the skin and generalized weakness.
- Koilonychia (spoon-shaped finger nails) is an important feature in iron deficiency anemia and the patients often exhibit increased brittleness and cracking of the finger nails.
- Splitting of hair is also commonly seen.

ORAL MANIFESTATION

- Pallor of the oral mucosa and gingiva with atrophy and loss of keratinization (atrophic mucositis).
- In some patients, atrophic mucositis in the aerodigestive tract or oropharynx may predispose to the occurence of squamous cell carcinoma.
- Atrophic glossitis with patchy or diffuse loss or flattening of tongue papillae and glossodynia (painful tongue), etc.
- The tongue appears smooth, bald and red with a glazed appearance, it may be tendered and have burning sensations (glossopyrosis).
- Dysphagia (difficulty in swallowing), recurrent aphthous ulcer and candidiasis of the oral mucosa.
- Abnormal bleeding from the ulcers, faulty wound healing and angular cheilitis are common.
- **Angular cheilitis** is often caused by candida albicans and it presents reddening, cracking, fissuring and discomfort in the angle of the mouth or commissural region.
- A manifestation of Iron deficiency anemia is **Plummer-Vinson syndrome** which presents a triad of symptoms comprising of dysphagia, stomatitis (inflammation of the oral mucosa) and atrophic glossitis.

- This syndrome primarily affects the middle-aged woman and these patients are susceptible to oral cancers and pre-cancers.

DIFFERENTIAL DIAGNOSIS

- Atrophic candidiasis
- Hypothyroidism
- Other anemias
- Chronic depression
- Allergic conditions.

DIAGNOSTIC ASSESSMENT

- Peripheral blood smear shows small (microcytic) and pale (hypochromic) red blood cells.
- Hemoglobin level is decreased to as low as 3.6 g/100 ml.
- Total RBC count is dropped moderately but rarely it goes to below 3 million per mm^3.
- Estimation of serum ferritin is also useful.
- MCV, MCH and mean cell hemoglobin concentration (MCHC)—all are reduced.
- Serum iron level is decreased to 10 mg (normal 50–150 mg).
- Hemosiderin is completely absent from the bone marrow.
- If GI tract bleeding is the suspected cause of iron deficiency anemia, then the following additional investigations are to be done.
  - X-rays (GI tract series)
  - Stool examination for occult blood
  - Esophagoscopy, gastroscopy and sigmoidoscopy, etc.

HISTOPATHOLOGY

Tongue shows atrophy of the covering epithelium with loss of papillae.

Leukocytic infiltrations in the spinus cell layer as well as in the underlying connective tissue.

TREATMENT

300 mg ferrous sulfate tablet, 3 to 4 tablets per day for 6 months.

APLASTIC ANEMIA

Aplastic anemia is a rare life threatening hemorrhagic disease characterized by general lack of bone marrow activity, that results in decreased formation of RBC, WBC and platelet cells.

Decreased production of RBC is anemia, decreased production of WBC is leucopenia and decreased production of platelets is thrombocytopenia, whereas severe depletion of all cell types of blood is often known as **pancytopenia** which often develops in dysplastic anemia. In aplastic anemia, the bone marrow shows lack of maturation of the hemopoietic stem cells.

ETIOLOGY

The exact etiology of aplastic anemia is not known, probably it is an autoimmune disorder. There are some other crucial factors which can trigger the disease:

- Hereditary factor; e.g. Fanconi's syndrome and dyskeratosis congenita.
- Drugs and chemicals such as:
  - Chloramphenicol
  - Phenyl butazone
  - Sulphonamides
  - DDT, benzene, etc.
- Radiation
- Infections–tuberculosis, viral hepatitis
- Idiopathic.

CLINICAL MANIFESTATIONS

The systemic and oral manifestations of Aplastic anemia are almost similar to leukemia (in terms of anemic severity, bleeding tendency and susceptibility to infections).

- It is more common in young adults and elderly individuals.
- Weakness, lightheadedness with dyspnea and fatigue due to slight physical exertion.
- Marked pallor of the skin and petechiae.
- Frequent episodes of epistaxis and bruises.
- Numbness and tingling of the extremities.
- Generalized edema of the body and tachycardia.
- Fever and severe infections often occurs due to neutropenia.
- Severe and fatal hemorrhages.

ORAL MANIFESTATIONS

- Petechiae, ecchymoses, purpuric spots and frank hematoma formations in the oral cavity.
- Spontaneous gingival bleeding, occasional uncontrolled hemorrhage and epistaxis, etc. frequently occur due to platelet deficiency.

- Extreme pallor of the oral mucous membrane.
- Multiple areas of ulcerations in the oral mucosa, gingiva and pharynx. Periphery of the ulcer shows minimal erythema.
- Persistent oral infections including candidiasis.
- Gingival hyperplasia is also sometimes associated with aplastic anemia.
- Fulminating conditions like bacteremia and septicemia, etc. may develop from simple oral infections.

HISTOPATHOLOGY

Histologically oral mucosa exhibits accumulation of numerous microorganisms with extreme lack of inflammatory cell infiltration in the connective tissue.

DIAGNOSTIC ASSESSMENT

- RBC count is usually below 1 million/mm^3.
- WBC count may be as low as 2000/mm^3.
- Platelet count may fall below 20000/mm^3.
- Bone marrow is fatty and contains only few developing blood cells.
- Bleeding time prolonged but clotting time is normal.

TREATMENT

Blood transfusion, antibiotics, splenectomy and bone marrow transplant, etc. Approximately, 50 percent patients die within 6 months after detection of the disease due to severe infections and hemorrhage.

HEMOLYTIC ANEMIA

DEFINITION

Anemia occurring due to increased hemolysis in the body, which the bone marrow can not compensate even by increasing the production of RBCs.

In case of recurrent hemolysis, a compensatory erythroid hyperplasia of the bone marrow occurs, which enhances the rate of erythropoiesis or the production of RBC. However, when due to some reason, the renewed rate of erythropoiesis is also unable to compensate for the increased hemolysis, anemia develops, which is termed as 'hemolytic anemia'.

CAUSES

A. *Hereditary causes*

- Hereditary spherocytosis
- Glucose 6–phosphate dehydrogenase deficiency (G6PD)
- Sickle cell anemia
- Thalassemia.

B. *Acquired causes*

I. *Antibody- mediated haemolytic disorders:*
- Acquired autoimmune hemolysis
- Paroxysmal cold haemoglobinuria
- Erythroblastosis fetalis.

II. *Haemolysis due to physical, chemical or biological agents:*
- Physical agents: Hemolysis due to prolonged physical exercise
- Chemical agents: Chemical agents and drugs can cause damage to RBC cells to produce anemia.

  Important chemical agents, which can cause hemolysis are–arsenic, lead, sulphonamides, potassium chlorate, methyldopa, naphthalene, mefanamic acid, etc.
- *Biological agents:* Several microorganisms can cause hemolysis which include:
  - *Plasmodium falciparum*
  - *Clostridia*
  - *Streptococcus pyogenes.*

CLINICAL FEATURES

- Palor, weakness, lightheadedness and fatiguability.
- Jaundice, recurrent infections, leg ulcers, etc.
- Dyspnea or other cardiovascular symptoms.

ORAL MANIFESTATIONS

- Palor or yellow tinge of the oral mucosa.
- Discoloration of teeth in erythroblastosis foetalis.
- Gingival hemorrhage.

DIAGNOSTIC ASSESSMENT

- Blood Hb percentage is often below to 10 gm/dl.
- Erythrocyte survival rate about 12 days (normal 120 days).

- A fall in blood hemoglobin at the rate of 1 gm/ltr. per week should be regarded as a definite indication of excess hemolysis.
- Reticulocyte count: Raised.
- Unconjugated serum bilirubin: Raised.
- Fecal urobilinogen: Raised.
- Serum iron concentration: Raised.
- Coomb's test: Negative.
- Osmotic fragility of RBC cell: Decreased.

TREATMENT

Treatment of anemia and effective management of the underlying diseases.

- Blood transfusion in severe cases.
- Steroids may be used in case of immune mediated disorders.
- Splenectomy should be done in case of spherocytosis.
- Administration of folic acid.

THALASSEMIAS

Thalassemias are a group of inherited, chronic, hemolytic disorder, which are characterized by the production of extremely thin, fragile erythrocytes called **"target cells".**

These cells survive only few days in the peripheral circulation as they are readily recognized by the spleen and are destroyed. Destruction of target cells often causes microcytic hypochromic type of anemia in thalassemia patients.

In thalassemia, there is insufficient synthesis of α and β polypeptide chains of hemoglobin (these chains are otherwise completely normal).

Either α or β chains can be affected by their diminished synthesis (in α-thalassemia— α-chain synthesis slows down and in β-thalassemia— β-chain synthesis diminishes). As the β-thalassemia is more common, it is called **"classic or major thalassemia"** and its other name is **"Cooley's anemia."**

Thalassemia is a autosomal recessive disease, the heterozygous form of the disease is mild which is known as ***thalassemia minor***. The homozygous form of the disease is very severe and is known as ***thalassemia major***. A third form of the disease is also recognized, which is called ***thalassemia intermedia*** and is characterized by clinical features which are of intermediate severity between the major and the minor forms.

In thalassemia the RBC cells are functionally compromised and because of this more and more RBC cells are produced by the bone marrow to meet the oxygenation demand, this often leads to bone marrow hyperplasia.

CLINICAL MANIFESTATION

The disease is commonly detected in the first two years of life and siblings are commonly affected. The thalassemia minor patients are generally asymptomatic except the presence of persistent anemia and occasional splenomegaly.

The features of thalassemia are as follows:

- The patients often suffer from jaundice with yellowish palor of the skin.
- Fever, chills, marked anemia (microcytic and hypochromic), malaise, generalized weakness and lethargy, etc. are common.
- Hepatosplenomegaly is an important feature of the disease, which often cause bulging of the abdomen.
- Bone marrow hyperplasia often produces painless enlargement of mandible and maxilla, which often results in a typical "**chipmunk facies**".
- Cholelithiasis and leg ulcers also develop frequently.
- Reduced oxygenation may lead to severe infections in the tissue.
- Most of the patients have a **mongoloid facies** with prominent forehead, depressed nasal bridge, prominent cheek bones, protrusion of the maxillary anterior teeth and slanting eyes, etc.
- In severe form of the disease, the onset is in infancy and death often occurs in adolescence. High output cardiac failure is the common cause of death in these patients.
- Repeated blood transfusions may cause iron deposition in tissues (hemosiderosis), which may lead to dysfunction of many glands and other vital organs.

RADIOGRAPHIC APPEARANCE

- The skull bones radiographically exhibit thin, poorly defined, inner and outer cortex of bone and the trabaculae between them are coarse, elongated and bristle-like, which produce a typical "**hair-on-end**" or **a "crew-cut" appearance** on the surface of the skull.

Oral manifestations of thalassemia

- Bimaxillary protrusion with painless enlargement of the jawbones.
- Spacing or flaring of anterior maxillary teeth.
- Pallor of the oral mucosa.
- Xerostomia due to salivary gland dysfunctions as a result of iron overload.
- Severe malocclusion due to enlargement of the jaws with marked open bite.
- Prominent malar bones and mongoloid facies.
- Delayed pneumatization of maxillary sinuses.
- Retracted upper lips.
- Discoloration of teeth due to iron deposition.
- Zygomatic bones are pushed outwardly.
- Depressed nasal bridge in severe cases.

- In the jaws, generalized rarefaction of the alveolar bone, thinning of cortex and enlarged marrow spaces are found.
- Radiograph of the ribs exhibit a typical **'rib within a rib'** appearance due to increased radiodensity within or overlapping the medullary space of the ribs.
- Sometimes, the jaw bones show coarsening of some bony trabaculae and blurring or disappearance of others, it often produces a typical radiographic appearance called **"salt-and pepper effect"**.
- Delayed pneumatization of the paranasal sinuses, especially the maxillary sinuses

DIAGNOSTIC ASSESSMENT

Laboratory findings in thalassemia include the following:

- Target cells (abnormally thin, fragile cells) and other bizarrely shaped, nucleated RBC cells appear in the circulation.
- The characteristic **'safety-pin' cells** may be present in the circulating blood.
- WBC count may be raised up to 10,000 to 25,000 per cubic millimeter of blood.
- The serum billirubin and, fecal and urinary urobillinogen are elevated because of severe hemolysis.
- An elevated fetal hemoglobin is present.
- High percentage of HbF and HbA_2 result from the decrease in β-chains.
- Elevated HbA is found.
- Bone marrow is hyperplastic and produces large numbers of immature, primitive looking, stem forms of RBCs.
- Excessive accumulations of alpha chains within the RBCs are called inclusion bodies (**Fessas bodies**) and these bodies can be detected by supravital staining (**methyl violet**) of the peripheral blood.

Key points of thalassemia

- Thalassemia is an inherited, chronic, hemolytic disorder characterized by the production of extremely thin, fragile erythrocytes (target cells).
- These cells survive only few days in the peripheral circulation.
- In thalassemia, there is insufficient synthesis of α and β polypeptide chains of hemoglobin, if a polypeptide chain synthesis is diminished, it is called α- thalassemia and if β polypeptide chain synthesis slows down it is called β -thalassemia.
- As the β-thalassemia is more common, it is called **"classic or major thalassemia"** and its other name is **"Cooley's anemia."**
- Clinically patients have a **mongoloid facies** with prominent forehead, depressed nasal bridge, prominent cheek bones and protrusion of the maxilla, etc.
- They suffer from severe anemia and frequent jaundice with yellowish pallor of the skin, hepatosplenomegaly, fever, weakness and lethargy, etc.
- Patients of thalassemia almost always have bimaxillary protrusion with painless enlargement of the jawbones, prominent malar bones, spacing of anterior maxillary teeth, pallor of the oral mucosa, xerostomia and severe malocclusion, etc.
- Radiographically, the skull bone exhibits a typical "hair-on-end" or a "crew-cut" appearance and jaw bones also exhibits a 'salt and pepper' effect.

TREATMENT

Multiple blood transfusions and splenectomy, etc. Desferrioxamine, chelating agent may reduce the effect of iron overload in tissues.

SICKLE CELL ANEMIA

DEFINITION

Sickle cell anemia is an inherited defect in the synthesis of hemoglobin molecule, in which the erythrocytes assume a **sickle** or **crescent shape.** The defective erythrocytes are easily destroyed causing severe anemia.

PATHOGENESIS

Sickle cell anemia is an autosomal recessive type of inherited disease, which is characterized by a point mutation in the Hb gene, which results in an abnormal Hb molecule (HbS). Each person inherits one gene from each parent, which governs the synthesis of hemoglobin. HbS is less soluble than HbA (normal adult hemoglobin) and the former forms long fibers, which deform the RBC into sickle shape. This crescent shaped or sickle shaped RBC cells in sickle cell anemia are more prone to agglutination. More agglutinations (hemolysis) of RBC leads to more anemia and increased viscosity of blood, moreover increased risk of blocking of capillaries may result in ischemic damage in various organs and the situation is known as '**sickle cell crisis**'.

CLINICAL FEATURES

- Delayed physical growth and development of the patient.
- Malaise, weakness and jaundice with a yellow sclera.
- Pallor, loss of appetite, dehydration and muscle rigidity.
- Loss of consciousness is a common feature in severe cases (**sickle cell crisis**).
- Children do not develop any symptom until late in the first year of life.
- Extreme susceptibility to infections, renal failure and CNS disturbances are common.
- There can be death due to wide spread ischemia, hypoxia and hypothermia.
- Extreme pain in abdomen, lung, long bones and joints due to ischemia and infarction.
- Fever, swelling of the joints, hands and feet, etc. are also common.

ORAL MANIFESTATIONS

- Oral mucosal polar can be seen and sometimes the oral mucosa may be yellowish in color due to hemolytic jaundice.
- Asymptomatic pulpal necrosis, anesthesia and paresthesia of the mandibular nerve.
- Decreased bony density with coarse trabacular pattern between root apex of tooth and the inferior border of mandible.
- Extraction of tooth may lead to the development of osteomyelitis especially in mandible.
- Thrombosis of blood vessels and infraction in the jawbone often produce '**painful cries'.**

RADIOGRAPHIC FEATURES

- Skull radiographs reveal multiple, small icicle like spicules across the calvarium, which produces a "**hair-on-end**" appearance.
- Occasionally infarcts develop in the jawbones, which radiographically mimic osteomyelitis. The bony infarcts are radiolucent in the beginning and later on they become sclerotic.
- Intraoral periapical radiographs reveal **"step–ladder"** like trabeculae between contagious posterior teeth.
- Increased osteoporosis and hyperplasia of the bone marrow with thinning of individual cancellous trabaculae and cortex.

DIAGNOSTIC ASSESSMENT

Sickle cells are viewed on a stained smear of blood under microscope.

Total RBC count—Decreased.
Hb%—Lowered.
Hematocrit value—Decreased.
Serum unconjugated bilirubin—Raised.
Hb electrophoresis reveals the presence of (Hb-S) in blood.

TREATMENT

No specific treatment. Oxygen and blood transfusions in serious emergencies.

ERYTHROBLASTOSIS FETALIS

Erythroblastosis fetalis is a congenital hemolytic anemia of newborn, which occurs due to the Rh incompatibility. The disease results from the destruction of fetal RBC due to the reaction between maternal and fetal blood factors.

PATHOGENESIS

If the mother is Rh-negative, but the fetus is Rh-positive, then the mother's blood can develop antibodies (anti-Rh-agglutinins) against the Rh-factor of the fetus.

These antibodies may pass onto the fetus by crosing the placental and destroy its RBC cells, this often results in hemolysis, jaundice and anemia, etc.

ORAL MANIFESTATION

- Black, brown or bluish discoloration of the deciduous teeth in the child due to deposition of blood pigments.
- Enamel hypoplasia, which may produce a "**ring-like" defect** on the tooth crowns and is often termed as **"Rh-hump**".

POLYCYTHEMIA VERA

Polycythemia Vera is chronic disease characterized by excessive proliferation of RBC cells, usually with an increased Hb level and total blood volume.

Secondary polycythemia: It is commonly associated with hypoxia (cardiac or pulmonary disease), excessive production of erythropoietin, steroid therapy or chronic exposure to chemicals, etc.

CLINICAL FEATURES

- The disease usually develops in middle age, particularly among Jewish people.
- Polycythemia Vera has a gradual onset and is more common in males.
- Patient often complains of dyspnea, headache, dizziness, drowsiness and tinnitus, etc
- Often there is excessive sweating, weight loss, fullness of head and face and pruritus, etc.
- There is severe weakness, fatigue, impaired mental ability and visual disturbances, etc.
- Patients often have slurring of speech, mental confusion and are unable to concentrate.
- Patients may have a plethoric appearance and they develop splenomegaly, coronary thrombosis and paresthesia of the cranial nerves, etc.
- Peptic ulcers, epigastric pain along with intestinal, nasal or cerebral hemorrhages, etc. are very common during the course of the disease.
- A characteristic finding of the disease is the **"ruddy cyanosis"** or a reddish-purple hue of the face, extremities and lips due to the presence of deoxygenated blood in the cutaneous vessels.
- Polycythemia vera may cause generalized pruritus (itching sensations) without any skin rash, moreover there may be burning sensations with erythema of the extremities.
- Hepatomegaly may occur as a late feature of the disease.

ORAL MANIFESTATION

- Deep purplish red discoloration of the oral mucosa that is commonly reflected on the tongue, gingiva, cheek and lip surfaces.
- The gingiva appears engorged and swollen, and it bleeds profusely upon slight provocation.
- Submucosal petechiae, hematoma and ecchymoses, etc. are very common.

Key points of polycythemia vera

- Polycythemia Vera is chronic disease characterized by excessive proliferation of RBC cells, usually with an increased hemoglobin level and total blood volume.
- The disease occurs more in middle aged males and patients often complain of dyspnea, headache, dizziness, drowsiness and tinnitus, etc.
- Often there is excessive sweating, weight loss, severe weakness, fatigue, impaired mental ability, slurring of speech and visual disturbances, etc.
- A characteristic finding of the disease is the **"ruddy cyanosis"** or a reddish-purple hue of the face, extremities and lips due to the presence of deoxygenated blood in the cutaneous vessels.
- Oral manifestations of the disease include deep, purplish red discoloration of the oral mucosa over the tongue, gingiva, cheek and lip surfaces.
- The gingiva appears engorged and swollen, and it bleeds profusely upon slight provocation.
- Submucosal petechiae, hematoma and ecchymoses, etc. are also very common.
- Laboratory investigation reveals higher red blood cell count, which may be as high as 8 to 12 million/mm^3 of blood.

- Often there is increased varicosity in the ventral surface of the tongue.
- Engorgement of all organs related with blood.

LABORATORY FINDINGS

- The red blood cell count may be as high as 8 to 12 million/mm^3 of blood.
- The bone marrow is hyperplastic with decreased marrow iron and it appears dark-red and highly cellular.
- Striking increase in the total blood volume and gradual increase in the blood viscosity.
- Hemoglobin level may by 18 to 20 g/100 ml.
- Hematocrit level is greater than 54 percent in men and 49 percent in women.
- Platelet count is increased and often there is abnormal platelet aggregation.
- Leukocytosis also common.
- Serum uric acid level is increased up to 3 to 4 times normal.
- Increased granulocyte alkaline phosphatase activity.

TREATMENT

- Repeated phlebotomy (vene-section) may be done to lower the Hb%, hematocrits and RBC cell mass.
- 500 ml of blood is removed every 2 to 3 days till the hematocrit reaches a desired level.
- Chemotherapy is given with chlorambucil, malphalan or cytosine arabinoside to reduce the number of RBCs.
- There is an increased chance of thrombosis, if the patients are on bed rest and therefore patients should be kept ambulatory.

COMPLICATIONS OF POLYCYTHEMIA VERA

- Thrombophlebitis, myocardial and cerebral infarctions.
- Thrombotic occlusion of the splenic, hepatic, portal and mesenteric veins.
- Hemorrhage— nasal, intestinal and cerebral, etc.
- Digital gangrene and necrosis.
- Gout–Due to over production of uric acid.
- Congestive cardiac failure due to increased blood volume and hypertension.
- Acute leukemia may be a terminal complication of polycythemia vera.

LEUKEMIAS

Leukemia is a malignant disease of the blood-forming organs, characterized by increased proliferation of WBC cells in the bone marrow at the cost of other hemopoietic cells. Although, leukemia is a disease of the WBC cells, it often severely affects the other major cell types of blood, e. g. RBCs and Platelets, etc. The disease produces **anemia** due to decreased production of RBC cells, there is **increased susceptibility of infection** due to production of immature and functionally inefficient WBCs in large numbers and there is also **increased tendency for hemorrhage** due to reduced number of platelets in the blood.

INCIDENCE

Leukemia accounts for 8 percent of all human cancers and is the common malignancy in children and young adults. One-half of all leukemias are classified as acute, with rapid onset and progression of the disease resulting in 100 percent mortality within days to months without appropriate therapy. The remaining leukemias are classified as chronic, which have a more indolent course.

ETIOLOGY

Although, the exact cause of leukemia is unknown, several predisposing factors have been associated with this disease which include:

- Chromosomal abnormality—the presence of an abnormal chromosome, e.g. Philadelphia chromosome is associated with an increased incidence of chronic myelocytic leukemia (CML).
- Exposure to high doses of radiation therapy.
- Exposure to certain chemicals, e.g. benzene, phenyl butazone and chloramphenicol, etc.
- Following chemotherapy treatment for some other diseases, particularly with melphalan.
- Myeloproliferative disorders like-polycythemia vera, etc.
- Congenital or genetic abnormalities (e.g. Down's syndrome).
- Presence of primary immune deficiency.
- Infection with human leukocyte virus (HTLV-1—human T-cell Leukemia virus-1).

- Hereditary—Some families have increased incidences of leukemia than others.

CLASSIFICATION OF LEUKEMIAS

Leukemias are broadly classified into acute and chronic types.

Acute Leukemia

It is characterized by neoplastic proliferation of large number of abnormal, immature leukocytes in the marrow that infiltrate the lymph nodes, liver, spleen and eventually all body systems.

In addition to this, production of other blood cells (i.e. red blood cells and platelets) are inhibited, which results in inadequate oxygen transport, thrombocytopenia and immune system malfunction, etc.

According to the French-American-British (FAB) cooperative group, the acute leukemias are classified in the following manner:

Chronic Leukemias

These diseases have a gradual onset and a more protected course than the acute forms. The white blood cells produced are more mature and thus can better defend the body against invading microorganisms.

Chronic leukemias are again classified into two types:

A. Chronic myelogenous leukemia (CML).
B. Chronic lymphocytic leukemia (CLL).

CLINICAL FEATURES OF LEUKEMIAS

- Acute leukemias occur commonly either in children aged between 2 and 4 years and in adult patients aged 65 years or above. Chronic leukemias on the other hand occur in patients between the ages of 25 and 60 years.
- Both types of leukemia occur predominantly among males.
- Patients often complain of fatigue, generalized malaise and weakness.
- Easy bruising, epistaxis, headache, vomiting and generalized pain, etc.
- Most of the patients may have the feeling of abdominal fullness due to hepatosplenomegaly.
- Decreased production of RBC causes anemia and severe pallor.
- Persistent fever of unknown etiology due to depressed immunity.
- Weight loss and heat intolerance due to increased rate of body metabolism.
- Pain from infarction of the spleen.
- Scattered petechiae, ecchymosis over the skin and generalized lymphadenopathy.
- Generalized bone and joint pain, shortness of breath, tachycardia and dyspnea on slight exertion, etc. are the other common features of the disease.

Classification of leukemias

Acute Leukemia	***Chronic Leukemia***
Acute Lymphocytic Leukemia (ALL) L1—Common childhood leukemia. L2—Adult ALL. L3—Rare subtype, blast cells resemble Burkitt's lymphoma.	***Chronic myelogenous leukemia (CML)***
Acute Myeloblastic Leukemia (AML) *Granulocytic* M1—Myeloblastic leukemia without maturation. M2—Myeloblastic leukemia with maturation M3—Hypergranular promyelocytic leukemia *Monocytic* M4—Myelomonocytic leukemia M5—Monocytic leukemia *Erythroid* M6—Erythroleukemia	***Chronic lymphocytic leukemia (CLL)***

Oral manifestations of leukemia

Oral manifestations in leukemia may be caused by the basic disease process itself or the secondary infections or due to local irritations aggregated by plaque, food debris and ill fitting dentures, etc.

- **Gingival hyperplasia** with **severe bleeding tendency** is the most common oral manifestation of leukemia.
- Diffuse hyperplastic gingivitis with **cyanotic bluish discoloration** of the gingiva. Moreover the gingivitis is often associated with **mucositis**.
- The gingival tissue becomes **swollen** and edematous due to **leukemic cell infiltration** and the overgrowth of gingival tissue may cover the entire teeth of the dental arch (Figs 17.1 and 17.2).
- There can be **marked enlargement** of the **interdental papillae** and sometimes boggy, non-tendered, **tumor-like swellings** (often called leukemic cell deposits) may also be seen in the gingiva palate and salivary glands, etc.
- Thinning of the oral mucosa and bone marrow depression can allow **increased opportunistic infections** in the mouth.
- Bacterial infections in the oral cavity often lead to septicemia.
- **Infiltration of leukemic cells** into the periapical region of tooth often simulates conventional periapical lesions.
- Leukemic cells can **infiltrate into the extraction sockets** and cause delayed healing with severe bleeding and secondary infections.
- Blockade of the bone marrow vessels and secondary infections often lead to the development of **osteomyelitis** in the jaw after tooth extraction.
- Besides this, ulceration of the sulcular epithelium and necrosis of the connective tissue leads to severe, spontaneous gingival bleeding.
- Petechiae, mucosal pallor, **ecchymosis, hemorrhage and hematoma** formations in the oral mucosa are common (Fig. 17.3).
- Multiple large irregular **necrotic ulcers** develop in the oral mucosa due to secondary infection by various organisms, the ulcers are usually surrounded by a pale zone and these lesions produce excessive foul smell (Fig. 17.4).
- Large **hematomas** often develop on the lower lip.
- Oral infections, e.g. **candidiasis, histoplasmosis, aspergillosis and HSV infections** are common in leukemic patients due to the absence of mature, healthy WBC cells and these secondary infections may produce fatal complications.
- Palatal ulcerations and necrosis may herald the presence of mucormycosis of the nasal cavity and the paranasal sinuses.
- Deep, punched-out ulcers with grayish-white necrotic base may occur due to extreme neutropenia.
- Rapid loosening and spontaneous exfoliations of teeth due to necrosis of the periodontal ligament and destruction of the alveolar bone.
- Mental nerve neuropathy or the **'numb chin syndrome'** is a constant finding in leukemia.
- Leukemic cell infiltration in the dental pulp may sometimes cause atypical dental pain.
- Prolonged post-extraction bleeding can be a serious problem in acute leukemia.

- Hyperuricemia with renal pain and retinal hemorrhages.
- Severe infections like pneumonia and septicemia, etc. may develop in cases of severe leukemia.
- Cerebral hemorrhage, increased intracranial pressure and cranial nerve palsies.
- Leukemic cell infiltrations into the skin, mucosa and retina, etc.

DIAGNOSTIC ASSESSMENT

A comprehensive evaluation of all body systems is necessary for establishing the diagnosis and treatment plan for leukemia.

CBC VALUES (COMPLETE BLOOD COUNT)

Peripheral Blood Picture:

- WBC total count may be either normal, or abnormally low (less than 100/mm^3) or

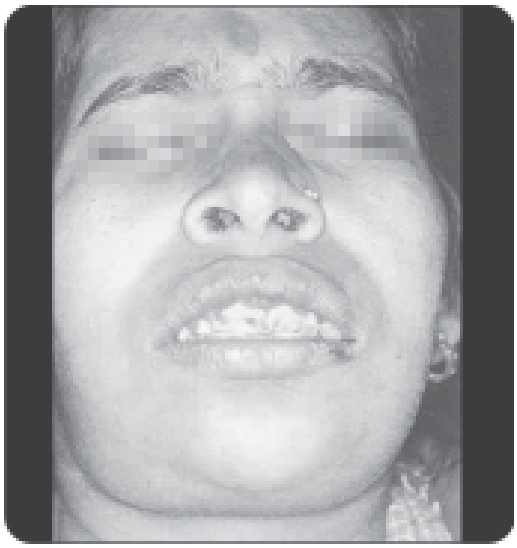

Fig. 17.1: Gingival swelling in a patient with acute myeloid leukemia

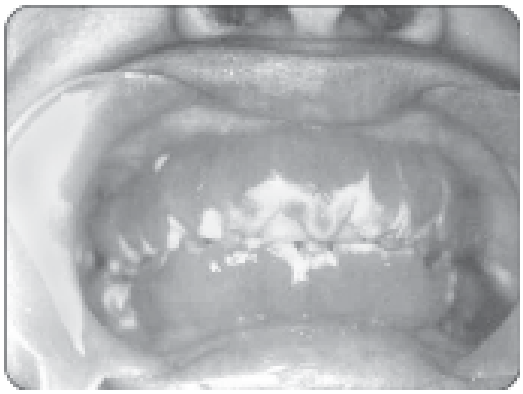

Fig. 17.2: Severe gingival swelling in the patient with acute myeloid leukemia

Fig. 17.3: Areas of ecchymosis of skin (extensor surface of hand) in the same patient

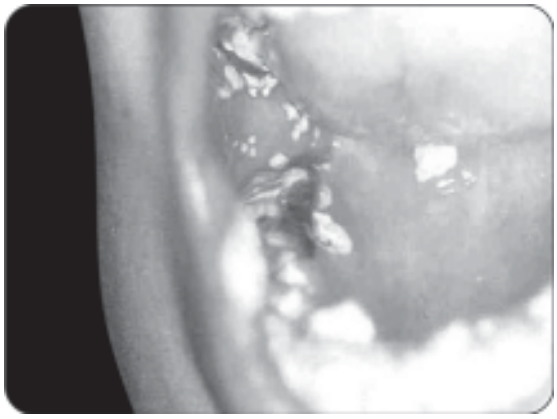

Fig. 17.4: Necrotic ulcerations of oral mucosa in the patient with acute myeloid leukemia

Key points of leukemia

- Leukemia is a malignant disease of the blood-forming organs, characterized by increased proliferation of WBC cells in the bone marrow at the cost of other hemopoietic cells.
- Leukemias are broadly divided into two groups—acute and chronic. Acute leukemias occur commonly in children while chronic leukemias are seen more commonly in middle aged adults and older people.
- Patients often complain of fatigue, weakness, easy bruising, epistaxis, ecchymoses, headache, vomiting and generalized weakness, etc.
- The other important features of the disease include hepatosplenomegaly, severe pallor and lymphadenopathy, etc.
- Oral manifestations of the disease include gingival hyperplasia with severe bleeding tendency.
- There is also presence of diffuse hyperplastic gingivitis with cyanotic bluish discoloration of the gingiva. Moreover the gingivitis is often associated with **mucositis**.
- The gingival tissue presents areas of tumor-like swellings, which occur due to deposition of leukemic cells within the tissue.
- Blood report shows total WBC has become abnormally high (more than 20,00,000/mm^3) with abnormal marrow activity.

extremely high (greater than 20,00,000/mm^3). Generally the WBC count of the peripheral blood ranges from 10,000 to 100,000 per 1 ml of blood.

- Differential count of WBC may reveal that one type of leukocyte is overwhelmingly predominant.

- There may be abnormal leukocytes, including immature blast forms in the peripheral blood.
- The platelet count and hemoglobin levels are usually low.

Bone marrow aspiration: Biopsy or bone marrow aspiration reveals an overall increase in the number of bone marrow cells, with an increase in the proportion of leukocyte series.

Lumbar puncture: It determines the presence of blast cells in the central nervous system.

Radiographic test: Radiographic tests may include the following:

- Chest X-ray—To detect the mediastinal involvement.
- Skeletal X-ray—To detect skeletal lesions.
- MRI and CT Scans—To detect lesions and sites of infection, especially in the head and neck areas.

Lymphangiogram: Lymphnode biopsy or lymphangiogram may be performed to locate malignant lesions and accurately classify the diseases.

TREATMENT

Antileukemic chemotherapy and radiotherapy. Repeated blood transfusions and administration of antibiotics.

AGRANULOCYTOSIS (GRANULOCYTOPENIA)

Agranulocytosis is a serious acute leukopenia, characterized by a significant decrease in the number of granular leukocytes (chiefly the neutrophils).

ETIOLOGY

The disease commonly occurs among adult females and interestingly it frequently affects the health professionals.

The exact etiology of agranulocytosis is not known, however, investigators believe that the disease may occur due to certain drugs and chemicals, which suppress the bone marrow. The agents and their effects are as follows:

- Toxic effects of some drugs, e.g. sulfonamides, chloramphenicol, anti-histaminics and chlorambucil, etc.
- Due to the hypersensitivity to drugs like aminopyrine.
- Long-term administration of analgesics (phenyl butazone), antithyriods, diuretics, cytotoxic drugs and anticoagulants, etc.
- Ionizing radiation, tuberculosis, typhoid fever and malaria, etc. may also induce agranulocytosis.

CLINICAL FEATURES

- The disease starts with high fever, chills and sore throat, etc.
- Patients gradually develop malaise, weakness, bone pain and increased prostrations.
- The skin appears pale and in many cases there may be sings of jaundice.
- Persistent bacterial infections develop in many parts of the body with regional lymphadenitis.
- Severe dysphagia, weak and rapid pulse, etc. are the other important features of the disease.
- Urinary tract infections with vaginal and rectal ulcerations are common.
- Without prompt antibiotic therapy the disease usually causes death within a week due to pneumonia, sepsis and shock, etc.

Oral manifestations of agranulocytosis

- Agranulocytosis causes narcotizing ulcerations called '**agranulocytic angina**' of the oral mucosa that involve the gingiva, soft palate, tonsils, lips, pharynx and cheek, etc.
- These ulcers are deep and are covered by a yellow or grey membrane, but there is absence of any red halo due to the lack of inflammation.
- Gingival bleeding, excessive salivations and dysphagia, etc. are also common.
- Halitosis and hemorrhagic ulcers are often present and the patients feel extreme difficulty in taking food.
- Excessive tendency for developing secondary infections, which develop rapidly and soon become overwhelming. These lesions often resemble acute necrotizing ulcerative gingivitis (ANUG).
- Opportunistic fungal infections are also common.

HISTOPATHOLOGY

Biopsy taken from the oral ulcer reveals numerous bacterial organisms both on the surface and deep inside the tissue. Inflammatory response in the tissue is very little.

DIAGNOSTIC ASSESSMENT

Diagnosis of arganulocytosis is made on the basis of the following:

- WBC count reveals severe leukopenia (500 to 3000/mm^3) with extreme reduction in neutrophil count (0 to 2%).
- Bone marrow examination reveals an absence of granulocytes, a maturational arrest of young developing cells or an increased number of myeloid precursors (signifying peripheral granulocyte destruction).
- Cultures of urine, blood and materials taken from lesions in the throat and mouth, etc. are positive for bacteria (usually gram-positive cocci).
- A history of exposure to an offending agent, plus all the above findings (especially in case of a person, who medicates himself or herself) are generally diagnostic for agranulocytosis.

TREATMENT

Elimination of causative factors, antibiotics, vitamins, antipyretics and high caloric soft diet.

CYCLIC NEUTROPENIA

DEFINITION

Cyclic neutropenia is an idiopathic disease characterized by episodic defects in neutrophil maturation in the bone marrow, resulting in periodic fall in circulating neutrophils at regular intervals of 3 to 4 weeks. **The condition is episodic in nature and is characterized by severe infections as the neutrophil count falls below the critical level,** moreover the symptoms subside as the neutrophil count rises towards normal.

CLINICAL FEATURES

- Cyclic neutropenia generally affects children and the patients often suffer from recurrent upper respiratory tract infections in uniformly spaced episodes.
- Patients develop short term fever on regular basis along with anorexia, malaise and lymphadenopathy, etc. which spontaneously resolve once the neutrophil count returns to normal.
- Aphthous-like ulceration in the month of short duration develop upon minor trauma, the areas commonly affected are lips, tongue, buccal mucosa and oropharynx, etc.
- Oral ulcers often have an erythematous 'halo' at the periphery.
- Cyclic neutropenia also characteristically produces rapidly progressive periodontal disease at an early age, which presents severe gingival recessions, rapid alveolar bone loss and tooth mobility, etc.

DIAGNOSTIC ASSESSMENT

- Total WBC count decreases to 3000 cells/cu mm of blood in every month.
- The neutrophil count falls below a critical level of 500/cumm for 3 to 5 days and then it rises, the same cycle repeats in about every 3 weeks.
- Blood monocyte and eosinophil count increases as the neutrophil count falls.
- In cyclic neutropenia, the neutrophil count is always far below normal even during the remission period also.
- Oral ulcer histologically shows absence of infiltrating neutrophils.

TREATMENT

No specific treatment.

PURPURA

Purpura is defined as the extra-vasation of small amount of blood into the skin or mucous membrane, causing petechiae, ecchymosis or spontaneous bruising, etc. The disease purpura results from platelet disorder or occasionally due to vascular defects and is characterized by prolonged bleeding time (BT) but normal clotting functions.

Drugs which may cause purpura

- Chloramphenicol
- Phenylbutazone
- Indomethacin
- Thiazide
- Diuretics
- Quinine
- Quinidine.

TYPES

The disease is of two types:
A. Idiopathic thrombocytopenic purpura (ITP)
B. Non-thrombocytopenic purpura

ITP refers to thrombocytopenia caused by an unknown, possibly autoimmune disease. This disorder is characterized by premature destruction of platelets due to the formation of antibodies against them. The platelets are then destroyed by phagocytosis in the spleen or in the liver.

Normally, platelet cells survive 8 to 10 days within the circulation but in ITP the platelet survival time is as brief as 1 to 3 days or less.

Non-thrombocytopenic purpura occurs due to the rupture of smaller blood vessels with resultant bleeding into the tissue.

Major forms of this disease are:
- Familial hemorrhagic telangiectasia
- Anaphylactoid purpura
- Toxic purpura.

CLINICAL FEATURES OF PURPURA

- Purpura commonly occurs among adults below 40 years of age and females are more frequently affected than males.
- The disease is characterized by sudden, spontaneous occurrences of **petechiae** (Fig. 17.5) (*small pinpoint hemorrhage under the skin or mucosa*), **ecchymosis** (*escape of blood into tissues producing a large bruise*) or **hematomas** (blood filled tumors) in the skin and mucous membrane.
- Purpuric spots are often seen on the palate, where the posterior border of artificial denture presses against the palatal mucosa.
- Excessive gingival bleeding and blood blisters in the oral mucosa, the blisters often rupture and leave ulcers (Fig. 17.6).

Fig. 17.5: Multiple petechial spots on the skin of a patient with thrombocytopenic purpura

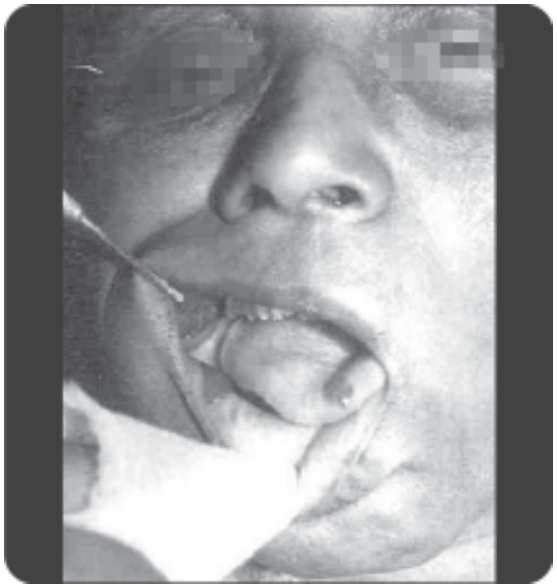

Fig. 17.6: Spontaneous bleeding from gingiva and buccal mucosa in the patient with purpura

- Localized oral purpura is a condition characterized by development of blood blisters on the oral mucosa due to minor trauma.
- In purpura, the bleeding spots on the skin or mucosal surfaces do not blanch upon pressure.
- Excessive bruising tendency, epistaxis, hematuria, melena and hematemesis are common.

- Spontaneous bleeding often does not occur unless the platelet count is below 20,000 per cu mm of blood.
- Women may have extremely heavy menses or bleeding between periods.
- The disease causes prolonged bleeding after surgery or injury.
- Bleeding into the diaphragm may result in pulmonary complications.
- Intracranial hemorrhage may produce paresthesia of the cranial nerves and hemiplegia.
- Bleeding into the muscles and joints may cause difficulty in movements.
- Prolonged oozing of blood from different sites may occur in severe cases, despite local measures to curtail bleeding.
- Interestingly, the spleen is not palpable and if it is palpable, leukemia should be suspected rather than purpura.

DIAGNOSTIC ASSESSMENT

- Platelet count below 100,000/mm³ of blood (normal platelet count is 2.5 to 4 lac/cumm of blood).
- Spontaneous bleeding occurs if the platelet count goes below 20000/mm³.
- Prolonged bleeding time with normal coagulation time.
- Increased capillary fragility as demonstrated by '**tourniquet test**'.
- Positive platelet antibody screening.
- Bone marrow aspirates contain normal or increased number of megakaryocytes.
- Examination of urine reveals proteinuria or hematuria.
- Gingival tissue biopsy with PAS stain reveals fibrin deposits within the small capillaries.

Oral manifestations of purpura

- Profuse gingival bleeding and development of blood blisters, which occurs either spontaneously or upon slight provocation.
- Bleeding starts typically after a short delay following injury as platelets and vascular response provide initial phase of hemostasis.
- Persistent uncontrolled hemorrhage may continue for days and untreated patients often die.
- Petechiae or ecchymosis occurs very frequently on the palatal mucosa (where posterior border of the denture presses into the palatal mucosa), however other intraoral structures may also be involved.
- Excessive uncontrolled bleeding occurs following minor surgical procedures including dental extractions (however unlike hemophilia, bleeding in purpura ultimately stops spontaneously as a result of normal coagulation of blood).
- Submucosal hematomas often develop in the oral cavity following trauma, and these lesions appear as large, dark tumors.
- Bleeding into the facial muscles may cause difficulty in opening and closing the mouth.
- Bleeding into the temporomandibular joint results in pain and trismus.

Key points of purpura

- Purpura is the extravasation of small amount of blood into the skin or mucous membrane; causing petechiae, ecchymosis or spontaneous bruising, etc.
- It results from decreased platelet count or occasionally due to vascular defects and is characterized by prolonged bleeding time (BT) but normal clotting time (CT).
- Purpura is of two types—Idiopathic thrombocytopenic purpura (ITP) and non-thrombocytopenic purpura.
- Clinically, the disease presents sudden, spontaneous occurrences of petechiae, ecchymosis and hematomas over the skin and mucous membrane.
- Oral manifestations of the disease include purpuric spots on the oral mucosa (especially palate), excessive gingival bleeding and blood blisters in the oral mucosa.
- Excessive bruising tendency, epistaxis, hematuria, melena and hematemesis are common.
- Blood report reveals platelet count below 100,000/mm³ of blood.
- Spontaneous bleeding occurs if the platelet count goes below 20000/mm³ of blood.

TREATMENT

By steroid therapy and repeated blood transfusions. Splenectomy and immunosuppressive drug therapy may be required.

HEMOPHILIA

Hemophilia is a potentially fatal inherited bleeding disorder characterized by profound hemorrhage due to the genetic deficiency of clotting factors. The disease occurs in males but is transmitted by females and the incidence rate is 1 in 8,000 to 10,000 populations.

ETIOLOGY

- Heredity
- Sex-linked recessive trait
- Spontaneous mutations may sometimes cause the condition (when the family history is negative for the disease).

TYPES

There are three major types of hemophilia.

A. Hemophilia A (classic hemophilia)
B. Hemophilia B (Christmas disease)
C. Von Willebrand's disease

Since, the classic hemophilia constitutes about 80 percent of all hemophilias, the discussion on clinical features and treatments, etc. will be made mostly in reference to this entity.

CLINICAL FEATURES OF HEMOPHILIA

- The disease is seldom diagnosed in infancy unless serious bleeding occurs from the umbilical cord or following circumcision.
- It is usually diagnosed after the child becomes active.
- The disease is mostly characterized by easy bruising and prolonged bleeding, particularly after minor accidental, surgical or dental trauma.
- Bleeding into muscles and joints in affected children cause pain, swelling and difficulty in movement of the affected organ.
- Spontaneous bleeding into the subcutaneous tissue or internal organs leads to recurrent soft tissue hematoma formation.
- Interestingly, no petechial spots are found on the skin or mucosal surfaces.
- Severe fatal epistaxis after injury to the nose.
- Gastric hemorrhage may occur in case a gastric ulcer is present.
- Recurrent hemarthrosis (bleeding into the joints) occurs commonly in elbow, knee and ankle joints, etc. and untreated or recurrent cases may result serious joint deformity and permanent crippling.
- Joint problems mostly occur due to degenerative changes in the joint structures, osteoporosis and muscle atrophy, etc.
- Patients often have spontaneous hematuria and intracranial hemorrhage.

Oral manifestation of hemophilia

- Severe hemorrhage from the gingival tissue after surgical incision, curettage or dental extraction.
- Bleeding may even start after brushing the teeth with a hard toothbrush.
- Following the surgical or traumatic injury bleeding starts after a short delay as the normal platelet or vascular responses provide initial phase of hemostasis. Severe bleeding however starts after this, which if not controlled may continue for weeks or until the patient dies.
- Slight trauma (e. g. common bumps or fall in small babies) may lead to ecchymosis or hematoma formations in the tongue, lips or palate, etc.
- Severe bleeding unexpectedly occurs from the tiny injection sites in the mouth.
- Internal bleeding into the glottis with subsequent air-way obstruction may occur following pterygomandibular-block-anesthesia, which may cause death of the patient.
- Recurrent subperiosteal hematoma with reactive new bone formation may cause tumor-like malformations of the jaw (such lesions are called **pseudo-tumor** of hemophilia).
- Hemophilic patients often carry a high caries index and severe periodontal disease.
- Deep tissue bleeding in oropharyngeal region is often a feared complication of hemophilia as it can obstruct the airway and therefore require emergency intubations.

- In cases of mild hemophilia, no major bleeding symptoms are present unless there is an injury or any surgical intervention carried out in the patient.

LABORATORY INVESTIGATIONS

- Clotting time is prolonged or sometimes it may test normal.
- Platelet count and bleeding time is normal.
- Prothrombin time is normal.
- Prothrombin consumption—Decreased.
- Activated partial thromboplastin time is prolonged.
- Thromboplastin generation—Increased.
- Genetic counseling and carrier detection by biologic and immunologic assays.
- Blood grouping and cross matching.
- Specific quantitative assays for factor VIII will determine the severity of the disease.

Common complications in hemophilia

- Airway obstruction due to hemorrhage into the neck and pharynx, down to glottis, occurs following inferior alveolar nerve block anesthesia.
- Even simple submucosal infiltration anesthesia may lead to serious consequenes.
- Intestinal obstruction due to bleeding into intestinal walls or peritoneum.
- Compression of nerves with paralysis due to hemorrhage into deep tissues.
- Intracranial bleeding.
- Death may occur due to intracranial bleeding or from exsanguinations following any serious hemorrhage.

TREATMENT

- Immediate transfusion of factor VIII or IX concentrate is the primary treatment.
- Although plasma and cryoprecipitate contain factor VIII, the concentrates have a known AHG content and carry less risk of blood volume overload.
- As the procoagulant activity of AHG disappears rapidly, patients need transfusions every 12 hours until bleeding stops.
- Transfusion of packed red blood cells or white blood cells are used only to replace blood volume when there has been severe loss.
- Prophylactic transfusion of factor VIII to a level of 50 percent above normal is recommended in cases of minor injury or dental extractions.
- Topical bleeding can be temporarily controlled by applying pressure to the injured site or packing the area with fibrin foam, and by applying topical hemostatic agents such as thrombin.
- Analgesics and corticosteroids reduce joint pain and swelling.
- Joint immobilization and local chilling (packing ice around the joint) may give relief in case of hemarthrosis. If the pain is severe it may be necessary to aspirate blood from the joint.
- In mild hemophilia, the use of intravenous desmopressin (acts by increasing factor VIII activity) may eliminate the need of AHG.

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CHAPTER 18

Periodontal Diseases

The periodontium consists of several tissues namely the gingiva, the periodontal ligaments, the cementum and the alveolar bone, etc. The periodontal diseases are a group of heterogenous, chronic destructive inflammatory diseases of the periodontium.

EPIDEMIOLOGY

Although there is evidence that at least, clinically, several distinct types of chronic destructive periodontal diseases may exist. The term gingivitis is used to designate inflammatory lesions that are confined to the marginal gingiva. Once the lesions extend to include destruction of the connective tissue attachments of the tooth and loss of alveolar bone, the disease is designated periodontitis.

Chronic inflammatory periodontal diseases of varying severity affect practically all dentate individuals. Gingivitis is common in children, even by the age of 3 years, and early periodontitis may be detected in teenagers; in general, the extent and severity of disease increase with age. This does not imply that all gingivitis will eventually progress to periodontitis. Since the adoption of the Community Periodontal Index of Treatment Needs (CPITN), epidemiological data from various parts of the world can be compared. This has confirmed that virtually all adult individuals show some evidence of early periodontitis but the advance disease affects only about 10-15 percent of the population. Tooth loss as a result of periodontal destruction is uncommon before the age of 50 years unless the patient has some other systemic diseases.

Etiological factors of periodontal diseases

Local Factors	• Microorganisms • Calculus • Food impaction • Faulty restorations • Tooth malposition • Mouth breathing habit • Use of different drugs or chemicals.
Systemic Factors	• Nutritional deficiency • Pregnancy • Diabetes • Allergy • Heredity • Immunological disorders • Psychogenic factors

THE ROLE OF BACTERIA AND DENTAL PLAQUE IN PERIODONTAL DISEASE

- Epidemiological studies conducted by different investigators in many parts of the world suggest that there is a strong relationship between the periodontal disease and the dental plaque.
- Clinical trials in humans and animals clearly indicate that lack of maintenance of proper oral hygiene causes accumulation of plaque, which results in the initiation of gingivitis and restoration of the proper plaque control measures rapidly prevents the disease and brings back the gingival health.

Important microorganisms in periodontal disease

- *Actinobacillus actinomycetemcomitans*
- *Actinomyces viscosus*
- *Capnocytophaga* group
- *Eikenella corrodens*
- *Fusobacterium nucleatum*
- *Porphyromonas gingivalis*
- *Prevotella intermedia*
- *Treponema*
- *Wolinella*

- Administration of different antimicrobial agents are proved to prevent the gingivitis and this again establishes the role of plaque bacteria in the causation of periodontal disease.
- Bacteria isolated from human dental plaque are capable of inducing periodontal disease when introduced into the mouths of gnotobiotic animals.
- Several species of pathogenic bacteria have been isolated from periodontal pockets that have the capacity to invade tissue and evoke destructive inflammatory changes.
- Healthy periodontal tissues of humans are associated with a scanty flora located almost entirely supragingivally on the tooth surface. The microbial accumulations are 1 to 20 cells in thickness and comprise mainly gram-positive bacteria Streptococcus and *Actinomyces* species predominate, for example *S. sanguis, A. naeslundii, A. viscosus*, etc.
- In developing gingivitis, the total mass of plaque is increased and the microbial cell layers often extend to 110 to 300 cells in thickness. Members of the genus *Actinomyces* predominate, but there is a substantial increase in strict anaerobes and gram-negative organisms. In long-standing gingivitis, gram-negative organisms may account for 35 to 40 percent of the flora. The majority are located subgingivally.
- Microbial examination of subgingival plaque in periodontitis has revealed a complex flora rich in gram-negative rods, motile forms, and *spirochetes*.
- Black-pigmented bacteroid group are the predominant cultivable organisms in most subjects and they have been reclassified as *Porphyromonas* or *prevotella* species, for example *Porphyromonas gingivalis, prevotella melaninogenica, and prevotella intermedia*, etc.
- The development of gingivitis and periodontitis is associated with sequential colonization and a progressively more complex flora, characterized by an increase in anaerobic, gram-negative and motile organisms rather than a mere increase in the amount of plaque.

CALCULUS

Sometimes, the dental plaque may become mineralized due to the deposition of calcium and other ions (which are coming either from the saliva or the blood serum) and this mineralized plaque is known as calculus.

The calculus may also contribute to the development of periodontal diseases, either by harboring the plaque bacteria or by causing irritation to the gingival tissues.

Factors causing accumulation and stagnation of plaque

- Calculus
- Food impaction
- Overhanging restoration
- Malocclusion
- Deep pockets
- Mouth breathing

OTHER LOCAL FACTORS

Local factors include the anatomy of teeth, gingiva, and alveolar bone, alignment and occlusal relationship of teeth, and proximal restorations, etc. and these factors may affect the accumulation and growth of plaque or interfere with its removal.

THE ROLE OF SYSTEMIC FACTORS

Although dental plaque is the essential etiological agent in periodontal disease, there are many systemic factors, which may alter the host's response to local irritants and, therefore, could influence the development and progression of the lesion.

Several systemic factors have been associated with an increased incidence and severity of periodontal disease or with modifying the course of that disease.

Diabetes Mellitus

- The relationship between diabetes and periodontal disease is controversial. It is commonly held that periodontal disease is more severe and progresses faster in diabetics than in non-diabetics.

- Vascular changes and defects in cellular defence mechanisms have been suggested as possible mechanisms in which diabetes could increase the susceptibility of periodontal tissue to irritants from dental plaque.

Pregnancy and Sex Hormones

- Severity of a pre-existing gingivitis increases in pregnancy from the second to the eight month of gestation and then decreases.
- Increased level of circulating hormones are thought to be responsible, but the fact that so-called pregnancy gingivitis can be resolved by adequate plaque control emphasizes that the hormonal changes simply modify the tissue response to dental plaque and do not cause the gingivitis themselves. Increased levels of sex hormones or their metabolites are found in inflamed gingiva.
- The aggravation of gingivitis during pregnancy is related mainly to progesterone, which affects the function and permeability of the gingivial microvasculature.
- Localized gingivial hyperplasia also occurs during pregnancy (pregnancy epulis). Increased levels of gingivitis occurring around puberty and in some women taking oral contraceptives may also be related to the concentration of circulating sex hormones.

Nutrition

- Nutritional factors can modify the course of, but not initiate periodontal diseases.
- In human, the relationship between nutrition and periodontal disease is controversial except in rare cases of gross deficiency states.
- Advanced periodontal disease has been reported in rural Nigerians who eat a protein–deficient diet and in such children this is an important factor predisposing to cancrum oris.
- Severe and prolonged deficiency of vitamin C causes scurvy, which may be associated with haemorrhagic gingivitis and generalized edematous enlargement of the gingiva.

Blood Diseases

- Acute leukemia may be accompanied by a generalized enlargement of the gingivia mainly due to infiltration and packing of the tissues by leukemic cells.
- Other oral signs of the disease can be related to the associated pancytopenia and include mucosal pallor, necrotizing ulceration (particularly of the oropharynx) petechial hemorrhages, gingival bleeding, and gingival ulceration, etc.
- Candidiasis and recurrences of herpetic infection are also common.
- Alveolar bone loss and severe periodontal destruction have also been reported which, in some patients, are caused by leukemic cell infiltration.

Drugs

With the exception of phenytoin, cyclosporine, and nifedipine, which are associated with generalized gingival hyperplasia.

Drugs which affect inflammatory and immune responses, such as immunosuppresents and non-steroidal antiinflammatory agents, might be expected to influence the course of periodontal diseases, by modifying the response of the host to product from microbial plaque. The common drugs, which can affect the periodontal tissue include, azathioprine, cyclosporine, naproxen sodium, nifedipine, verapamil, estrogen and progesterone, etc.

Acquired Immunodeficiency Syndrome (AIDS)

Several epidemiological studies indicate that the periodontal status of many HIV-positive patients is similar to that of the general population. However, severe and atypical forms of periodontal diseases may be seen in some patients, particularly those with AIDS.

Smoking

There is ample evidence that tobacco smoking is an important risk factor for the development and progression of periodontal diseases. Smoking probably impairs the phagocytic function of Polymorphonuclear neutrophils (PMN).

PATHOGENESIS OF PERIODONTAL DISEASE

Host-parasite relationship—In healthy condition a balance exits between the challenge to the tissue from microorganisms in dental plaque and the host defense mechanisms. Disturbances in this

host-parasite relationship lead to the development of periodontal disease, but the transition from healthy condition to gingivitis is not precisely identifiable.

Host-parasite relationship in periodontal disease

Microbial plaque	Host defences
Direct injury Toxic products Enzymes Antigenic challenge	Salivary factors Crevicular fluid Epithelial barrier Transmigrating of neutrophils immune response

POTENTIAL FOR TISSUE REGENERATION AND REPAIR

The host may be able to adapt to the imbalance in the relationship so that a new equilibrium is established and the disease may become arrested and remain stable over long periods of time. Transient imbalances in the host-parasite relationship are likely to occur frequently and yet the natural history of periodontal disease in humans usually spans decades, suggesting that equilibrium is rapidly restored and that for most of the time destruction is not continuous but is episodic in nature.

The etiopathogenesis of periodontal disease following withdrawal of oral hygiene procedures and the accumulation of dental plaque has been described as occurring in four stages:

Stages of periodontal disease

• The initial lesion • The early lesion • The established lesion	Gingivitis
• The advanced lesion	Periodontitis

The Initial Lesion

- The initial lesion of gingivitis develops within 2 to 4 days following the onset of plaque accumulation. The changes are histological and cannot be detected clinically.
- The lesion is localized to the tissue around the base of the histological sulcus and involves portions of the junctional and sulcular epithelium and a microscopic area of underlying gingival connective tissue.
- It is essentially an acute inflammatory response and within the inflammed area the vessels become dilated, accompanied by the formation of both a fluid and cellular exudates.
- Large numbers of predominantly polymorphonuclear neutrophilic leucocytes (PMN) extravasate from the vessels and migrate through the connective tissue to infiltrate the intercellular spaces of the junctional epithelium. They continue to migrate coronally and eventually enter the oral cavity through the base of sulcus.
- This transmigration of the junctional epithelium by PMN is a response to chemotactic stimuli released into and elaborated within the sulcular area.
- The transmigration of PMN causes disruption of the junctional epithelium and widening of the intercelluar spaces, which impairs the barrier functions of this tissue.
- Exudation of protein–rich fluid, due to increased vascular permeability, accompanies the cellular exudate. As the disease develops and the volume of fluid-exudate contains all classes of plasma proteins, notably immunoglobulins and complement, which may also play a role in controlling the initial bacterial challenges.

The Early Lesion

- The early lesion develops within 4 to 7 days following the onset of plaque accumulation and overlaps with and evolves from the initial lesion with no clear-cut dividing line.
- It develops at the site of the initial lesion, but as it evolves, the area of inflammed gingival connective tissue expands laterally and apically, particularly as a narrow band beneath the junctional epithelium, extending towards the cemento-enamel junction.

Clinical Features of Gingivitis

- Gingival tissue will become red or bluish red in color.
- It becomes swollen, which may be either localized or generalized in nature.
- The gingiva has a boggy or spongy consistency.

- Bleeding occurs either spontaneously or by slight provocation (e.g. tooth brushing) from gingiva.
- The gingival attachment level on the tooth surface remains unchanged.
- Radiographic changes in the bone are absent, as it is a superficial lesion.

The Established Lesion

- The established lesion of gingivitis develops within 2 to 3 weeks of the onset of plaque accumulation and evolves from the early lesion.
- Histologically, there is accentuation of the features of the initial lesion, but these changes are confined to a narrow band beneath the junctional and pathologically altered epithelium.
- There is further deepening of the gingival sulcus and further growth of subgingival plaque.
- The characteristic feature of the established lesion, which distinguishes it from the early lesion, is the shift in the inflammatory cell population within the infiltrated gingival connective tissue from predominantly lymphocytic (T cell) to predominantly plasma cell (B cell) type.
- Large amounts of immunoglobulins are present throughout the connective and epithelial tissue.
- There is continuing loss of collagen as the area of inflammation slowly expands.
- In areas away from the zone of destruction, there may be varying attempts at repair characterized by the formation of fibrous tissue.

Degradation of Extracellular Matrix

- Degradation of the extracellular matrix, especially collagen, in periodontal disease is of major importance, since destruction of the connective tissue attachment results ultimately in loss of the tooth.
- In health, normal collagen turnover is reflected in a balance between the relative rates of synthesis and degradation.
- The loss in disease could, therefore, be the consequence of a decreased rate of synthesis, increased rate of degradation, or a combination of both.
- Although, damage to fibroblasts in the inflammed area would result in decreased synthesis, increased degradation involving enhanced enzyme activity is the major factor.
- The destruction of the extracellular matrix may involve the activity of bacterial enzymes from the plaque, but is effected mainly by a family of enzymes, the metalloproteinases derived from host cells.
- These enzymes principally collagenase and stromalysin, are produced mainly by fibroblast, macrophages, and neutrophil leucocytes.
- In periodontal disease, the release of metalloproteinases is increased due to activation of host cells by a variety of cytokines , especially interleukin-1, generated in the inflammatory response to microbial plaque.

The Advanced Lesion–Chronic Periodontitis

- The advanced lesion corresponds to chronic periodontitis, a disease characterized by destruction of the connective tissue attachment of the root of the tooth, loss of alveolar bone, and pocket formation (Figs 18.1 and 18.2).
- Gingivitis in some patients may remain stable for years, in other, it either progresses slowly to periodontitis or, in a minority of patients, there may be rapid progression and advanced bone loss occurring at an early age.
- The earliest histological evidence of the progression of gingivitis to periodontitis is the extension of inflammation beneath the base

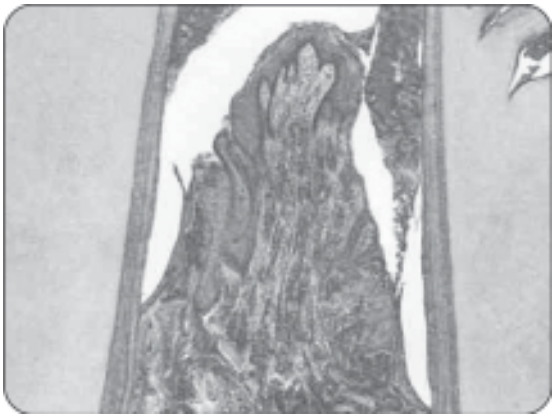

Fig. 18.1: Photomicrograph of periodontal pocket

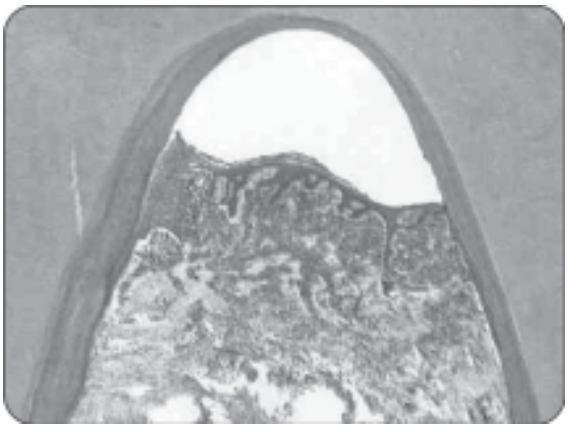

Fig.18.2: Photomicrograph of advance periodontitis with furcation involvement

of the junctional epithelium into the supra-alveolar connective tissue.

- Plasma cells dominate the infiltrate at all stages of the advanced lesions, although lymphocytes and macrophages are also present.
- As the area and density of the infiltrate increases there is destruction of collagen in the supra-alveolar connective tissue and the fibers loose their attachment to cementum.
- This is accompanied by apical migration of the junctional epithelium to cover the denuded root surface resulting in early true pocket formation.
- As the disease extends into the supporting tissue, there is progressive destruction of the fibers of the periodontal ligament accompanied by osteoclastic resorption of the alveolar bone.
- The junctional epithelium continues to migrate apically, resulting in progressive deepening of the pockets.
- As the junctional epithelium migrates apically, the more coronal and inflamed tissue loses its specialized attachment and is converted into pocket epithelium.

PATHOLOGICAL FEATURES OF ESTABLISHED PERIODONTITIS

- **Persistence of the features of established gingivitis**
- **Apical extension of destructive inflammation into:**
  - supra-alveolar connective tissue
  - alveolar bone
  - periodontal ligament
- **Predominance of plasma cells among the inflammatory infiltrates.**
- **Loss of connective tissue attachment into:**
  - destruction of collagen
  - apical migration of junctional epithelium
  - pocket formation
- **Destruction of alveolar bone**
- **Periods of quiescence/stability; episode of destruction**
  - attempts at healing

Clinical classification of periodontitis

Prepubertal periodontitis	A rare form affecting the deciduous dentition, that may be localized or generalized. Genetic factors and a variety of medical conditions may be associated.
Juvenile periodontitis	An uncommon form with onset in puberty and adolescence and relativity well-defined clinical features.
Rapidly progressive periodontitis	An uncommon form with onset in late adolescence and early adulthood, characterized by episodes of localized or generalized periodontal destruction. Many cases have associated with defects in leukocyte function.
Adult type periodontitis	The most common form of periodontitis typically seen in adults over the age of 30 years.

CLINICAL FEATURES OF PERIODONTITIS

Prepubertal Periodontitis

- Prepubertal periodontitis is a rare form of periodontitis presenting in childhood and involving the deciduous, and subsequently, the permanent dentition.
- It is characterized by extensive destruction of alveolar bone and is associated with a variety of uncommon systemic disease.
- Most involved abnormalities in number and/or function of PMN. Because of the deficient or defective neutrophils such patients are prone to severe systemic infections.

Conditions causing widening of periodontal ligament space

- Periapical abscess
- Current orthodontic therapy
- Trauma from occlusion
- Scleroderma
- Osteosarcoma of the jaw.

- The Papillon-Lefevre syndrome is characterized by skin lesions of palmar-plantar hyperkeratosis and severe periodontal destruction involving both the deciduous and permanent dentitions.
- It is probably transmitted as an autosomal recessive trait, but the mechanisms underlying the oral changes are uncertain, although a neutrophil abnormality has been reported.

Juvenile Periodontitis

- Juvenile periodontitis is a rare form of periodontitis, which commences in young people and is clinically distinct from the usual form of periodontitis seen in adults.
- It commences around puberty and there is a higher incidence in females.
- The disease is characterized by rapid destruction of alveolar bone with vertical bone loss resulting in deep infrabony pockets (Fig. 18.3).
- Initially, the permanent first molar and/or maxillary incisor teeth are affected, usually symmetrically, but the number of teeth involved increase with age.
- The pattern of involvement of teeth tends to follow their sequence of eruption.

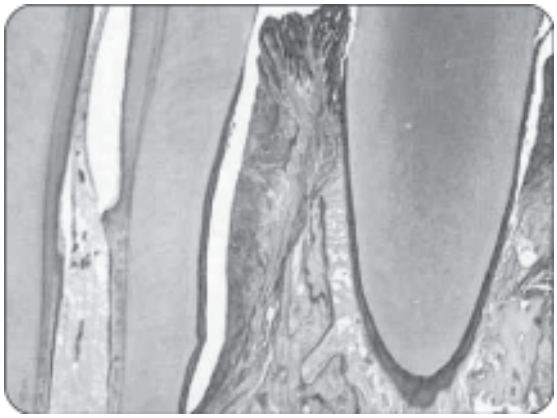

Fig.18.3: Photomicrograph of infrabony periodontal pocket

- The etiology and pathogenesis of the condition remain obscure.
- The lesions are inflammatory and bacterial plaque is the prime etiological factor, but the degree of destruction is not commensurate with the generally small amounts of plaque present.
- However, the subgingival flora in juvenile periodontitis is dominated by gram-negative anaerobic rods, particularly *Actinobacillus actinomycetemcomitans*. *Capnocytophaga* species and *Eikenella corrodens* may also be of etiological significance.
- In addition to a unique flora, host factors have also been implicated. In particular, a familial pattern has been found in several cases and there is increasing support for the suggestion that genetic factors are involved.
- Abnormalities in cell-mediated immunity and in PMN function have also been demonstrated.

Rapidly Progressive Periodontitis

- Less common than juvenile periodontitis, rapidly progressive periodontitis has an onset between puberty and 30 years of age but lacks well-defined characteristic.
- The periodontal lesions are severe and generalized with evidence of rapid bone destruction occurring within a few weeks or months.
- The gingiva my appear actually inflamed or relatively normal, and the amounts of microbial deposits are highly variable.
- Almost the entire dentition is usually affected and the disease may either progress without remission to tooth loss or subside and become quiescent.
- Vertical or angular bone loss occurs with marked difference in attachment loss between adjacent teeth or different surfaces of the same tooth.

Adult Type Periodontitis

- Adult type periodontitis is by far the most common form of chronic periodontal disease and is characterized by its chronicity.
- The onset of disease is in early adult life (or even before). But in the majority of patients

does not progress to tooth loss until after 50 years of age.
- A generally regular pattern of predominantly horizontal bone loss is seen with suprabony pocket formations.
- The entire dentition is usually involved, with the lower incisors and molar tending to show the maximum bone loss.

Factors affecting the prognosis of periodontal diseases

- Oral hygiene status
- Patient motivation
- Age of the patient
- Tooth factor
- Host resistance

GINGIVAL HYPERPLASIA

An increase in the number of cells causing tissue growth is called **hyperplasia** while an increase in the size of cells causing tissue growth is called **hypertrophy**.

Gingival hyperplasia refers to the excessive, exuberant proliferation of gingival tissue causing swelling or overgrowth of the gingiva.

Gingival hyperplasia may be of two types:

A. Inflammatory hyperplasia
B. Fibrous hyperplasia.

CAUSES OF GINGIVAL HYPERPLASIA

***Causes of inflammatory hyperplasia*:**
- Vitamin C deficiency (scurvy)
- Leukemias
- Chronic hyperplastic gingivitis
- Endocrine imbalance (puberty/pregnancy)
- Sarcoidosis
- Crohn's disease.

***Causes of fibrous hyperplasia*:**
- Heredity (genetic)
- Drug intake
- Orofacial angiomatosis
- Wegner's granulomatosis
- Idiopathic.

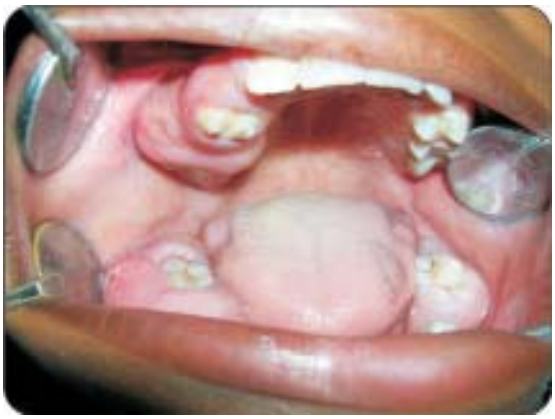

Fig. 18.4: Drug-induced gingival hyperplasia

Common drugs associated with gingival hyperplasia (Figs 18.4 and 18.5)

Anticonvulsants
- Phenytoin
- Carbamazepine
- Ethotoin
- Felbamate
- Mephenytoin
- Phenobarbital
- Sodium valproate

Calcium channel blockers
- Amlodipine
- Bepridil
- Diltiazem
- Nifedipine
- Verapamil

Cyclosporine

Erythromycin

Oral contraceptives

Gingival Hyperplasia Associated with Vitamin C Deficiency

Vitamin C helps in the synthesis of collagen by helping in the hydroxylation of proline and lysine.

Defective collagen synthesis in Vitamin C deficiency produces scurvy and the disease will have the following manifestations:
- The gingiva becomes tendered, edematous and swollen.
- It has a spongy consistency and bleeds frequently.

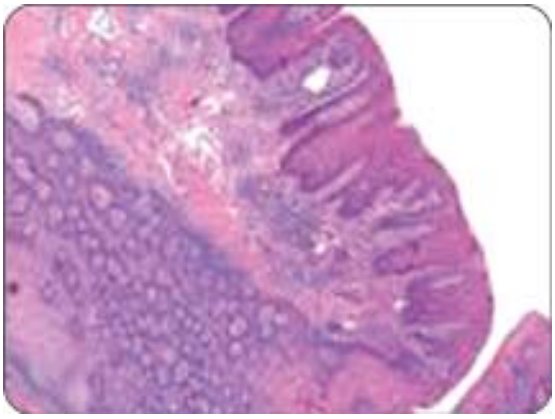

Fig. 18.5: Histopathology of drug-induced gingival hyperplasia

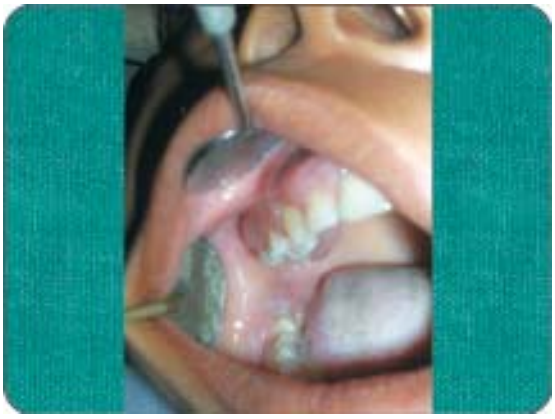

Fig. 18.6: Localized gingival hyperplasia

- The crest of the interdental papillae appear "red or purple"
- Ulceration and necrosis of the gingival tissue occurs commonly.
- Gingival sulcus is often filled with blood clot and there may be hemorrhage from any part of the body following slight trauma.
- Foul smell is often present in the mouth.

Administration of Vitamin C and improvement of the oral hygiene will cure the disease.

Gingival Hyperplasia Associated with Leukemias

Acute monocytic, lymphocytic or myelocytic leukemias often manifest intraorally by gingival hyperplasia, which occurs predominantly due to the infiltration of malignant cells into the gingival tissue.

Clinically the following manifestations develop:

- The gingiva becomes soft, edematous and swollen
- It is usually painful and has a purplish, glossy appearance.
- Pallor in the surrounding mucosa with development of petechiae or ecchymosis is often observed.
- Ulcerations and severe hemorrhage often occur in the gingiva. The diagnosis is confirmed through hematological investigations.

Gingival Hyperplasia Associated with Endocrine Imbalance

Abrupt hormonal changes often take place in the body during puberty or pregnancy, etc. and these conditions are often associated with gingival hyperplasia.

Hormonal imbalance mostly increases the proliferative potential of the gingival tissue in response to the irritations caused by plaque bacteria and local irritants.

Clinically the following manifestations will develop

- The gingiva becomes red, edematous and swollen.
- It may or may not be painful but bleeds frequently.
- Sometimes, a localized "tumor-like" growth may develop on the gingiva during pregnancy and it is often known as "pregnancy tumor" (Fig. 18.6).
- The condition regresses spontaneously after the pregnancy period is over.

No treatment is required except oral prophylaxis and maintenance of oral hygiene.

Gingival Hyperplasia Associated with Crohn's Disease

The Crohn's disease is characterized by granlomatous superficial ulceration of the intestinal epithelium, with frequent development of multiple fistulas. The disease produces the following oral manifestations.

- Granular, erythematous swelling of the gingiva.
- Ulceration and occasional bleeding is also reported.
- "Cobble-stone" appearance of the buccal mucosa with many linear hyperplastic folds
- Diffuse indurated swelling on the lips.
- Multiple ulcerations on the palate.

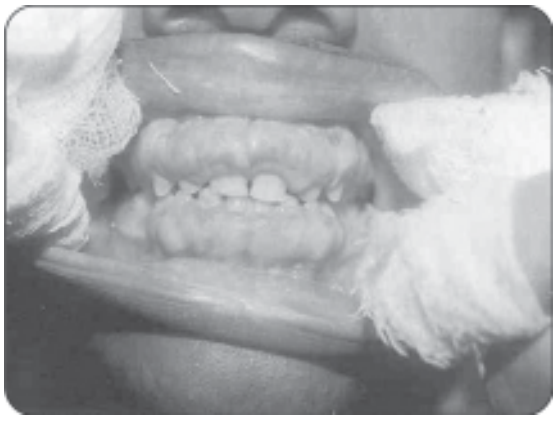

Fig.18.7: Dilantin hyperplasia of gingiva

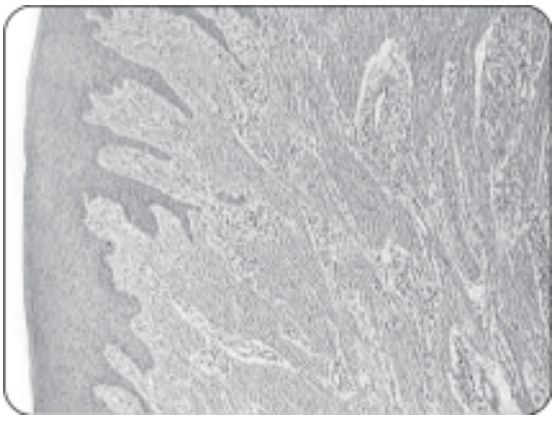

Fig. 18.8: Photomicrograph of dilantin hyperplasia

Gingival Hyperplasia Due to Dilantin Sodium Therapy

Dilantin sodium is an antiepileptic drug and use of this drug may induce gingival hyperplasia (as its side effect) (Figs 18.7 to 18.9).

Clinically the following Manifestations Develop

- The disease begins with painless enlargement of the interdental papilla.
- The swelling is rough, lobulated and has a pebbly surface.
- The gingival tissue is of normal color and often there is an increase in stippling.
- It is firm and dense, with no tendency to bleed.
- The gingival growth ceases after the drug therapy is stopped.

Beside dilantin sodium, gingival hyperplasia may also occur due to other drugs, e.g. nifedipine and cyclosporine, etc.

Hereditary Gingival Hyperplasia

Hereditary or familial gingival hyperplasia occurs among several members of the same family.

The gingiva is usually firm and resilient and is of normal color. Pain and hemorrhage, etc. are usually absent. In some patients, the gingival growth is so severe that it may cover up the entire crowns of the teeth and may even prevent the eruption of teeth in younger individuals.

Gingival Hyperplasia in Orofacial Angiomatosis

Angiomatous proliferation of the gingival blood vessels may sometimes cause gingival hyperplasia and in such cases, the gingiva clinically appears swollen and red. The enlargements may cause false gingival pocket formation on few occasions.

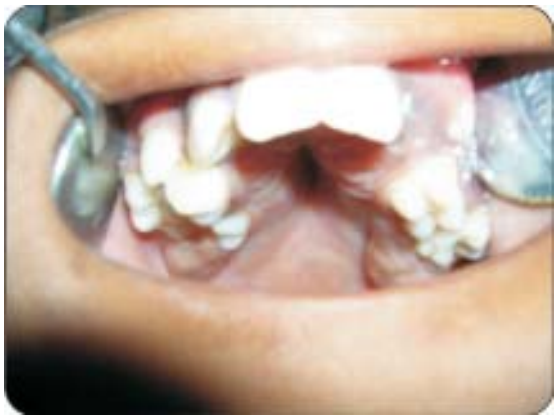

Fig. 18.9: Gingival fibromatosis

Gingival Hyperplasia in Wegener's Granulomatosis

Focal or diffuse gingival swelling can occur in Wegener's granulomatosis and the lesion is characterized by epithelial proliferation and dense inflammatory cell infiltration.

DESQUAMATIVE GINGIVITIS

DEFINITION

Desquamative gingivitis refers to the condition in which the gingival epithelium sloughs spontaneously or can be scrapped off with gentle rubbing.

Desquamative gingivitis is not a disease entity but a clinical term applied to the gingival manifestation of several different diseases.

CLINICAL FEATURES

- Clinically gingival tissue appears smooth, red, and edematous with loss of stippling; and there are areas of superficial ulceration, erosion or spontaneous desquamation of varying severity.
- Vesicles or bullae (filled with clear fluid or blood), white flecks or striae may also be seen depending on the underlying etiology.
- Severe pain, burning sensation and difficulty in food intake are the common complaints.
- The disease has a gradual onset and it initially affects only limited part of the gingiva, however with time, the disease spreads to involve larger areas of the gingival tissue.
- The involvement is patchy but the buccal and labial gingivas are more commonly affected than lingual or palatal tissues.
- The condition is more common in females (80 percent) than males and most cases occur after 30 years of age.
- Mucous membrane pemphigoid and lichen planus account for most cases of clinical desquamatic gingivitis.
- Other cases my represent local hypersensitivity reactions to various substances, for example tooth pastes, cosmetics. chewing-gums, and cinnamon, etc.
- The gingival reaction associated with chewing-gum hypersensitivity (has also been referred to as "plasma-cell gingivitis") widespread distribution of large numbers of plasma cells throughout the gingiva.
- Several other uncommon etiological factors have also been suggested, which include hormonal disturbances in menopausal females, unusual manifestations of chronic infection.
- Abnormal responses to dental plaque will exacerbate the inflammation and maintenance of adequate oral hygiene is important in management, but may be difficult because of soreness and bleeding associated with erosions.

ACUTE NECROTIZING ULCERATIVE GINGIVITIS (ANUG)

Acute necrotizing ulcerative gingivitis is a relatively rare condition and is characterized clinically by severe necrosis of the free gingival margin, the crest of the gingiva and the interdental papillae, etc.

Acute necrotizing ulcerative periodontitis is the advanced lesion of the same ulcerative process (ANUG) and occurs when the necrotizing process causes loss of epithelial attachment and spreads into the deeper tissues of periodontium, leading to periodontitis

ETIOLOGY

Acute necrotizing ulcerative gingivitis is a fuso-spirochetal disease and is caused predominantly by the fusiform bacilli and a spirochete called *Borrelia vincentii.*

Microorganisms often implicated in ANUG

- *Borrelia vincentii*
- *Fusobacterium fusiformis*
- *Prevotella intermedia*
- *Porphyromonas gingivalis*
- *Selenomonas sputigena*
- *Leptotrichia buccalis*

Interestingly, it has been observed that, the disease affects multiple numbers of people staying under the same living conditions. This often gives a false impression of the contagious nature of this disease.

Precipitating factors in ANUG

- Immunosuppression (AIDS, infectious mononucleosis)
- Sudden change in lifestyle.
- Poor nutritional status.
- Poor oral hygiene.
- Lack of rest and sleep.
- Local tissue damage local trauma.
- Recent debilitating diseases, (e.g. bacterial infections, diabetes, blood dyscrasias, etc).
- Emotional and professional stress.
- Down's syndrome
- Smoking.

CLINICAL FEATURES

- Acute necrotizing ulcerative gingivitis usually occurs among young and middle aged adults, between the ages of 15 and 35 years and males suffer more often than females.
- Stressed professionals like army recruits tend to suffer more (7 percent) from the disease than the normal population (1 percent).
- Moreover, young children suffering from malnutrition are also more vulnerable to the disease.
- Initially the gingiva becomes red, edematous, hemorrhagic and painful.
- Later, on, a sharply demarcated "**punched-out" crater-like erosion** of the interdental papillae occurs.
- The gingiva is often covered by a gray "**pseudomembrane**" with accumulation of necrotic tissue debris.
- Patient have pronounced spontaneous bleeding tendency, exquisite pain and an extremely unpleasant fetid odor in the mouth.
- Rarely, the gingival lesion may extend to the mucosal surfaces of soft plate and tonsils; and thereby resulting in the condition called **necrotizing ulcerative stomatitis**.
- Patients often develop headache, fever, malaise and lymphadenopathy, etc.
- Often there is difficulty in taking food due to increased salivation and a metallic taste in the mouth.
- When the necrotizing process leads to the development of periodontiris with loss of epithelial attachment the condition is called '**necrotizing ulcerative periodontitis**'.
- Most of the patients develop systemic manifestations in the form of leukocytosis, tachycardia and GI disturbance, etc.
- When the necrotizing process of ANUG extends further through the oral mucosa and reaches to the extraoral skin surface, the condition is called 'noma' or cancrum oris.

Key points of ANUG

- Predominantly affects young adult males
- People with smoking habits and history of minor respiratory infections are more prone.
- Punched-out ulcers occur at the tip of interdental papilla which spreads along the gingival margins.
- Gingival bleeding, soreness and extreme foul breath.
- The disease is caused by spirochaetes and fusiform bacilli.
- No significant fever, lymphadenopathy or systemic complications
- Responds well to metronidazole and good oral hygiene care.

HISTOPATHOLOGY

- The affected gingival tissue shows inflammation, ulceration and extensive necrosis.
- The gingival stratified squamous epithelium is often replaced by a thick, fibrinopurulent "pseudomembrane".
- The pseudomembrane usually consists of microorganisms, polymorphonuclear neutrophil (PMN), and necrotic tissue debris, etc.
- The unaffected areas of the gingival tissue show a general lack of keratinization.
- The underlying connective tissue shows intense hyperemia and inflammatory cell infiltration by PMN.

DIFFERENTIAL DIAGNOSIS

- Primary acute herpetic gingivostomatitis
- Erosive lichen planus
- Cicatricial pemphigoid
- Drug allergy.

TREATMENT

- Local debridement of necrotic tissue with H_2O_2.
- Administration of metronidazole, tetracycline and penicillin, etc.
- Oral hygiene motivation.

LATERAL PERIODONTAL ABSCESS

DEFINITION

The lateral periodontal abscess is a localized area of suppurative inflammation arising within the periodontal tissue alongside a tooth and is distinct from the more common periapical abscess.

ETIOLOGY

Most lesions arise in patients with pre-existing advanced periodontitis and it may occur either as a direct result of an increase in virulence and toxic factors released by plaque organisms or secondary to reduction in host resistance.

- Obstruction to the drainage of exudate from a pocket predispose to abscess formation. This may occur particularly in infrabony pockets pursuing a tortuous course around the root, or where fibrosis or edema in the superficial parts of the pocket causes tight approximation of the soft-tissue wall to the neck of the tooth.
- Impaction of foreign material, such as food debris, into a pocket may also lead to abscess formation.
- Following a traumatic injury to a tooth
- Lateral perforation of the root in endodontic therapy
- Stab infections, which arise when a foreign object, such as a toothbrush bristle or fish bone, penetrates the tissue introducing infection into the periodontal ligament.

CLINICAL FEATURES

- Clinically, periodontal abscess may be acute or chronic.
- An acute abscess develops rapidly and is accompanied by throbbing pain, redness, swelling, and tenderness of the overlying mucosa.
- The affected tooth is extremely sensitive to palpation, tendered to percussion but it is mostly vital.
- There can be sensitivity, mobility and/or extrusion of the adjacent teeth.
- The abscess may discharge spontaneously through the mouth of a pocket, but in deep-seated lesions or where drainage is obstructed, it may track and present with a sinus opening on the mucosa somewhere along the length of the root.
- Foul taste in the mouth is almost always present.
- The associated general symptoms include fever, malaise and lymphadenopathy, etc.
- Discharge of pus relieves the acute symptoms and the lesion may heal or become chronic with intermittent discharges.
- The chronic abscess may be asymptomatic or give rise to episodes of dull pain. Acute exacerbations are common.

RADIOGRAPHIC FEATURES

- Radiographic appearances are very variable and are influenced by the extent of previously existing bone destruction, the stage of the abscess, and its location.
- There is often extensive pocketing and abscess formation may be accompanied by rapid deepening of such defects, but in the early stages of an acute lesion there may be no associated radiographic changes.
- In deep-seated lesions, there may be a discrete radiolucent area along the lateral aspect of the root.

TREATMENT

- Drainage
- Antibiotics
- Elimination of the etiologic factors
- Surgical intervention.

PERICORONITIS

DEFINITION

Pericoronitis is inflammation of the soft tissue overlying the crown of an impacted or partially erupted tooth; and is seen commonly in association with mandibular third molars.

CAUSES

Pericoronitis mostly occurs due to accumulation of bacterial plaque and food debris in the space between the crown of the impacted or partially impacted tooth and the overlying gum flap; leading to inflammation. Other factors which may aggravate the condition include –opposing tooth biting on the gum overlying the impacted tooth and acute ulcerative gingivitis, etc.

CLINICAL FEATURES

- Inflammatory edema in the pericoronal tissue leads to swelling and pain in the gum flap around the tooth.

- The swollen pericoronal tissue predisposes to further trauma from the opposing teeth and this leads to exacerbation of the pain and inflammation.
- The usual symptoms of pericoronitis include pain, swelling, erythema, tenderness in the gum flap and a bad taste; it is associated with occasional oozing of pus from beneath the flap.
- Because of the pain and swelling it is difficult to close the jaws.
- The pain is generally very severe, which often radiates to the ear and floor of the mouth.
- Limitation of mouth opening due to trismus and discomfort on swallowing may be frequently present.
- Recurrent inflammation can result in severe localized ANUG-like necrosis of the tissue.
- In severe cases, an acute pericoronal abscess may develop, which can either remain localized or spread diffusely leading to cellulitis and space infections.
- In some cases, the inflammation in the pericoronal tissue may be chronic in nature; in which the clinical symptoms are very little.

TREATMENT

Treatment is done by antibiotic therapy, elimination of obstruction in the path of eruption of the involved tooth or extraction of the tooth whenever necessary.

STAINING OF TEETH

(A) EXTRINSIC STAINS OF TOOTH

Causes

- Tobacco
- Coffee, tea and cold drinks, etc.
- Chromogenic microorganisms
- Mouth washes, e. g. chlorhexidiene gluconate

Mostly the brown, black, green or orange stains are produced by the chromogenic bacteria and these occur commonly on the labial surfaces of maxillary anteriors in children.

Common Stains in Teeth

Yellow-Brown Stains

Chlorhexidine produces yellow-brown discoloration, especially on the proximal surfaces of teeth near the cervical region.

Black-Gray Stains

These staining mostly occur due to amalgam restorations and are more intense in young individuals as they have more open dentinal tubules.

Brown or Black Stains

These stains are produced by sulphides or silver nitrates. Brown and black stains appear either as a thin line along the gingival margin or as wide band on the tooth surface. These stains are commonly seen on the teeth located adjacent to the salivary gland duct orifices.

Brown Stains

Tobacco, tea and coffee, etc often cause brown discoloration of teeth; Smokers do have discoloration of lingual surfaces of mandibular incisors.

Green Stains

Green stains are generally produced by metals, e. g. copper and nickel, etc and these stains are usually seen on the labial surface of upper anterior teeth as a band and are probably caused by the blood pigments secondary to gingival hemorrhage. Green stains are produced due to excessive consumption of chlorophil containing foods.

Orange or Yellow Stains

Orange or yellow stains are formed on the gingival third of the teeth and are easily removed.

(B) INTRINSIC STAINS OF TOOTH

Causes of intrinsic stain	Color change in tooth
Aging	Yellow-brown
Death of pulp (non-vital tooth)	Gray-black
Fluorosis	White-yellow or yellow-brown
Tetracycline	Yellow-brown
Minocycline	Blue-gray
Internal resorption	Pink
Dentinogenesis imperfecta	Blue-gray
Amelogenesis imperfecta	Yellow-brown
Congenital porphyria	Yellow or brown-red
Erythroblastosis fetalis	Yellow-green
Jaundice	Yellow-green
Lepromatous leprosy	Pink or red

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CHAPTER 19

Oral Aspects of Dermatological Disorders

A large number of dermatological disorders may present with some oral lesions, either as a part of their manifestations or as the sole feature of disease. Most of these disorders have a diverse etiopathogenicity and, more importantly, few of them are potentially malignant in nature.

Diagnosis of dermal lesions usually depends on their oral and cutaneous manifestations, histopathology and immunohistochemistry, etc.

The features of some of the important dermatological diseases will be briefly discussed in this chapter.

HEREDITARY ECTODERMAL DYSPLASIA

Hereditary ectodermal dysplasia is an inherited X-linked recessive disorder, characterized by the defective formation of ectodermal structures of the body (e.g. skin, teeth, nails, sweat glands, sebaceous glands and hair follicles).

CLINICAL FEATURES (FIGS 19.1 TO 19.3)

- The three most outstanding features of ectodermal dysplasia are **hypohydrosis (lack of sweating), hypotrichosis (absence of hair) and hypodontia (absence of teeth).**
- The disease occurs more frequently among males than females.
- The patients often have soft, dry and smooth skin with little or no tendency for sweating; due to decreased number of sweat glands.
- Patients may have an unexplained fever, as release of heat from body through sweating is not possible and moreover they cannot endure warm temperature.
- The hair over the scalp, eyelashes and eyebrows are often fine, scanty and blond (Fig. 19.1).
- The sebaceous glands are also absent (asteatosis).

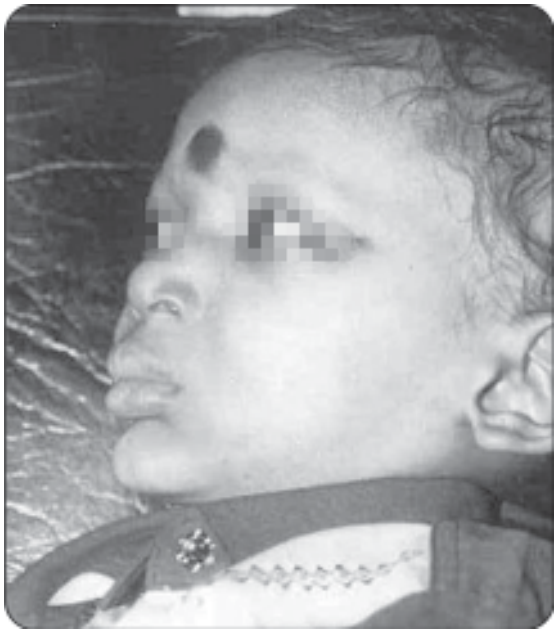

Fig. 19.1: Hereditary ectodermal dysplasia (typical facial profile)

- There is fine wrinkling and hyperpigmentations over the periocular skin.
- Patients have malformed finger nails which are often brittle.
- **Complete or partial anodontia** occurs that involves both deciduous as well as the permanent dentition (only the canines are often present).
- The teeth which may be present are often small and abnormal in shape; e.g. the incisors look tapered, conical or pointed while the molars look narrow and much smaller in diameter (Fig. 19.2).
- **Xerostomia** is a constant feature which occurs due to the decreased salivary secretion.
- The patient may also have rhinitis, sinusitis, pharyngitis, etc. with dysphagia and hoarsenoess of voice.

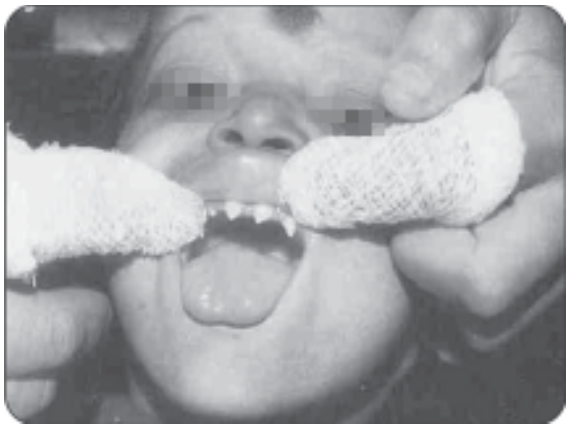

Fig. 19.2: Hereditary ectodermal dysplasia patient showing formation of only few conical shaped teeth

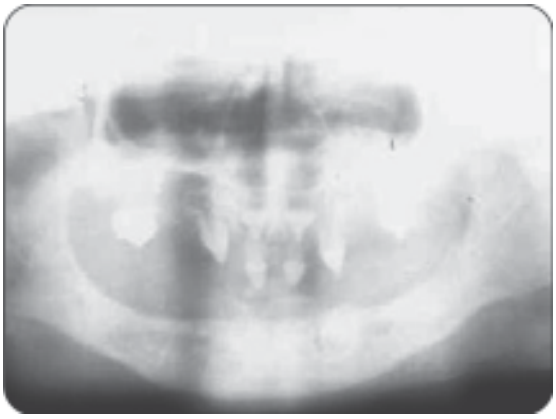

Fig. 19.3: Hereditary ectodermal dysplasia X-ray showing almost complete lack of tooth formation in lower jaw

- The patient frequently exhibits "pili torti" (kinky hair), cleft palate and popliteal pterygium.
- Patient with ectodermal dysplasia always have a typical facial appearance characterized by depressed nasal bridge, frontal bossing and protuberant lips, and because of this, most of the patients are often mistaken for siblings.

TREATMENT

The typical clinical manifestations always confirm the diagnosis of this disease and there is no specific treatment for it. Artificial dentures (with soft liners) are constructed and are changed from time to time to cope up with the growth of the jaws and artificial saliva is given to keep the mouth moist.

Key points of hereditary ectodermal dysplasia

- Ectodermal dysplasia is a hereditary disorder characterized by defective formation of ectodermal structures of the body, e.g. skin, teeth, nails, sweat glands, sebaceous glands and hair follicles.
- Hypohydrosis, hypotrichosis and hypodontia are the three most outstanding features of ectodermal dysplasia.
- Hypohydrosis or lack of sweating causes difficulty in releasing the body heat through sweating and the patients thus always have high body temperature.
- There is complete or partial lack of development of tooth and patients require artificial prosthesis from young age.
- **Xerostomia (dry mouth)** is a constant feature due to decreased salivary secretion.
- Patient have a typical facial appearance with depressed nasal bridge, frontal bossing, protuberant lips, etc.

PSORIASIS

Psoriasis is a common self-limiting, chronic inflammatory dermatological disease of unknown etiology. Some investigators believe that its occurrence is genetically determined. Psoriasis exhibits an increased proliferative activity of skin and mucous membrane.

CLINICAL FEATURES

- The disease occurs predominantly in the second and third decade of life. There is no sex predilection.
- Psoriasis clinically presents well-demercated, painless, dry, erythematuos patches with silvery scale on the surface.
- These lesions often develop on the skin over the elbows, knees, scalp, chest, face, etc.
- The patches are well-circumscribed and may be present for years on the skin, few lesions can even produce sterile pustules.
- The lesions enlarge at the periphery and the disease often shows periods of remissions and exacerbations.
- These skin lesions are often symmetrically distributed and these are more severe during

the winter and the condition is much better during the summer.
- The psoriatic lesions are mostly asymptomatic besides occasional complains of itching.
- Mental anxiety or stress often increases the severity of the disease.
- If the deep scales on the surface of the lesion are removed, one or two tiny bleeding points are often disclosed and this phenomenon is known as **"Auspitz's sigh".**
- Although rare, oral lesions of psoriasis present erythematous patches with white scaly surfaces over the lips, palate, gingiva, cheek, etc.
- Some lesions in the oral cavity may appear as well-defined, grayish-white or yellowish-white papules.
- In some cases, these oral lesions may resemble "*geographic tongue*".
- Sometimes psoriasis may be accompanied by arthritis and the condition is often called **"psoriatic arthritis"** and it can affect the TM Joint as well.

MICROSCOPIC FINDINGS

- The oral epithelium shows atrophy with hyperparakeratosis, absence of granular cell layer and elongation or clubbing of the rete-pegs.
- Intraepithelial microabscess formation (**abscess of Munro**) is an important histological finding of psoriasis.
- There is always an increased mitotic activity seen in the psoriatic skin or mucous membrane.
- The sub-epithelial connective tissue shows many dilated capillaries and perivascular infiltrations of lymphocytes or histiocytes.

TREATMENT

No treatment is required as the disease undergoes spontaneous regression.

PITYRIASIS ROSEA

Pityriasis rosea is a rare mucocutaneous disease, which probably develops as a result of some viral infections.

CLINICAL FEATURES

- The disease commonly occurs in children or young adults and it affects several people at a time.
- This disease often shows seasonal outbreaks and it is mostly **noticed during spring or autumn**.
- Clinically, pityriasis rosea presents **superficial, light red macules or papules over the skin**, which cause slight itching.
- A typical bright-red skin rash is present in the affected area about 10 to 15 days prior to the development of original macules or papules and this primary skin rash is known as "**herald patch**".
- Sometimes, the disease may be accompanied by low grade fever, headache, lymphadenopathy, etc.
- In the oral cavity pityriasis rosea develops **erythematous macules over the cheek, tongue, palate, etc**. These macules often have a central grayish area of desquamation.
- Oral mucosa in the affected areas also exhibits ulceration, vesicle formation and hemorrhage, etc.

HISTOPATHOLOGY

- The oral epithelium in pityriasis rosea exhibits hyperorthokeratosis or parakeratosis along with mild degree of acanthosis.
- Ulceration, hemorrhage and chronic inflammatory cell infiltration are found in the basal epithelium as well as in the juxta-epithelial connective tissue.

TREATMENT

Since, it is a self-limiting condition, no treatment is usually necessary.

INCONTINENTIA PIGMENTI

It is a relatively rare, serious type of inherited genodermatosis; which is transmitted as a sex-linked dominant trait.

CLINICAL FEATURES

- The disease occurs mostly during infancy. Although, it is more common among females, it is often **lethal among males**.

- Clinical manifestation begins to appear shortly after birth and is characterized by slate-grey pigmentation of the skin with formation of vesicles or bullae over the trunk and limbs.
- Lichenoid, papillary or verrucous lesions also develop in the skin.
- Oral mucosa exhibits patchy, plaque-like or verrucous looking white lesions on the buccal mucosa.
- Patients may also have epilepsy, strabismus with nystagmus, partial anodontia, etc.
- The teeth are small and cone shaped and the condition affects both deciduous as well the permanent dentitions.

HISTOPATHOLOGY

- During the verrucous stage of the disease, intra-epithelial vesicle formation is often seen with accumulation of large number of eosinophils.
- Dermal or submucosal accumulations of macrophages and melanin granuals are also seen.
- White areas display hyperorthokeratosis or parakeratosis with acanthosis.
- Individual cell keratinization is also sometimes seen.

TREATMENT

No specific treatment is available.

ERYTHEMA MULTIFORME

Erythema multiforme is an acute inflammatory dermatological disorder characterized by extensive blistering and ulcerations. The disease frequently involves skin, mucous membrane and sometimes the internal organs.

ETIOLOGY

Although the exact etiology of erythema multiforme is obscure, some precipitating factors have been identified, which are shown below in the table.

CLINICAL FEATURES

- Erythema multiforme frequently occurs between the age of 15 and 40 years and males are affected more often than females.
- The prodromal symptoms occur about one week before the onset of the disease and these include fever, malaise, headache, cough, sore throat, etc.
- Soon after rapidly developing round erythematous macules, papules or vesicles appear over the skin.
- These lesions develop symmetrically over the hands and arms, legs and feet, face and neck, etc.
- In severe cases, large bullae may also develop over the skin.

Precipitating factors in erythema multiforme

Infections	• *Tuberculosis* • *Herpes simplex (Type I and Type II) infections* • *Mycoplasma pneumoniae* • *Infectious mononucleosis* • *Histoplasmosis*.
Drug hypersensitivity	• *Barbiturates* • *Sulfonamides* • *Phenylbutazone* • *Salicylates* • *Oral pills*
Hyperimmune reactions	*Results formation of antigen-antibody complex against the sub-mucosal and dermal blood vessels.*
Miscellaneous factor	• *Radiation therapy* • *Crohn's disease* • *Vaccinations*

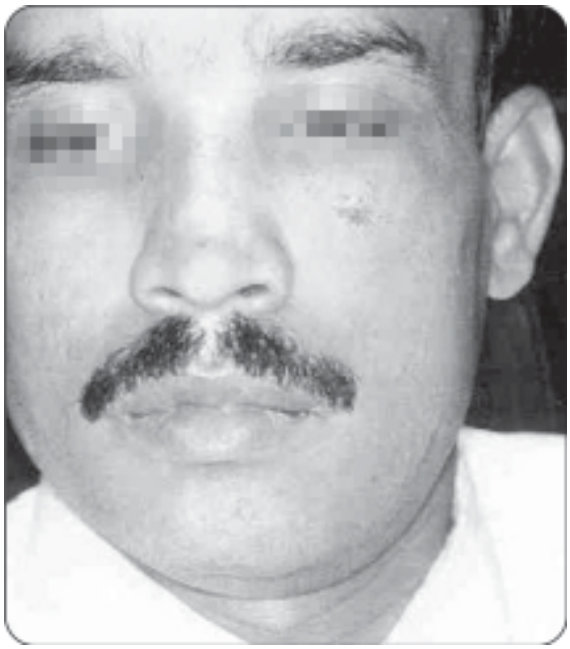

Fig. 19.4: Erythema multiforme showing ulceration of the facial skin with erythematous change

- The classic dermal lesions of erythema multi-forme which often appear on the extremities are called **"target", "iris" or "bull's eye",** etc.
- The target lesions are red macules of one centimeter or more in diameter with a bluish cyanotic center.They often consists of concentric erythematous rings separated by rings of near normal color on the skin.
- Severe form of erythema multiforme may cause widespread sloughing and ulceration of the skin, and the mucous membrane of the entire body (Fig. 19.4).
- Mucosal lesions in this disease also consist of macules, papules or vesicles, etc. and these are mostly seen on the tongue, labial mucosa, buccal mucosa, floor of the mouth, etc.
- The oral mucosal lesions are sometimes more prominent than the skin lesions and sometimes they are the only ones present.
- The vesicles of the mucosal surfaces are often short-lived and they readily become eroded or ulcerated and bleed profusely.
- However, new vesicles appear in the oral mucosa in about 10 days time and the process continues for nearly three to four weeks.
- The ulcers are diffuse, extremely painful, have irregular borders and are normally covered by a slough. These ulcers can be secondarily infected in many cases.
- Patients often complain of foul smell in the mouth and difficulty in eating or swallowing, these often lead to severe weakness and dehydration.
- The cutaneous and mucosal lesions may occur either separately or simultaneously.
- The entire disease process may recur in a cyclic order at an interval of few months and the cycle may characteristically continue for one to two years, with increasing in severity after every recurrence.
- Patients with erythema multiforme may also develop tracheobronchial ulcerations and pneumonia, etc.
- Erythema multiforme is a self limiting disease and it regresses spontaneously.
- The disease is uncommon among children and older individuals, however, if it occurs in the older people, the possibility of an internal carcinoma should not be ruled out.

Stevens-Johnson Syndrome

It is a severe form of erythema multiforme (**also known as erythema multiforme major**) that simultaneously involves the skin, eyes, oral mucosa and genitalia. This condition is often triggered by a drug and not by an infection.

The clinical features of this condition are as follows:

Skin Lesions

- Severe lesions of macules, papules, vesicles, bullae, etc. (as discussed earlier).

Oral Mucosal Lesions

- Large vesicles or bullae often develop which rupture and leave painful ulcers (Fig. 19.5).
- Pain and hemorrhage from the ulcers cause difficulty in taking food.
- Ulceration and bloody encrustation are often present on the lips.
- Mucosal lesions are self-limiting and complete healing, usually occurs in about two to three weeks time. Recurrence is common.

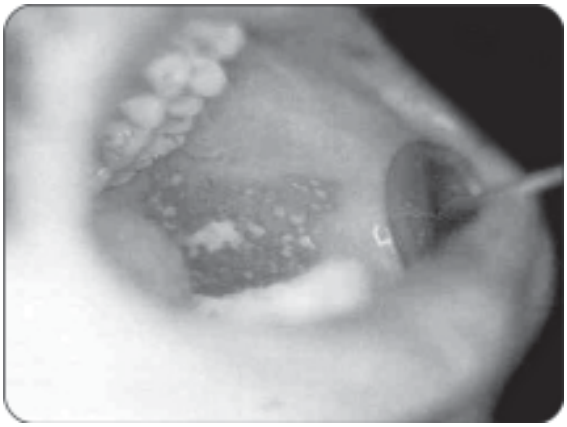

Fig. 19.5: Erythema multiforme producing intensely erythematous ulcerations of the buccal mucosa

Eye Lesions

- Photophobia
- Conjunctivitis
- Corneal ulceration
- Uveitis
- Blindness due to secondary infection.

Genital Lesions

- Urethritis
- Balanitis
- Vaginal ulceration.

HISTOPATHOLOGY

- The microscopic findings of erythema multiforme are often nonspecific, and they usually consist of acanthosis, intra- or intercellular edema alongwith widespread necrosis of the basal keratinocytes, etc.
- Vesicles or bullae may form within the epithelium or at the epithelium-connective tissue junction.
- Subepithelial connective tissue shows edema and perivascular infiltration of lymphocytes, neutrophils, eosinophils, macrophages, etc.

DIFFERENTIAL DIAGNOSIS

- Acute primary herpetic stomatitis
- Aphthous ulcers
- Pemphigus
- Pemphigoid
- Erosive lichen planus.

Key points of erythema multiforme

- Erythema multiforme is serious type of dermatological disorder characterized by extensive blistering and ulcerations of the skin and mucous membrane.
- Initially the disease produces rapidly developing round, erythematous macules, papules or vesicles over the skin.
- These classic dermal lesions of erythema multiforme often characteristically appear as **"target", "iris" or "bull's eye",** etc.
- Vesicles also appear over the oral mucosa, which rupture and produce diffuse, are extremely painful irregular ulcers with bleeding tendency.
- Stevens-Johnson Syndrome is the most severe form of Erythema multiforme; which simultaneously affect skin, mucosa, eyes and genitalia.
- The disease can cause trachea-bronchial ulceration and pneumonia.
- Sometimes erythema multiforme indicates the possibility of internal carcinoma.

TREATMENT

Topical and systemic steroid therapy, coupled with antibiotics.

DERMATITIS HERPETIFORMIS

Dermatitis herpetiformis is a rare chronic recurrent mucocutaneous disease of unknown etiology. The disease has some connection with the dietary gluten.

CLINICAL FEATURES

- The disease commonly occurs among middle-aged males.
- Initially there is pruritis with severe burning sensation in the affected areas of skin.
- Gradually, there is appearance of erythematous, papules or vesicles on the skin or mucous membrane.
- These lesions are commonly seen over the extremities, buttock, face, scalp, etc. and they often resemble *Herpes simplex*.
- The vesicular lesions often develop in crops and are symmetrically distributed.
- Oral lesions appear initially as vesicles but soon they rupture and leave painful ulcers.

HISTOPATHOLOGY

- Disruption of the superficial epithelium with subsequent ulcerations.
- Aggregation of eosinophils and neutrophils at the apex of the connective tissue papilla with formation of microabscesses.
- Subepithelial bullae or vesicle formation with destruction of basement membrane.

TREATMENT

Gluten-free diet and administration of Sulfapyridine.

KERATOSIS FOLLICULARIS

Keratosis follicularis is a hereditary disorder of the skin and is characterized by the formation of multiple crusted, greasy lesions that often produce foul odor.

CLINICAL FEATURES

- The lesions commonly develop over the face and neck of the young individuals.
- In the oral cavity, small white papules may appear on the gingiva, tongue, hard palate, cheek, etc.
- The erythematous hyperkeratotic papules develop on the skin over the trunk and scalp. These usually measure about 2 to 3 mm in diameter.
- The papules become grayish-brown with age.
- Smaller lesions coalesce together and thus gradually enlarge with time.
- Accumulation of keratin often gives a rough texture to the lesion. Moreover, bacterial desquamation of these keratin often produces foul smell in the lesion.
- Nails often have longitudinal lines or painful cracks.

HISTOPATHOLOGY

- Lack of cohesiveness among the surface epithelial cells is the hallmark of keratosis follicularis; and the disease microscopically reveals the presence of multiple clefts and lacunae within the epithelium.
- Often these clefts or lacunae contain two types of cells. The grain-like keratinized epithelial cells named **"corps grains"** and esoinophilic cells named **"corps ronds"**.
- Sometimes intra-epithelial bullae may appear with acantholysis and suprabasilar split and in such cases the lesions resemble pemphigus vulgaris.
- The epithelial rete ridges are narrow, elongated and they often have a '**taste-tube**' like shape.
- The epithelium is often hyperplastic with presence of chronic inflammatory cell infiltration in the lamina propria .

TREATMENT

By high doses of vitamin A therapy or steroids.

ACANTHOSIS NIGRICANS

Acanthosis nigricans is a rare cutaneous disease, which usually affects the flexural surfaces of skin and it has an occasional oral mucosal component.

TYPES

The disease usually has three types:

Benign type: Present at birth or during puberty. It is inherited as autosomal dominant trait and is never associated with internal malignancy. The benign type of acanthosis nigricans often occurs in association with various disease conditions, e.g. diabetes mellitus, hypothyroidism, acromegaly, Crouzon syndrome, chronic steroid therapy, etc.

Malignant type: Usually, develops after the age of 40 years and is invariably associated with internal malignancies like adenocarcinoma or lymphoma of the GI tract.

Pseudoacanthosis type: It is the most common form of acanthosis nigricans and in this type, lesions develop around body creases as a result of obesity.

CLINICAL FEATURES

- Skin lesions clinically present numerous, fine, velvety, confluent plaques with brownish pigmentation.
- These lesions predominantly occur on the flexural surfaces of skin over axilla, palms, soles, face, etc.

- Oral lesions are mostly seen in association with the malignant form of the disease.
- Dorsum of the tongue exhibits hypertrophy of the filiform papilla with development of a shaggy appearance.
- Tongue also presents some areas of papillomatous growth.
- Lip is grossly enlarged (mainly the upper lip) and its surface is dotted with small papillomatous nodules especially at the commissure.
- Gingiva also exhibits hyperplastic changes and the lesions are clinically similar to that of the fibromatosis gingivae.
- Buccal mucosa and palate exhibit a velvety white appearance with papillary projections in some areas.
- The pigmentations which are seen in the cutaneous lesions of the disease are often absent in the mucosal areas.

HISTOPATHOLOGY

- Thickening of the epithelium with marked acanthosis.
- Hyperorthokeratinization of the surface epithelium.
- Malignant form of the disease shows marked epithelial hyperplasia and acanthosis.

TREATMENT

There is no definitive treatment for this condition.

DYSKERATOSIS CONGENITA

It is a rare hereditary disorder of skin, which is inherited as a recessive trait.

CLINICAL FEATURES

- The disease commonly occurs during early childhood and it shows a definite male predominance.
- Nails exhibit abnormal dystrophic changes and they gradually shed in few days time.
- Skin shows grayish-brown pigmentations over the trunk, neck and thighs.
- Facial skin appears red due to atrophic or telangiectatic changes.
- Patients may also have mental retardation, thrombocytopenic purpura, aplastic anemia, dysphagia, deafness and hyperhydrosis of the palms, soles, etc.

ORAL MANIFESTATIONS

- Vesicles and bullae develop over the oral mucosa especially in the tongue and cheek; these lesions are followed by mucosal erosions and subsequent development of white leukoplakic patches.
- Oral mucosa may also have red, macular lesions or erythroplakic patches with superadded candidal infections.
- The leukoplakia lesions in the oral mucosa may turn into squamous cell carcinoma.
- Severe periodontal tissue destruction and loss of alveolar bone is often seen.

HISTOPATHOLOGY

- Oral mucosa exhibits hyperortho or hyperparakeratosis and acanthosis.
- In many cases there is presence of epithelial dysplasia.
- Skin lesions show increased vasculitis and increased number of melanin containing chromatophores.

DIAGNOSIS

Presence of anemia, leukopenia, thrombocytopenia, Fanconi's syndrome, etc.

TREATMENT

No treatment is needed. Periodic evaluations of the oral lesions are required to look for any suspected malignant transformation.

WHITE SPONGE NEVUS

White sponge nevus is a hereditary skin disease characterized by the occurrence of white, thickened, corrugated mucosal lesions in the oral cavity that often affects several members of the same family. The condition is genetically determined and occurs due to a defect in the normal keratinization process of the oral epithelium.

CLINICAL FEATURES

- The disease generally occurs at birth or during childhood and there is no sex predilection.
- Clinically oral lesions exhibit **symmetrically, thickened, white, folded or corrugated diffuse plaques, which develop bilaterally over the cheek.**

- The other common intraoral sites of this lesion include the palate, labial mucosa, tongue, gingiva, floor of the mouth, etc.
- Sometimes, these lesions may even develop in relation to the nasal, rectal or genital mucosa, etc.
- The oral lesions are asymptomatic, soft and spongy and they have a peculiar opalescent hue.
- Sometimes the shaggy white thickening can involve the entire oral mucosa.
- The surface of the lesion sometimes exhibit areas of desquamation.
- The border of the lesion is not clearly demarcated and the edges fade away gradually in the normal oral mucosa.

Key points of white sponge nevus

- White sponge nevus is a hereditary skin disease; which affects several members of the same family.
- Oral lesions produce symmetric, thickened, white, folded or corrugated diffuse plaques; which occur bilaterally over the cheek.
- The oral lesions have a peculiar opalescent hue and microscopically the disease presents mild to moderate hyperparakeratosis of the epithelium.
- Thickening of the spinus cell layer and intercellular edema often seen and there may be presence of some large "vacuolated" cells in the spinus layer.
- The abnormally prominent epithelial cell membranes produce a typical 'basket-weave' appearance.
- This is a self regressing disease and no treatment is required.

DIFFERENTIAL DIAGNOSIS

- Hereditary benign intraepithelial dyskeratosis
- Lichen planus
- Leukodema
- Hyperplastic candidiasis
- Leukoplakia
- Verrucous carcinoma

HISTOPATHOLOGY (FIG. 19.5A)

- White sponge nevus microscopically presents mild to moderate hyperparakeratosis of the epithelium with acanthosis and intercellular edema.
- There may be presence of some large "vacuolated" cells in the spinus cell layer having pyknotic nuclei.
- An eosinophilic condensation is sometimes noticed in the perinuclear region of the superficial epithelial cells.
- The abnormally prominent epithelial cell membranes produce a typical **"basket-weave"** appearance.
- The underlying connective tissue shows mild or no inflammatory cell infiltrations.
- Parallel striae of condensed parakeratin traverse the surface layers in oblique planes.
- There is no epithelial atypia or dysplasia seen in the epithelium.
- Individual cell keratinization may be seen in the spinus layer.

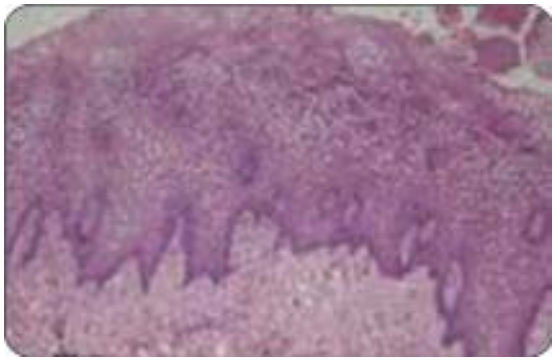

Fig. 19.5A: White sponge nevus

TREATMENT

No treatment is required for this self-regressing disease.

POLYMYOSITIS

Polymyositis is an inflammatory myopathy of unknown etiology, which commonly affects the skin.

CLINICAL FEATURES

- The acute form of the disease affects the people between the ages of 50 to 60 years while the chronic form of the disease occurs in children between the age of 5 to 15 years.
- In both forms, there is a definite female predilection observed.

- The disease clinically presents muscle pain, fever, malaise, arthralgic pain , weight loss, etc.
- A violaceous rash commonly develops over the cheek, eyelids and hands, etc.
- Death often occurs due to cardiorespiratory failure or infections.
- Oral mucosa reveals erythematous patches having lichen planus like appearance with swelling.
- Sometimes mucosal lesions may transform into malignancy and moreover some lesions of polymyositis may be associated with an internal carcinoma.

DIAGNOSIS

- Hypergammaglobulinemia
- Positive Rheumatoid factor
- Positive antinuclear factor.

TREATMENT

There is no specific treatment for this condition.

PEMPHIGUS

Pemphigus is a group of vesiculobullous lesions of the skin and mucosa membrane, which is characterized by the formation of intraepithelial vesicles or bullae causing separation of the epithelium above the basal cell layer.

Types of pemphigus

- ***Pemphigus vulgaris***
- ***Pemphigus vegetans***
- ***Pemphigus foliaceus***
- ***Pemphigus erythematosus***
- ***Brazilian pemphigus***

ETIOPATHOGENESIS

An **"autoimmune mechanism"** plays the major role in the development of pemphigus. Actually the patient develops immunoglobulin G (IgG) and complements in his or her body, which are specifically targeted against the intercellular cement substances **(desmosomes)** of the skin and mucous membrane.

Deposition of such **autoantibodies** in the skin or mucous membrane initiates an immune reaction, that eventually causes **destruction and dissolution of the desmosomal attachments** between the cells leading to the loss of adhesion between one cell to the other **(acantholysis).** Further accumulation of fluid in the region eventually leads to the development of **intra-epithelial bullae and a suprabasilar split in the epithelium.**

According to another theory, which is known as the "protease theory", deposition of auto-antibodies within the epithelium induces a proteolytic activity by activating the tissue plasminogens. This in turn generates proteolytic enzyme called "plasmin" that destroys the desmosomes.

Note

- ***Autoantibodies:*** When specific antibodies are produced against some of the body's own tissues or cells or cellular components.
- In case of pemphigus the antibodies are produced against the antigenic components of the desmosomes or the intercellular cement substances (desmoglein-3 and desmoglein-1).
- These autoantibodies attach to the desmosomal components and inhibit the molecular reaction that is responsible for cell to cell binding in the epithelium.

CLINICAL FEATURES OF PEMPHIGUS (FIGS 19.6 TO 19.10)

Pemphigus Vulgaris

- It is the most common type of pemphigus, which occurs between the ages of 40 to 70 years and it is more prevalent among females.

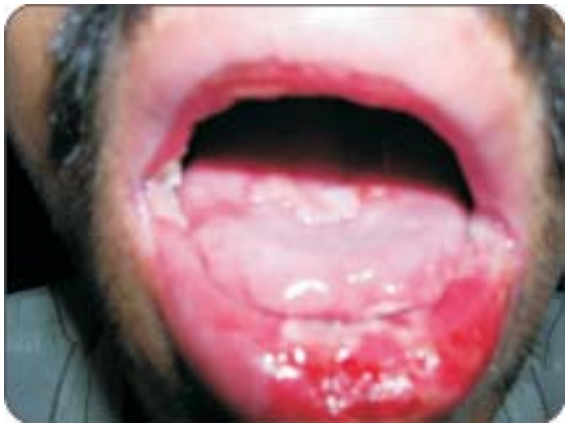

Fig. 19.6: Pemphigus-I

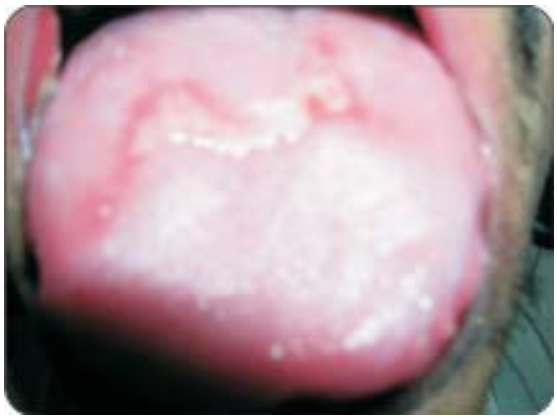

Fig. 19.7: Pemphigus vulgaris of tongue

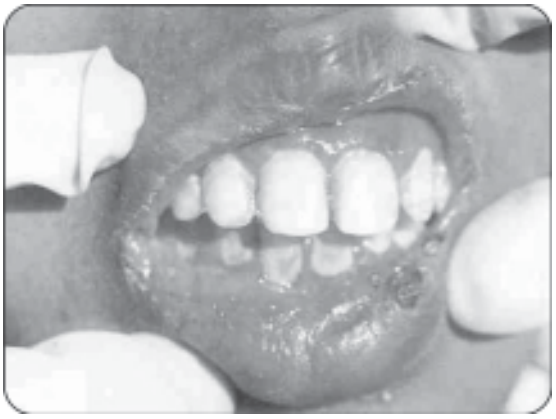

Fig. 19.10: Pemphigus vulgaris of the oral mucosa

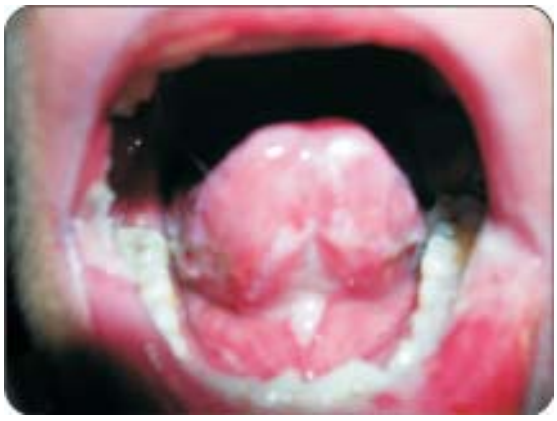

Fig. 19.8: Pemphigus-II

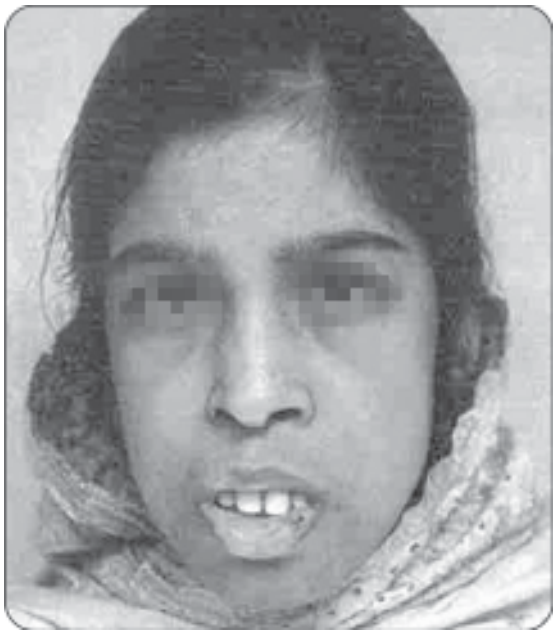

Fig. 19.9: Pemphigus vulgaris of lip

- Oral lesions often begin as **"bleb-like" blisters** or as **diffuse gelatinous plaques**.
- Soon rapidly developing vesicles or bullae on several areas of the skin and mucous membrane are found.
- The vesicles contain clear fluids initially but later on there is formation of pus.
- Often these lesions develop in the mouth and then spread widely on to the skin.
- The vesicles or bullae are fragile and rupture almost as soon as they form.
- Ruptured vesicles in the oral cavity often leave extremely painful, superficial, erythematous ulcers with ragged borders.
- The ulcers often bleed profusely and may be covered with blood-tinged exudates.
- Gentle traction or oblique pressure on the unaffected areas around the lesion causes denudation or stripping of the normal skin or mucous membrane, this phenomenon is known as **"Nikolsky" sign".**
- Skin lesions in pemphigus vulgaris usually appear over the scalp, trunk and umbilical area.
- Oral lesions of pemphigus vulgaris can be fulminating in nature since they not only exhibit widespread involvement of the oral mucosa but they can also spread rapidly to eyes and skin.
- Sometimes, the disease involves the entire body and in these cases the patient's condition becomes as serious as a severely burnt case, especially in terms of fluid loss and risk for secondary infections.

- Patient may die of dehydration and septicemia, etc.
- Skin lesions of pemphigus usually heal by scar formation but the mucosal lesions heal without scarring. However, oral mucosa often shows the formation of keratotic lesions following healing.
- Oral lesions in pemphigus vulgaris may involve any part of the oral cavity but are more frequently found in those areas which are often subjected to trauma, e.g. cheek, labial mucosa, ventral surface of tongue, palate gingiva, etc.
- Some ulcers can be very large in size causing severe pain and they usually take much longer time to heal.
- In over 60 percent cases of pemphigus vulgaris, oral lesions precede the skin lesions and in about 25 percent cases, they are the only manifestations of the disease.
- Patients with oral pemphigus vulgaris often have sore mouth with severe pain, excessive salivation, bleeding, difficulty in taking food and an extremely foul smell in the mouth.
- In some cases of pemphigus vulgaris, ocular lesions may develop in the form of bilateral conjunctivitis.

Pemphigus Vegetans

This is a common form of pemphigus lesion, which resembles the pemphigus vulgaris in all respects, but it has been observed that a papillomatous hyperplasia (vegetation) often occurs in this lesion following the rupture of the bullae.

Oral lesions are present in about 50 percent of cases of pemphigus vegatans.

The so-called 'cerebriform tongue' is a typical clinical sign of this disease.

Pemphigus Foliaceus and Pemphigus Erythematosus

Both are rare forms of pemphigus lesions and here the bullae formation is often associated with marked erythema of the involved skin. Both these lesions resemble exfoliative dermatitis and, rarely, there are any oral manifestations.

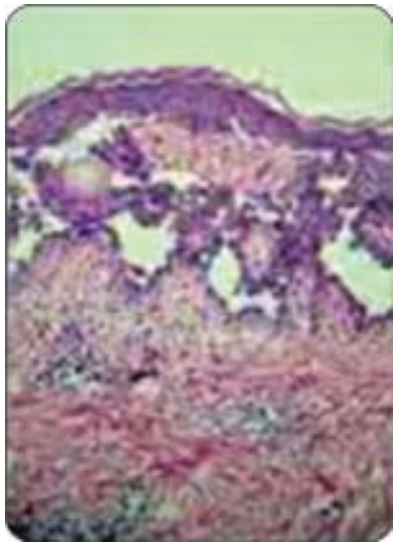

Fig. 19.11: Photomicrograph of pemphigus vulgaris showing suprabasilar split of the epithelium

Brazilian Pemphigus

It is an endemic form of pemphigus, which affects several members of the same family and is commonly seen in the costal areas of Brazil.

HISTOPATHOLOGY OF PEMPHIGUS

Pemphigus is, histopathologically, characterized by the following features:

- Formation of the vesicle or bullae within the epithelium that often results in a **supra-basilar spilt or separation (Fig. 19.11).**
- Following this suprabasilar spilt in the epithelium, the basal cell layer remains attached to the lamina propria, and it often appears as a row-of-tomb stones.
- Loss of intercellular bridges and collection of edema fluid result in **acantolysis** within the spinus cell layer, which causes **disruption of the prickle cells.**
- As a result of acantholysis, clumps of large hyperchromatic epithelial cells desquamate that are often seen lying free within the vesicular fluid, these desquamated cells are often rounded and smooth in appearance and are known as **"Tzanck cells"**.
- Small number of polymorphonuclear neutrophil (PMN) and lymphocytes may be found within the vesicular fluid, but there is

minimum inflammatory cell infiltration in the underlying connective tissue (unlike any other vesiculobullous lesion).

IMMUNOHISTOCHEMISTRY

- In pemphigus, immunofluoresence tests of the perilesional tissue often demonstrate the deposition of specific immunoglobulines (IgG), within the intercellular areas of epithelium.
- The intensity of the fluorescence is the greatest in the suprabasilar region (spinous cell layers), and gradually it becomes decreased towards the surface of the epithelium.
- Circulating autoantibodies against epithelial intercellular desmosomes are of disgnostic importance.

Key points of pemphigus

- Pemphigus is a vesiculobullous lesion of the skin and mucosa membrane; which occurs due to autoimmune destruction of the intercellular cement substance between cells.
- The disease produces rapidly developing vesicles or bullae on several areas of the skin and mucous membrane.
- Ruptured vesicles in the oral cavity often leave extremely painful, superficial erythematous ulcers with ragged borders.
- Gentle traction or oblique pressure on the unaffected areas around the lesion causes stripping of the normal skin or mucous membrane, this phenomenon is known as "Nikolsky's sign".
- Histologically, the disease is characterized by formation of intraepithelial vesicles or bullae, which causes separation of the epithelium above the basal cell layer.
- Loss of intercellular bridges and collection of edema fluid result in acantholysis within the spinus cell layer.
- Disruption of the spinus cells causes clumps of large hyperchromatic epithelial cells accumulating within the vesicular fluid; these desquamated cells are known as "Tzanck cells".
- The disease is treated by high dose of steroid therapy.

DIFFERENTIAL DIAGNOSIS

- Pemphigoid
- Erythema multiforme
- Bullous lichen planus
- Dermatitis herpetiformis
- Desquamative gingivitis
- Toxic epidermal necrolysis
- Aphthous ulcers
- Epidermolysis bullosa.

TREATMENT

- High dose of steroids
- Immunosuppressive drugs, e.g. azathioprine or methotrexate
- Antibiotics to prevent secondary infections
- Fluid and electrolyte balance must be strictly maintained.

PEMPHIGOID

Pemphigoid is a group of relatively uncommon, autoimmune vesiculo-bullous lesion; characterized histologically by the **subepithelial bullae formation in the basement membrane zone (BMZ)** of the skin and epithelium.

PATHOGENESIS

Progression of the disease pemphigoid occurs in the following mechanisms:

Formation of autoantibodies in the body against the antigenic components of the basement membrane zone.

↓

Binding of autoantibodies to hemidesmosome associated antigens in the basement membrane.

↓

Activation of complements, which attract inflammatory cells.

↓

Synthesis of chemotactic factors.

↓

Release of proteolytic enzymes (especially protease) by inflammatory cells.

↓

Protease causes destruction of hemidesmosomal junctions of the basement membrane zone.

↓

Formation of subepithelial vesicles or bullae.

Unlike pemphigus, **pemphigoid lesions usually heal up by scar formation (cicatrication).** However, the scarring mostly occurs in eye lesions and sometimes it can cause even blindness.

Although a large number of clinical variants of pemphigoid exist, the most common and the best understood among them are: (A) **cicatricial pemphigoid**, and (B) **bullous pemphigoid**.

The former lesion occurs commonly in relation to the mucous membrane, while the later one occurs frequently in relation to the skin. Pemphigoid is seen twice as common in females as in males and the mean age of occurrence is above 60 years. The disease is not life-threatening and though, it often runs a chronic course for many years.

Cicatricial Pemphigoid

Cicatricial pemphigoid is also known as benign mucous membrane pemphigoid (BMMP), and it frequently affects the middle-aged or elderly females.

The most common site of occurrence is the oral mucous membrane, followed by the conjunctiva. Sometimes the disease also involves the nose, pharynx, larynx, esophagus, genitalia, etc.

Clinical Features

Oral Lesions

- In the oral cavity, cicatricial pemphigoid usually produces slowly progressive, mild erosion or desquamation of the gingival tissue.
- Vesicles or bullae arise from mucosal areas, which become erythematous earlier (Fig. 19.13).
- In severe cases, large vesicles or bullae may develop on the palate, cheek, alveolar mucosa or tongue, etc.
- Bullae are sometimes quite large in size and they persist for several days (In contrast, the vesicles or bullae in pemphigus do not persist and they rupture as soon as they form).
- Skin lesions occur in about 5% cases and mucosal lesions always precede the skin lesions.
- The mucosal bullae are often tense and are relatively tough because these are usually covered by a full thickness epithelium.

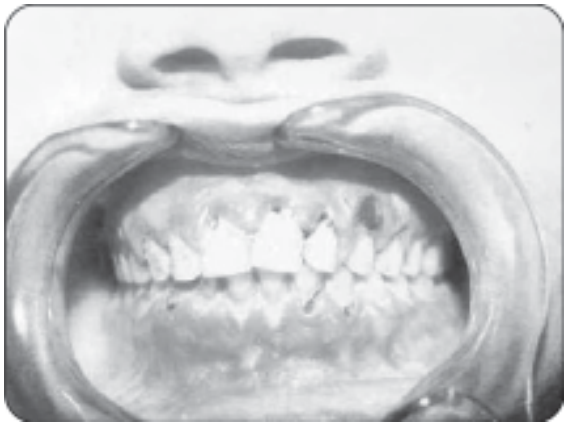

Fig. 19.12: Ulcerative lesions of gingiva in a patient with pemphigoid

- Bleeding into the bullae can make them look like blood blisters.
- Once the bullae rupture, they leave large painful, eroded or ulcerated areas, which heal up slowly (Fig. 19.12).
- Further erosions may occur in the adjoining areas and the process continues for long.
- The gingival lesions are very common (seen in about 90 percent cases) and they characteristically present either patchy erythema with mild discomfort or severe erythema, widespread desquamation, ulceration, etc.
- Sometimes these gingival lesions are the only manifestations of pemphigoid and the so called **desquamative gingivitis** can be the only manifestation of the disease.
- Pain and bleeding are the common complaints and **Nikolsky's sigh** is typically positive.
- Irritation from denture, calculus and plaque can exacerbate the condition.
- Secondary infection often occurs in pre-existing pemphigoid lesions and oral lesions usually heal up by scar formation.
- Involvement of the pharynx, esophagus and larynx may produce discomforts like sore throat, dysphagia, strictures, etc. some patients may develop septicemia.

Eye Lesions

- Conjunctivitis.
- Blister formation in the eye.
- Corneal ulceration.
- Swelling of the fornix and corneal opacity.

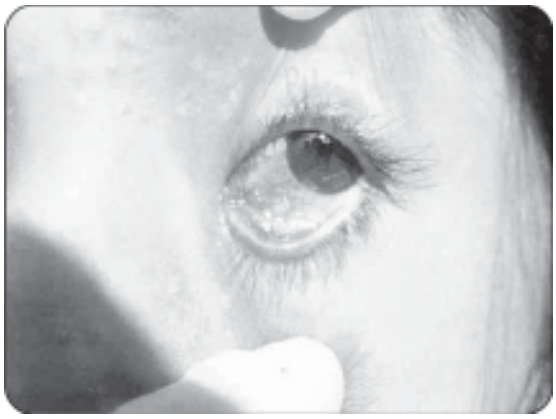

Fig. 19.13: Vesicle formation near the inner canthus of eye in pemphigoid

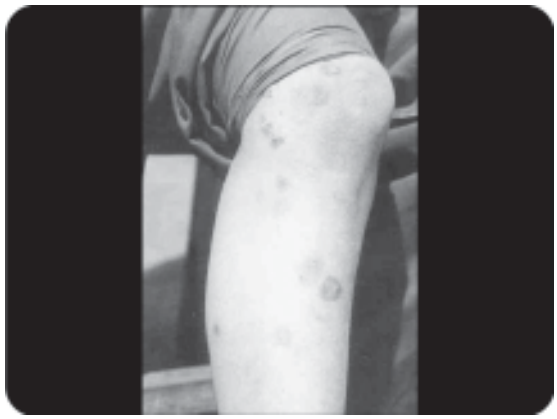

Fig. 19.14: Vesiculobullous lesion of skin in pemphigoid

- Fibrosis and scarring of the lacrimal ducts, which often leads to "**dry eye**".
- Scarring may cause adhesions between the bulbar and the palpebral conjunctiva.
- Scarring of the conjunctival mucosa results in blindness.

Skin Lesions

The skin lesions are rare in cicatricial pemphigoid and occasionally few large, tense and fluid-filled vesicles or bullae may appear over the face, scalp or neck.

Bullous Pemphigoid

Bullous pemphigoid occurs more commonly on the skin and it seldom affects the oral mucosa.

Clinical Features

- These lesions also follow the usual clinical patterns of vesiculation, followed by ulceration and finally healing (without scarring).
- Elderly people in the age group 70 to 80 years are usually affected, and there is no gender predilection.
- The skin lesions mostly occur over the trunk and limbs, and usually undergo spontaneous regression (Fig. 19.14).
- Skin lesions begin as red, eczematous plaques which eventually progress to the formation of bullae.
- Skin lesions always precede the mucosal lesions and these mucosal lesions are always smaller than that of the cicatricial pemphigoid.
- Bullous pemphigoid having oral lesions may be associated with internal malignancy.

Histopathology of Pemphigoid

- Extracellular edema and vacuolation in the basement membrane zone are the earliest histological changes in cicatricial pemphigoid.
- Gradually, there is formation of subepithelial vesicles or bullae (Fig. 19.15).
- The subepithelial bullae cause separation of the full thickness epithelium from the underlying lamina propria and thus the epithelium forms the roof of an intact bullae till it is ruptured.
- Acantholysis and epithelial degenerative changes are absent.
- Polymorphonuclear neutrophils (PMN) may be found within the vesicular fluid.

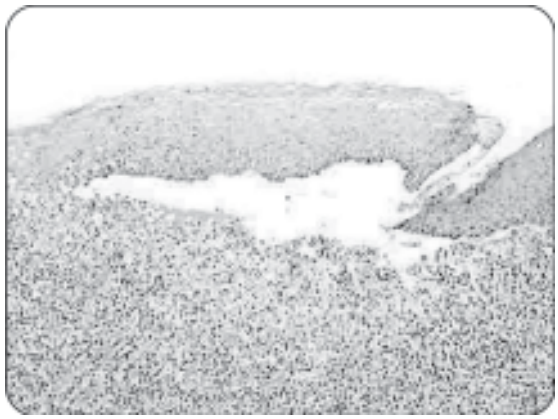

Fig. 19.15: Photomicrograph of pemphigoid showing subepithelial bullae formation

Key points of pemphigoid

- Pemphigoid is a relatively uncommon, autoimmune vesiculobullous lesion. It is characterized by subepithelial bullae formation in the basement membrane zone (BMZ).
- The disease produces large vesicles or bullae in the skin and mucous membrane; which rupture after a certain period and leave painful ulcers.
- Pain, bleeding and secondary infection are the common problems caused by these ulcers.
- Nikolsky's sigh is typically positive in this disease.
- Besides the dermal lesions eye lesions also commonly develop in Pemphigoid.
- The eye lesions include conjunctivitis, blister formation in the eye, corneal ulceration, fibrosis of the lacrimal duct leading to dry eye, etc.
- Histologically, pemphigoid presents formation of subepithelial vesicles or bullae at the basement membrane zone which causes separation of full thickness epithelium from the underlying connective tissue.
- Systemic steroid therapy is the treatment of choice.

- Subepithelial connective tussue shows inflammatory cell infiltration by lymphocytes, macrophages and eosinophils in the perivascular areas.
- Blood vessels are often dilated and prominent in the superficial part of the lamina propria.

Treatment

Systemic steroid therapy is the treatment of choice in both forms of the disease.

EPIDERMOLYSIS BULLOSA

Epidermolysis bullosa is a generalized desquamating condition of the skin and mucosa which is often associated with scarring, contractures and dental defects.

In epidermolysis bullosa, there is a separation of the epithelium from the underlying connective tissue with formation of large blisters, which often heal with extensive and often immobilizing scar formation.

Several forms of epidermolysis bullosa have been recognized, and these lesions are divided into two broad categories:

A. Hereditary epidermolysis bullosa
B. Acquired epidermolysis bullosa.

The hereditary forms of epidermolysis bullosa include epidermolysis bullosa simplex, epidermolysis bullosa dystrophic and junctional epidermolysis bullosa.

There is only a single form of acquired epidermolysis bullosa, and it is named as epidermolysis bullosa aquisita. This acquired from of the disease may be associated with multiple myeloma, diabetes mellitus, tuberculosis, amyloidosis, crohn's disease, etc.

CLINICAL FEATURES

- All forms of the disease are characterized by the formation of multiple vesicles or bullae on the pressure areas of the skin (i.e. elbows and knees).
- Dystrophic type is the most severe from of the disease and it may cause death secondary to septicemia.
- The bullae rupture and leave raw, painful ulcers, which heal up with scarring.
- The healing of skin lesions cause extensive scarring with pigmentation or depigmentation of the area.
- Nails often shed or exfoliate due to formation of blisters in the nail beds.
- The hereditary forms of the disease are usually very severe in nature and occur during infancy or early childhood, whereas the acquired form of the disease is common during adulthood only.
- Patients with hereditary epidermolysis bullosa may also exhibit stunted growth, mental retardation, ectodermal dysplasia, etc.
- The patients may have alopecia and claw-like hands due to repeated scarring and contractures.
- Many such patients die during childhood.

ORAL MANIFESTATION

- Oral lesions are particularly common and severe in relation to the hereditary forms of the disease.
- The features include rapidly developing, multiple, fragile and hemorrhagic blisters or bullae in the areas of trauma (particularly in the palate).

- The lesions rupture soon and leave painful ulcers, which later on heal by scarring.
- Repeated blistering and scarring around the oral cavity result in decreased mouth opening (microstomia), ankyloglossia and loss of vestibular sulci.
- Some patients may develop perioral and perinasal crusted and hemorrhagic granular lesions.
- Sometimes oral lesions may transform into squamous cell carcinoma.
- Hypoplastic pitted enamel of the molar teeth may occur in a few cases of epidermolysis bullosa.
- Patients may exhibit delayed eruption of tooth, increased caries susceptibility and increased periodontal diseases.

HISTOPATHOLOGY

- Extensive destruction of the basal or the suprabasal layers of the oral epithelium, results in the formation of vesicles or bullae.
- Bullae formation may also be seen within enamel organ of the developing tooth germ.
- Mucosal bullae formation occurs at different planes in various forms of epidermolysis bullosa and these are explained in the following sections.

Mucosal bullae formation

Disease types	Level at which bullae forms
Simplex type	Intraepithelial bullae.
Junctional type	At the level of lamina lucida
Dystrophic type	At the level of sublamina densa
Acquired type	At the level of sublamina densa.

TREATMENT

- Systemic steroid therapy
- Immunosuppressive drug therapy
- Avoidance of trauma.

LUPUS ERYTHEMATOSUS

Lupus erythematosus is an autoimmune disorder, characterized by the destruction of tissue due to the deposition of autoantibody and immune complexes within it. Production of autoantibody, particularly the **antinuclear antibody** is the hallmark of lupus erythematosus.

PATHOGENESIS

Pathogenesis of lupus erythematosus is not clearly known. It is believed that autoimmune reactions cause changes within the basal cells of the skin or mucous membrane along with the collagen and vascular tissues. Autoantibodies to DNA and other nuclear and ribonuclear protein antigens are present in blood. The circulating autoantibodies cause cross reactivity with antigenic determinants on multiple tissues.

The disease occurs in two basic forms.

A. Systemic lupus erythematosus (SLE), and
B. Discoid lupus erythematosus (DLE).

Systemic Lupus Erythematosus (SLE)

SLE frequently produces lesions in the skin and oral mucous membrane, and besides this, it also involves certain other body systems.

Clinical Features of SLE

Skin lesions

- Systemic lupus erythematosus (SLE) occurs in about 0.1 to 0.4 percent individuals.
- Skin lesions of SLE are characterized by the development of fixed, erythematous rashes that often have a **"butterfly configuration" (Fig. 19.16)** over the malar region and across the bridge of the nose.
- In some cases, the rashes may spread diffusely and have a wide area of skin involvement.
- These skin rashes produce itching or burning sensation, which is often aggravated by the

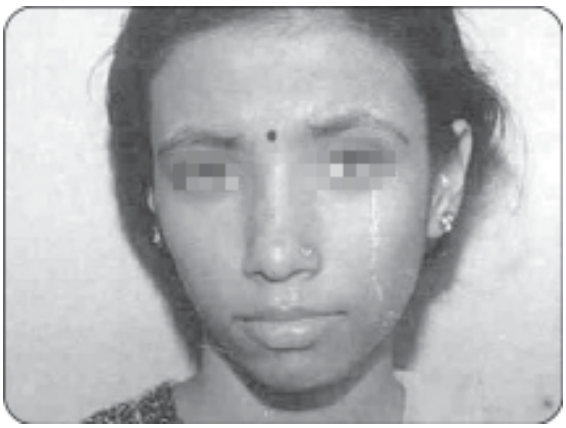

Fig. 19.16: SLE patient showing erythematous rash on the facial skin

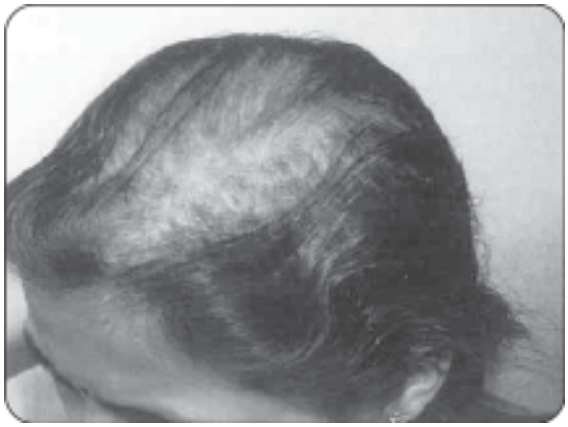

Fig. 19.17: SLE patient showing loss of hair over the scalp

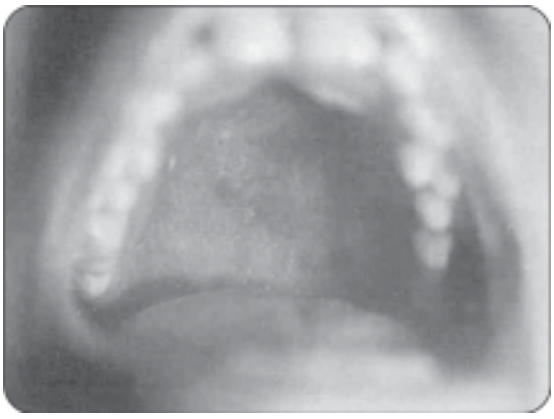

Fig. 19.18: Intense erythema in the oral mucosa with areas of ulcerations in SLE patient

exposure to sunlight. The disease often causes hyperpigmentation of the skin.

- The diseases affect females five times more often than males and it is mostly detected in the fourth decade of life.
- Patchy or extensive loss of hair from the scalp is a very common (Fig. 19.17) clinical finding in lupus erythematosus (hair may grow once again after successful treatment in case of SLE, but not in case of DLE).

Oral Lesions

- Oral lesions occur in about 20 percent cases of SLE and these lesions are usually white, hyperkeratotic plaque-like areas and resemble lichen planus.
- Oral and nasopharyngeal ulcerations are recognized as the major diagnostic manifestations of SLE (Fig. 19.18).
- Occasionally, there may be presence of erythematous lesions in the oral cavity.

Systemic manifestations of SLE

General problems	Fever, weight loss, fatigue, malaise, vomiting, diarrhea, anorexia, lymphadenopathy, etc.
Skin	Rashes with itching sensation and the rash often have butterfly configuration
Serous membrane	Pleurisy and endocarditis
Lung problem	Pneumonitis
G I Tract involvement	Pancreatitis, hepatomegaly and splenomegaly
Ocular disturbances	Conjunctivitis and retinal damage
CNS disturbances	Neuroses, psychoses, depression, strokes and cranial nerve palsies.
Hematologic disorders	Anemia, purpura and leukopenia
Cardiac problems	Vegetations in the heart valves (Libman-Sacks endocarditis) and myocarditis.
Renal problems	Profuse proteinurea, nephritic syndrome and fibrinoid degeneration of the glomerular capillaries, which may lead to renal failure.
Joint problems	Non-deforming arthritis and arthralgia
Mouth	Stomatitis and Sjogren's syndrome
Disease often coexisting with SLE	Sjogren's syndrome, Raynaud's phenomenon, scleroderma, pemphigoid, erythema multiforme and pemphigus

- Often there is formation of hemorrhagic macules in the oral mucosa that becomes frequently ulcerated.
- Ulcerated lesions are often painful and are surrounded by a red halo.
- Severe burning sensation in the oral mucosa is often present and the affected area is extremely tendered to palpation.
- Oral lesions mostly occur over the buccal mucosa, palate, gingival, etc.
- The vermillion border of the lower lip is sometimes affected and the condition is known as "**lupus cheilitis**".
- Purpuric lesions, e.g. petechiae and ecchymosis, etc. are frequently seen in the oral mucosa.
- **Secondary infections** frequently occur to these mucosal lesions (mostly candidiasis).
- There may be involvement of salivary glands in SLE, which causes **secondary Sjogren's syndrome** and severe **xerostomia**.
- Besides xerostomia, patients may also suffer from altered taste sensations, sore mouth, chronic periodontal disease, nasopharyngeal ulcerations, etc.
- In some cases, oral lesions may undergo malignant transformations.

Key points of lupus erythematosus

- Lupus erythematosus is an autoimmune disorder, characterized by destruction of tissue due to the deposition of autoantibody and immune complexes within it.
- The disease occurs in two forms- Systemic lupus erythematosus (SLE) and Discoid lupus erythematosus (DLE).
- Systemic lupus erythematosus presents characteristic fixed, erythematous rashes with a "butterfly configuration" over the malar region and across the bridge of the nose.
- In the oral cavity SLE produces white, hyperkeratotic plaque-like and resembles lichen planus. Involvement of salivary glands in SLE often results secondary Sjogren's syndrome and severe xerostomia.
- Systemic manifestations of SLE include hepatosplenomegaly, pneumonia, cardiac problem, renal problem, GI disturbances, neural problem, etc.
- DLE clinically presents multiple, white plaques with central atrophy, shallow ulcers, reddish purple erosions, etc.
- Histologically, SLE produces atrophy with hyperkeratinization and liquefactive degeneration of the basal cell layer of epithelium.
- Systemic steroid therapy is the treatment of choice in both forms of the disease.

Histopathology

The oral lesions present the following histopathological findings:

- Atrophy with hyperkeratinization of the oral epithelium
- Liquefactive degeneration of the basal cell layer
- Edema of the subepithelial connective tissue with vascular dilatations
- Lymphocytic infiltration and fibrinoid degeneration of the collagen fibers.

Discoid Lupus Erythematosus (DLE)

DLE is a dermal lesion in which, oral lesions are also commonly seen and unlike SLE this disease is not associated with autoantibody productions. DLE also occurs commonly among females and the usual age is the third and fourth decades of life. The disease commonly involves the skin over the back, chest and extremities, and the oral mucous membrane.

Clinical Features of DLE

Skin Lesions (Fig. 19.19)

- These are slightly elevated, red or purple macules, which are often covered by a yellow or gray scale.
- Skin lesions of DLE also present a butterfly distribution over the malar region and across the nose.
- Upon forceful removal of the covering scale, numerous "carpet track" extensions of the pialo-sebaceous channels appear.
- Skin lesions in DLE usually enlarge at the periphery and in some cases, epidermoid or basal cell carcinoma may develop from these lesions.

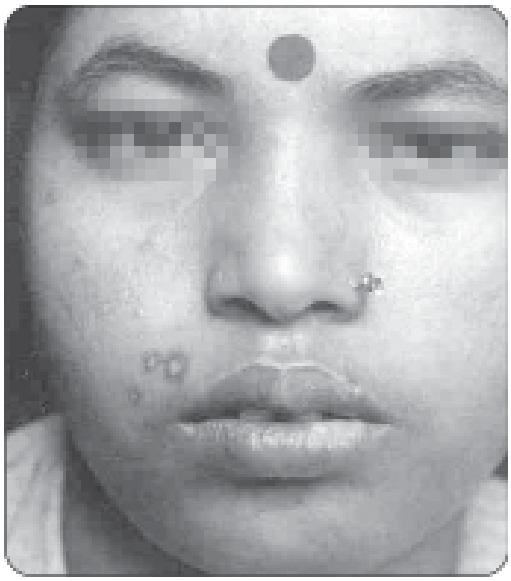

Fig. 19.19: Small erythematous lesions on the facial skin in a patient with DLE

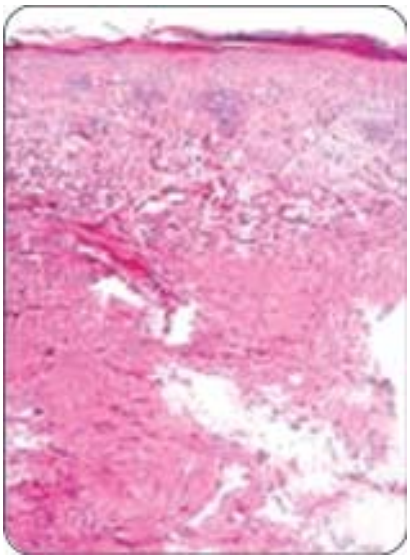

Fig. 19.20: Photomicrograph of mucosal lesion of DLE

- Involvement of scalp with loss of hair is also common.

Oral Lesions

- The oral lesions of DLE include multiple white plaques with central atrophy, shallow ulcers, reddish purple erosions, etc.
- These mucosal lesions frequently involve cheek, lips, gingiva, palate, etc.
- The lesions initiate at a particular point and then gradually extend peripherally to cover a wider area.
- As the white plaque of the oral cavity extends peripherally, its central area becomes red and ulcerated while the border remains white and keratotic.
- Small white dots are often present on the oral mucosa with a slightly elevated border.
- Pain and burning sensations are common in the mouth in DLE.
- Small slit-like ulcers are often seen near the gingival margin.
- Often these oral lesions resemble leukoplakia.
- Erythema or ulcerations in DLE may be surrounded by a white keratotic border, which can also have radiating striae.

Histopathology (Fig. 19.20)

Oral lesions of DLE present the following histologic findings:

- Hyper-ortho or parakeratinization of the surface epithelium.
- The epithelium may be atrophic in some cases.
- Few lesions exhibit keratin plugging, acanthosis and pseudo-epitheliomatous hyperplasia.
- Liquefactive degeneration of the basal cell layer.
- Basophilic degeneration of the collagen with sign of hyalinization and perivascular lymphocytic infiltration in the lamina propria.
- Inflammatory cell infiltration typically extends deep into the connective tissue.
- PAS positive thickening of the basement membrane zone and narrow blood vessels are seen, which occur due to deposition of antigen-antibody complex.
- Vasculitis occurs commonly in SLE but it is not seen in DLE.

LABORATORY INVESTIGATIONS OF LUPUS ERYTHEMATOSUS

Lupus erythematous ("LE") cell inclusion phenomenon: It is a specific laboratory test for SLE. If the serum from a patient suffering from SLE is added to the buffy coat of normal blood, a typical **"LE" cell** will develop. These are neutrophil leukocytes, which have phagocytosed other leukocytes. LE cell is characterized by a large, circular, basophilic inclusion within a neutrophil. Positive LE cell test is rare in DLE.

Other laboratory tests include the following:

- Antinuclear antibodies are present in the serum.
- Anti-DNA antibodies are also present.
- Polyclonal hyperactivity of the B-lymphocytes.
- Decrease in the number of suppressor cells.
- Blood examination reveals-leukopenia, thrombocytopenia and hemolytic anemia.
- Hypergamaglobulinemia and profuse proteinuria.

Direct immunofluorescence test: This test will reveal the deposition of immunoglobulins (e.g. IgG, IgA, IgM and Complement 3) in the basement membrane zone of the epithelium and skin, in case of both SLE and DLE.

***Indirect immunofluorescence test*:** Reveals prominent circulating auto-antibodies.

Treatment

Systemic steroid therapy is the treatment of choice in lupus erythematosus.

SCLERODERMA

Scleroderma or progressive systemic sclerosis is a complex multisystem autoimmune disease characterized by progressive **diffuse subcutaneous fibrosis (sclerosis)** of the skin, widespread **submucous fibrosis** in oral cavity and **disorders** in multiple internal organs including the G I tract, lungs, heart , kidney, etc.

PATHOGENESIS

Blood circulation insufficiency in the tissue because of the abnormalities in the arterioles and blood capillaries; cause replacement of the normal connective tissue by the dense collagen bundles and this results in the fibrosis or sclerosis of the tissue.

TYPES

Scleroderma usually occurs in two basic forms:

A. **Localized or morphea form**
B. **Generalized or diffuse form (it is the more common type).**

The localized form of scleroderma is characterized by fibrosis with development of single or multiple, red or ivory colored, smooth, hard patches on the skin. Although, facial skin is frequently affected, it does not have any oral manifestations. Childhood "morphea" form of scleroderma may be responsible for the development of facial hemihypertrophy.

The generalized or diffuse form of scleroderma usually occurs among children or young adults, and it frequently affects females. Scleroderma is more prevalent in areas where silicosis is a common environmental hazard.

Clinical Features of Diffuse Scleroderma (Figs 19.21 and 19.22)

- Females between the ages of 30 to 50 are very frequently affected by scleroderma.
- The disease begins with edema of the skin over the face, hands or trunk.
- The affected skin becomes thinned and stiff and it is fixed firmly to the underlying tissues, e.g. muscles, bones, etc.
- The affected skin is also marked by multiple telangiectasias and contractures.
- The skin often appears reddish and scaly and it also frequently exhibits scarring.
- Fixation and stiffness of the skin causes progressive loss of mobility of hands and joints as well as restricted movements of many internal and external organs.

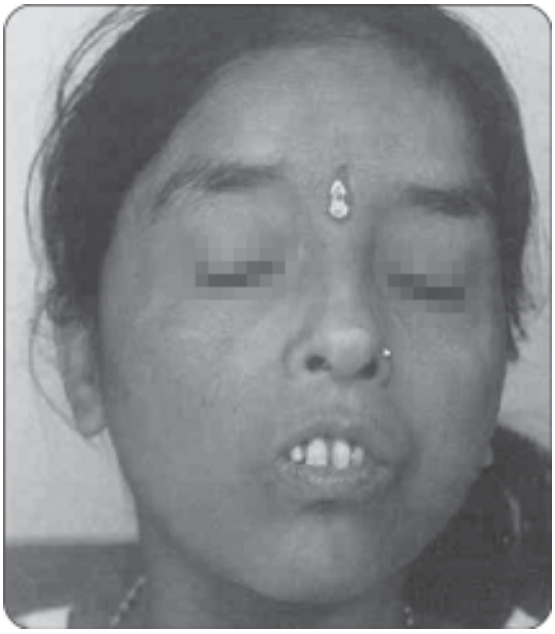

Fig. 19.21: Facial profile of a patient with scleroderma

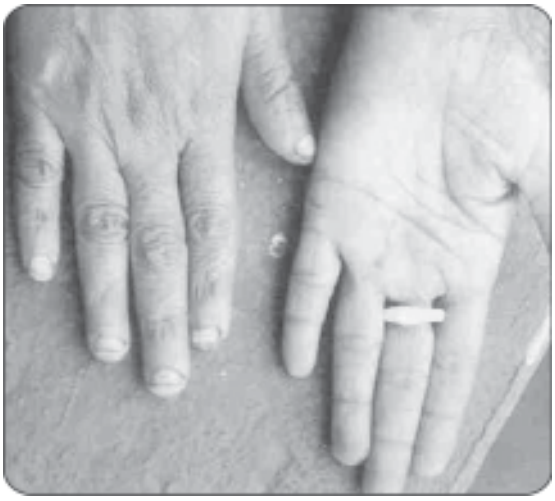

Fig. 19.22: Stiffness of the fingers in patient with scleroderma

- Resorptions of terminal phalanges and flexion contractures often produce a typical "**claw-like**" appearance of the fingers. In this situation, the patient is unable to straighten the fingers.
- Ulcerations may occur on the finger tips due to fibrosis (abnormal collagen deposition) and reduced vascularity.
- Widespread involvement of the disease causes wasting of muscles and body fat, with weakening of the limbs.
- Patients develop arthritis and arthralgia, along with neuralgia and paresthesia of the skin.
- As the disease progresses, the **skin becomes yellow, gray or ivory white** in color and it shows a waxy appearance.
- The skin gradually becomes thin or atrophic with areas of pigmentation and subcutaneous calcium deposition (**calconosis cutis**).
- Due to fixation or toughness of the facial skin, "**wrinkles" (lines of facial expression)** do not form and eyes also become narrow. These causes a **"mask-like"** appearance of the face. This type of typical facial appearance or expression in scleroderma is also named as "**Mona Lisa face**" (Fig. 19.21).
- Atrophy of the ala of the nose often gives rise to a "**pinched**" appearance of the nose; which often produces a "**mouse facies**".
- Restriction of movements occurs in all the voluntary and involuntary muscles as a result of fibrosis, and later on, the patient becomes **completely bed-ridden**.
- Fibrosis of the viscera causes dyspnea, dysphagia, pulmonary hypertension, loss of vision, etc.
- Finally all the internal organs, e.g. GI tract, heart, lungs, kidneys, etc. become affected by the fibrosis and these organs gradually loose their respective functions. Among which cardiac failure is the most threatening.
- **CREST syndrome** is often associated with scleroderma and it includes the following component features:

Features of CREST syndrome

C—Calcinosis cutis	Cutaneous deposition of calcium salts
R—Raynaud's phenomenon	When patient's hands and feet are exposed to cold temperature, the digits become dead white in appearance initially due to vasospasm and later on they become bluish due to venous stasis.
E—Esophageal dysfunction	Fibrosis of the esophageal submucosa with stricture formation.
S—Scleroductyly	Abnormal collagen deposition causes stiffness and flexure of fingers with a claw-like deformity.
T—Telangiectasia	Bleeding from superficial dilated capillaries produces multiple red macules on the skin, especially on the face.

- Besides this, scleroderma may also coexist with some other systemic diseases like-Sjogren's syndrome, rheumatoid arthritis, polymyositis and lupus erythematosus.

Oral Manifestation of Diffuse Scleroderma

- **Mask-like** expressionless face (**Mona Lisa face**) as wrinkles (lines of facial expression) does not develop due to the stiffening of facial skin.
- Multiple telangiectatic spots may be seen on the facial skin.

- Complete loss of facial esthetics and expression.
- Patient may have a "pinched" appearance of the nose, as the ala of the nose becomes atrophic due to fibrosis this often gives the patient a typical "**mouse facies"**.
- Intraorally, the disease mostly involves the tongue, cheek, lips, soft palate, larynx, etc.
- Fibrosis and stiffening of the periarticular tissue cause restricted movements of the TM Joint with development of varying degrees of "**trismus**" (Fig. 19.23).
- Pain, clicking sounds and crepitations in the temporomandibular joint.
- The restricted movements of the TM Joint may be due to fibrosis, muscle wasting, skin tightening, calcinosis, etc.
- The lips of the patient in scleroderma may appear **"pursed"** (lips appear as if the patient is about to blow whistle by the mouth) with radiating furrows and it occurs due to constriction of the mouth aperture (microstomia) resulting from fixation and rigidity of the lip muscles.
- Moreover the constricted lip of the patient often produces a typical facial appearance; which is called **"fish mouth"**.
- Stiffening and restricted movements of the facial muscles and tongue cause difficulty in speech.
- Oral mucosa shows edema, which is often followed by atrophy and indurations.
- Atrophy of the minor salivary glands often causes dry mouth (xerostomia). Moreover Sjogren's syndrome may also be associated with the disease in few cases.
- Stiffness of the tongue muscles cause narrowing of the tongue (**chicken tongue**) with restricted movements. This along with xerostomia may cause difficulty in speech and swallowing. The surface of the tongue often looks smooth.
- Esophageal fibrosis or stricture causes increased abnormal gastroesophageal reflux which often results in dysphagia, heartburn and severe erosions of tooth.
- Palatal rogue areas become flattened.
- Trigeminal neuralgia can also be associated with scleroderma.

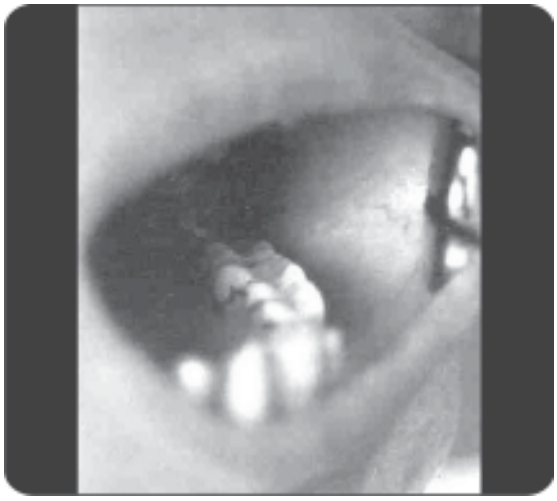

Fig. 19.23: Stiffness of the oral mucosa with a blanched appearance in scleroderma

- Decreased salivary secretion causes dry mouth (xerostomia) and increased susceptibility to dental caries and candidal infections.
- Gingival tissue becomes pale and firm. Moreover there can be severe gingival recession due to loss of attached gingiva. Alteration of the fibrous components of gingiva may also result in advanced periodontitis
- Looseness of teeth as periodontal ligaments expands with more and more collagen deposition and loss of alveolar bone.
- Failure of implants is common in this disease due to xerostomia and mucosal as well as submucosal tissue abnormality.
- Weakness of hands, decreased mobility of the TM joint, decreased mouth opening, decreased salivary secretions, etc. lead to poor oral hygiene.

RADIOLOGICAL FEATURES

- There is generalized widening or thickening of the periodontal ligament space.
- Resorption of bone occurs in some areas of the condyle or ramus of mandible due to persistent pressure from the contracting facial skin, muscles and joints.
- In untreated cases, severe mandibular bone resorption occur, which can lead to pathological fracture and even development of osteomyelitis.

Key points of oral manifestations of Scleroderma

Affected orofacial area	*Signs and symptoms*
Lips	"Pursed" lips with constriction of mouth opening
Mouth	Microstomia
Face	Mask-like expressionless face, no wrinkles on skin
Facial muscles	Weakness and muscle wasting
Oral mucosa	Edematous and atrophic, candidiasis often present
Salivary glands	Decreased salivary secretion (xerostomia), Sjogren's Syndrome
T M Joint	Restricted movements with trismus, pain and clicking sound
Tongue	Stiffness with difficulty in speech and swallowing
Esophagus	Fibrosis and stricture causing increased gastro-esophageal reflex.
Gingiva	Becomes pale and firm
Palate	Loss or flattening of palatal rogue
Teeth	Premature loss of teeth due to advanced periodontitis and alveolar bone loss
Nerves	Trigeminal neuralgia (occasionally)

HISTOPATHOLOGY

- Oral epithelium becomes atrophic with flattening of the rete pegs.
- Areas of pigmentations are often present on the epithelium.
- Thickening and hyalinization of the collagen fibers occur in the connective tissue with atrophy of the minor salivary glands.
- In the early stages, perivascular infiltrates of mononuclear inflammatory cells are common.
- Blood vessels gradually become scanty and there is narrowing of the lumen of the remaining vessels due to the perivascular fibrosis.
- The thickness of the periodontal ligament is increased due to the increased synthesis of collagen and oxytalan fibers.
- Sweat glands, sebaceous glands and hair follicles are often absent in the skin.

TREATMENT

No specific treatment is available for scleroderma. Systemic steroid therapy may produce partial remission.

EHLERS-DANLOS SYNDROME

Ehlers-Danlos syndrome is a group of hereditary disorders characterized by defective or abnormal collagen synthesis in various body organs.

CLINICAL FEATURES

- The patient often exhibits **hypermobility of joints** and **increased laxity or hyperelasticity of the skin**, and because of this, the patient is often referred to as the "**rubber man**".
- Excessive bruising tendency and defective wound healing occurs due to increased fragility of the skin and blood vessels
- The skin is velvety, thin and hyperextensible. Moreover, it shows an abnormal scarring response when subjected to minor injuries (**Papyraceous scarring**); and the scarred area of skin appears as "crumpled cigarette papers".
- Development of aortic aneurysm and its rupture is the common life threatening factor for the patient.

Types of Ehlers-Danlos syndrome	
Type I	This is the classic and most severe form of the disease, it presents both hyper-extensibility of joints and hyper-elasticity of the skin; with easy bruisability. The skin often shows "cigarette–paper" scars.
Type II	Same as Type-I, but mild in nature.
Type III	Joint hypermobility is more prominent than skin change
Type IV	Excessive scars and hyperpigmentation of skin over the areas of bony prominence. The skin is so thin that the subcutaneous vessels are visible.
Type V	Patients may face sudden death due to rupture of large vessels and hollow organs.

ORAL MANIFESTATION

- Increased fragility of the oral mucosa.
- About half of the patients are able to touch the tip of the nose with their tongue (**Gorlin's sign**).
- Bleeding from the gingiva and oral mocosa.
- Mobility of teeth and marked periodontal weakness.
- Retarded wound healing.
- Enamel hypoplasia.
- Loss of normal scalloping of the dentino–enamel junctions of the tooth.
- Large pulp stones in the teeth and formation of irregular type of dentine.
- Hypermobility and subluxation of the temporomandibular joint.
- Difficulty in suturing the oral wounds due to extreme tissue fragility.
- Easy bruising and bleeding following minor oral surgical procedures.

LABORATORY INVESTIGATION

Clotting time is normal but the capillary fragility test is positive.

TREATMENT

No specific treatment is available.

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CHAPTER 20

Diseases of the Nerves and Muscles

Different types of pain in the orofacial region

A. Pain in the teeth and supporting structures
- Pulpitis
- Fracture of tooth
- Cracked tooth syndrome
- Apical periodontitis
- Acute periapical abscess
- Pericoronitis
- Lateral periodontal abscess
- HIV-associated periodontitis
- ANUG

B. Pain in the jaws
- Fractures
- Osteomyelitis
- Infected cyst
- Osteoradionecrosis malignant neoplasms
- Sickle cell infarcts

C. Pain in edentulous patients
- Trauma from denture
- Mucosal disease below the denture
- Jaw pathology
- Glossodynia
- Impacted tooth
- Broken root of tooth erupting under the denture
- Excessive vertical height of denture

D. Postoperative pain
- Dry socket
- Aerodontalgia
- Fracture of jaw
- Damage of TM Joint
- Postoperative osteomyelitis
- Damage to the nerve during treatment

E. Neurological pain
- Trigeminal neuralgia
- Herpes zoster
- Multiple sclerosis
- Post-herpetic neuralgia
- Migrainous neuralgia
- Causalgia
- Intracranial tumors
- Bell's palsy
- Glossopharyngeal neuralgia

F. Pain from extraoral sources
- Maxillary sinusitis
- Meningitis
- Carcinoma in maxillary antrum
- Acute parotitis
- Salivary calculi
- Sjogren's syndrome
- Malignant neoplasm of salivary gland
- Otitis media
- Cavernous sinus thrombosis
- Myocardial infarction
- Myofacial pain dysfunction syndrome (MPD)

G. Psychological pain
- Atypical (psychogenic) facial pain
- Burning mouth syndrome (MPD)

DISEASES OF THE NERVES

TRIGEMINAL NEURALGIA

Neuralgia can be defined as the pain along the distribution of nerves and, therefore, trigeminal neuralgia refers to the pain along the distribution of any branch of the trigeminal nerve. This is the most common neuralgia or nerve pain disorder.

The trigeminal nerve has three divisions- **ophthalmic, maxillary and mandibular;** out of these maxillary and mandibular branches are almost exclusively affected in trigeminal neuralgia.

ETIOLOGY

- Mostly idiopathic
- Traumatic compression of the nerve resulting in demyelination

- Biochemical change in the nerve cells
- Abnormal blood vessel causing compression of the nerve as it exists from the cranial foramen.

CLINICAL FEATURES

- This condition often causes severe, unilateral, '**lancinating**' type of pain in the orofacial region that is usually radiating in nature.
- The disease usually occurs among middle–aged people (above 35 years of age) and it occurs more in females than males.
- Most of the patients give the history of excruciating pain attacks, which feels like sharp stabbing or electric shock.
- The pain in trigeminal neuralgia lasts for only a few seconds or minutes and then disappears promptly. Between the attacks the people are relatively of pain free.
- Often the burst of pain attacks are precipitated by touching some **"trigger zones"** on the face. Presence of trigger zone is a definitive indicator of trigeminal neuralgia.
- Trigger zones may get stimulated and the pain starts due to touching, washing the face, tooth brushing, talking, eating, chewing, smiling, shaving or even if a strong breeze touches the face.
- Thus, the people with trigeminal neuralgia become plagued by intermittent severe pain that interferes with common daily activities, e. g. eating, sleep and shaving, etc.
- Patients try to avoid foods or drinks because of the fear of horrific pain.
- The pain in trigeminal neuralgia may produce spasmodic contractions of the facial muscles and because of this characteristic muscle spasms, the condition is often called '**Tic doulorreux**'.
- The pain may involve any part of the face on either side, depending upon which branch of the trigeminal nerve is affected. Generally, maxillary branch is more often affected than the mandibular branch (ophthalmic branch is least affected).
- If maxillary branch is involved the pain occurs in the cheek bone, entire nose, upper lips and teeth of upper jaw. Whereas, if mandibular nerve is involved the pain occurs in lower cheek, lower lip, lower teeth and jaw.
- However, right side of the face is affected more frequently than the left side and it rarely crosses the midline.
- Patients live in fear of unpredictable painful attacks, which result in insomnia, irritability, anticipatory anxiety and depression, etc. Suicidal tendency is also not uncommon.
- Surprisingly there is no detectable disease or pathology present in the jaw in patients with trigeminal neuralgia.

HISTOPATHOLOGICAL FINDINGS

In trigeminal neuralgia, focal areas of myelin degeneration can be seen within the gasserian ganglion or along the course of the nerve.

LABORATORY DIAGNOSIS

- History of the patient and normal neurological findings usually establish the diagnosis beyond doubt.
- MRI may be suggested for detection of any space occupying lesion or any vessel compression in the nerve root.
- CT scan and MRI of the head and neck region are advised to rule out suspected brain tumor, meningitis or any other neurological abnormality.

Key points of trigeminal neuralgia

- Trigeminal neuralgia refers to severe, excruciating, pain along the distribution of any branch of trigeminal nerve on one side of the face.
- The 'lancinating' or excruciating pain in trigeminal neuralgia lasts for only a few seconds or minutes and then promptly disappears.
- Often the burst of pain attacks are precipitated by touching some "trigger zone" on the face. Presence of this trigger zone is a definitive indicator of trigeminal neuralgia.
- The trigger zones on the face may get stimulated by any of the common actions, e. g. washing the face, tooth brushing, talking, eating, chewing, smiling, shaving, etc.
- The disease occurs more frequently among middle aged females and maxillary or mandibular branch of the trigeminal nerve is often involved.
- Pain in trigeminal neuralgia often characteristically produces spasmodic contractions of the facial muscles.

DIFFERENTIAL DIAGNOSIS

- Multiple sclerosis
- Migraine
- Atypical neuralgia
- Myofacial pain
- Cluster headache
- TM joint disorder
- Intracranial hemorrhage
- Acute pulpitis
- Fractured tooth.

TREATMENT

Trigeminal neuralgia can be treated by the following methods:

- Peripheral neurectomy.
- Injection of alcohol or boiling water into the gasserian ganglion.
- Injection of steroid or anesthetic in the ganglion
- Electrocoagulation of the same ganglion.
- Administration of carbamazepines and phenytoin, etc.
- A recent treatment called microsurgical decompression of trigeminal root being tried with good results.
  Unfortunately, none of these treatments can produce impressive and permanent results.

SPHENOPALATINE NEURALGIA

Sphenopalatine neuralgia is a distinctive syndrome of headache; characterized by a unilateral radiating pain in the region of the eye, maxilla, ears, teeth, cheek and nose, etc.

TYPES

There are two types of sphenopalatine neuralgia
A. Episodic
B. Chronic

CLINICAL PRESENTATION

- The pain begins very rapidly; it persists for few minutes to few hours and then disappears.
- Generally 1 to 3 short attacks of pain occur in a day.
- The condition often simulates toothache, however, unlike the trigeminal neuralgia; **no "trigger zone" is present** in this case.
- Sphenopalatine neuralgia occurs more frequently among females and sometimes it may be associated with other symptoms like sneezing, nasal discharges and watering of the eyes, etc.
- Interestingly in some patients the onset of pain is exactly at the same time every day and hence, it is referred to as the **"alarm clock" headache**.

GLOSSODYNIA AND GLOSSOPYROSIS

Glossodynia refers to the painful tongue, while glossopyrosis means burning sensation of the tongue.

Etiology of glossodynia and glossopyrosis

- Vitamin deficiency
- Anemia (especially pernicious anemia)
- Hormonal disorder, e. g. diabetes, hypothyroidism
- Xerostomia
- GI disturbances (hyper or hypoacidity)
- Psychogenic factor, e.g. cancer phobia, chronic anxiety and depression
- Trigeminal neuralgia
- Referred pain from tooth
- Angioneurotic edema
- Heavy metal poisoning, e. g. mercurialism
- Moeller's glossitis
- Postmenopausal syndrome
- Oral thrush
- Cervical nerve injury

CLINICAL FEATURES

- Glossodynia usually occurs among the middle-aged or elderly people, mostly among females.
- The sensations which are commonly encountered in this disease are pain and burning, itching or stinging sensations of the mucous membrane covering the tongue.
- However in glossodynia, the tongue appears normal and clinically there are no apparent lesions, e.g. discoloration or ulcerations, which can precipitate the symptoms.
- The pain is low or absent during morning, however, it gradually builds up as the day progresses.

TREATMENT

Topical anesthetics, analgesics, muscle relaxants and sedatives, etc. are given in case of glossodynia, although permanent remission is difficult to achieve. Low doses of benzodiazepines, tricyclic antidepressants or anticonvulsants may also be effective.

AURICULOTEMPORAL SYNDROME (FREY'S SYNDROME)

Frey's syndrome occurs due to anomalous repair of the damaged auriculo temporal nerve following injury, which results in the innervations of sweat glands by the parasympathetic salivary fibers.

The patients with this syndrome typically exhibit **flushing and sweating in the temporal area during meals.** Moreover, this can happen even when the patient sees or thinks or talks about certain foods that cause increased salivation. The condition usually occurs following the surgical procedures like removal of the parotid gland or resection of the ramus of mandible, etc.

GLOSSOPHARYNGEAL NEURALGIA

Glossopharyngeal neuralgia manifests itself by repeated episodes of sharp, shooting type of pain in the ear, pharynx, tonsillar area and the posterior part of the tongue, etc. The intensity of pain is almost similar to that of the trigeminal neuralgia and usually there is a **"trigger zone"** present in the tonsillar fossa region.

The pain occurs unilaterally, lasts for few seconds to few minutes and the condition mostly affects the older individuals. Pulse is often slow and fainting may occur if the pain is severe.

TRIGGERING FACTORS

- Chewing
- Coughing
- Talking
- Swallowing
- Laughing.

ETIOLOGY

The exact etiology of this syndrome is not clearly known and the probable initiating factors could be the following—abnormal blood vessels pressing down on glossopharyngeal nerve, growth at the base of the skull and tumor or infection in the mouth, etc.

BELL'S PALSY (FACIAL NERVE PARALYSIS)

Bell's palsy refers to the paralysis of facial nerve resulting in inability to control the facial muscles on the affected side of the face. The condition is named after Scottish anatomist **Charles Bell** who first described it.

Functions of facial nerve

- Blinking
- Closing eyes
- Smiling
- Frowning
- Lacrimation
- Salivation
- Taste sensation from the anterior two-third of tongue.

ETIOLOGY OF BELL'S PALSY

The disease may be precipitated by the following conditions:

- Change in the atmospheric pressure, e. g. while flying or diving, etc.
- Malignant tumors of the parotid gland and brain.
- Stroke.
- Surgical procedures in the parotid region
- Infections, e. g. acute otitis media and *Herpes simplex* virus infection.
- Melkersson-Rosenthal syndrome
- Meningitis
- Head injury
- Lyme disease
- Multiple sclerosis
- Exposure to common cold
- Following incorrect pterygomandibular block anesthesia
- Ischemic damage of the facial nerve.

CLINICAL FEATURES (FIGS 20.1 AND 20.2)

Paralysis of facial nerve causes loss of all or many of the above mentioned functions:

Fig. 20.1: Bell's palsy-I

Fig. 20.2: Bell's palsy-II

- Bell's palsy commonly affects the middle-aged females and mostly the condition occurs unilaterally.
- The paralysis is often rapidly progressing and it can be either complete or partial.
- The **patient cannot close the eye** on the affected side due to loss of muscle control which results in **constant watering from the eye**.
- As the eye is constantly open, there will be conjunctival dryness. Even ulceration may also occur.
- Drooping of the corner of the mouth on the affected side is often seen in Bell's palsy.
- Saliva may often run from the affected side of the mouth; which the patient can not control.
- The corner of the mouth on the affected side does not raise during smile and his gives the patient a typical **'mask–like'** expressionless appearance.
- Most of the patients complain of difficulty in speech (they have a slurred speech), difficulty in taking foods and there may be even loss of taste sensations.
- The patients **cannot raise their eyebrows** and there is **no wrinkle formation in their forehead**.
- Bell's palsy patients **fail to blow whistles** by their mouth when they try.
- Recurrent attacks of Bell's palsy can be associated with **"Melkersson–Rosenthal syndrome"**, which also have other features like cheilitis granulomatosa, fissured tongue and edema of the face, etc.
- On rare occasions Bell's palsy can affect bilaterally.

Key points of Bell's palsy

- Bell's palsy is the paralysis of facial nerve, resulting in inability to control the facial muscles on the affected side of the face.
- Patients with this disease cannot close their eye and are unable to raise their eyebrows on the affected side due to loss of muscle control,
- The disease results in constant watering from the eye and gives the patient a typical 'mask–like' expressionless face.
- Slurring of speech, inability to blow whistles by the mouth and difficulty in taking food, etc are the other common problems of Bell's palsy.
- The disease commonly affects the middle–aged females and it may be precipitated by several factors such as sudden exposure to cold, surgical injury to facial nerve, change in atmospheric pressure, head injury or meningitis, etc.

TREATMENT

There is no specific treatment for Bell's palsy. Administration of histamine or nicotinic acid has been beneficial in some cases. Physiotherapy is also helpful in some patients. The eye on the involved side has to be protected from infections by using protective glasses, eye drops and ointments, etc.

CAUSALGIA

Causalgia refers to the burning pain in the area of previous injury or surgical procedures; which results from damage to the peripheral nerve. In the oral cavity it can occur following tooth extraction.

CRITERIA OF CAUSALGIA

- Pain is spontaneous, severe and persistent.
- It should be present for at least 5 weeks.
- Pain should be felt distal to the proximal nerve injury.

TYPES

Causalgia can be of two types—**major** and **minor**, the difference is in the degree of severity of pain.

INJURIES THAT CAN CAUSE CAUSALGIA

- Bullet injury
- Head injury
- Polio
- Stroke
- Myocardial infarction
- Surgical injury
- Injury from a high velocity sharp instrument
- Tooth extractions.
- In few cases, causalgia may develop following tonsillectomy.

NATURE OF PAIN IN CAUSALGIA

The pain can be of several types, which are as follows: burning, tingling, searing, stabbing, crushing and lightening, etc .

The pain arises within a few days to several weeks after the tooth extraction, although the oral wound has already been completely healed-up by that time. Pain in causalgia is most commonly felt in the limbs.

Factors precipitating the pain in causalgia

- Emotional stress
- Visual stimulation
- Auditory stimulation
- Physical stimulation
- Gentle bridge
- Family arguments.

EAGLE'S SYNDROME

The 'Eagle's syndrome complex' was first described by Eagle and hence it is called Eagle's syndrome.

It is characterized by the following features:

- Elongation of the styloid process or ossification of the styloid ligament causing dysphagia; and pain in the throat, pharynx and ear, etc.
- Glossodynia
- Headache
- Vague orofacial pain and pain on the side of the neck.

Important causes of paresthesia or anesthesia of the lip

- Inferior alveolar nerve block
- Injury or fracture of the jaw
- Acute osteomyelitis
- Malignant or metastatic tumor of mandible
- Exposed mental foramen
- Herpes zoster
- Multiple sclerosis
- Tetany

DISEASE OF THE MUSCLES

GENERALIZED FAMILIAL MUSCULAR DYSTROPHY

Generalized familial muscular dystrophy is a rapidly progressing muscular disease, which predominantly affects the children and most of the patients are the sons of their carrier mothers.

CLINICAL FEATURES

- The earliest manifestation of the disease is inability of the child to stand, run or walk even after attaining a standard age.
- Most of the kids fall rapidly while making an attempt to stand or walk by themselves and

this happens due to the weakness of the muscles of extremities.
- In severe cases, all the muscles of the body including those of the facial, masticatory or ocular groups become involved.
- In generalized familial muscular dystrophy, most of the patients die by the age of 20 years due to pulmonary infections related to the respiratory muscle weaknesses.

ORAL MANIFESTATIONS

- Malocclusion
- Open-bite or cross-bite
- Macroglossia
- Expanded dental arch.

HISTOPATHOLOGY

Histologically, the involved muscles reveal gradual loss of muscle fibers, which are replaced by connective tissue or fat.

LABORATORY DIAGNOSIS

Elevation of serum creatine kinase is a significant laboratory finding.

TREATMENT

There is no satisfactory treatment for this disease.

MYASTHENIA GRAVIS

Myasthenia gravis is one of the best known autoimmune disease in which antibodies are produced against acetylcholine receptors of the muscle end plate of the neuromuscular junctions. This results in an impairment of acetylcholine signal transmissions across the neuromuscular junction there by causing muscle weaknesses and pronounced fatigability.

CLINICAL FEATURES

- This disease commonly affects middle-aged females.
- The patients often exhibit difficulty in mastication and deglutition
- Dropping of the jaw, slurring of speech, loss of taste sensation
- Dry mouth alongwith ulceration of the tongue, buccal mucosa and palate
- Dropping of head, diplopia, ptosis, weight loss and exhaustion
- Atypical facial pain, candidiasis
- Hyperplasia of thyroid gland
- Many patients die of respiratory failure but few patients survive and lead a relatively normal life.

Abnormal conditions with which myasthenia gravis is often associated are

- Systemic lupus erythematosus
- Sjogren's syndrome
- Progressive systemic sclerosis

TREATMENT

Intramuscular administrations of physostigmine improve the strength of the affected muscles readily, but the remission is temporary.

MYOSITIS OSSIFICANS

Myositis ossificans is a skeletal muscle disease of unknown etiology, which is characterized by the formation of bone (calcification) and connective tissues within the muscles.

TYPES

Non-hereditary type—This is the common type, in which ossification occurs following injury.

Hereditary type—It is known as myositis ossificans progressive and in this type the ossification occurs without injury.

Ossifications of the muscle may occur following an inflammatory process and the disease can involve either a single muscle (**focal**) or the entire group of muscles **(generalized).**

CLINICAL FEATURES

- Myositis ossificans occur frequently among children and young adults.
- Most patients develop a single or multiple, soft, fluctuant or firm, nodular, painless swellings on the body, which often arise following trauma to the affected area.
- In the later stages, some of the nodules disappear while the remaining nodules become bony hard and they often exhibit an overlying red skin.
- The condition can be painful especially when the affected muscle is used for any work.

- In the orofacial region the masseter muscle is often affected by this disease, which results in trismus and difficulty in food intake.
- Eventually, the entire group of muscles in the body becomes ossified and this transforms the patient into a rigid organism.
- In many cases the abnormal bone within the muscle becomes resorbed spontaneously

TREATMENT

There is no treatment possible for this disease, surgical treatment has limited success.

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CHAPTER 21

Oral Manifestations of Generalized Diseases

VITAMIN DEFICIENCIES

Name of the disease	Important oral manifestations
Vitamin A deficiency	Hyperkeratosis of oral epithelium, decreased salivary flow and dryness of mouth.
Hypervitaminosis A	Cortical thickening of bone, mucosal pigmentations, hemorrhages, retardation of growth.
Vitamin B_1 (Thiamine) deficiency	Edema of the tongue, loss of papillae, pain and paresthesia.
Niacin deficiency	Stomatitis and bleeding in the oral mucosa, glossitis and Sandwith's bald tongue (red, smooth and raw tongue).
Riboflavin deficiency	Reddening and inflammation of tongue with cyanosis and ulceration (magenta glossitis), angular cheilitis, sore throat, swelling and erythema of oral mucosa.
Nicotinamide deficiency	Glossitis, stomatitis and gingivitis.
Vitamin B_{12} deficiency	Glossitis, aphthous ulcer.
Pyridoxine deficiency	Cheilitis and glossitis.
Folic acid deficiency	Glossitis, aphthous ulcer.
Vitamin C deficiency	Widespread petechiae and ecchymosis of the oral mucosa along with hyperemia, edema and ulceration. Generalized enlargement of gingiva with spontaneous bleeding. Severe periodontal inflammation, alveolar bone loss, tooth mobility and premature loss of teeth. Failure of wound healing, breaking down of recent wounds and painful subperiosteal hemorrhage.
Vitamin D deficiency	Delayed tooth eruption, malpositioning of teeth, retardation of mandibular growth, development of class II malocclusion. Increased susceptibility to jaw fracture due to minimum injury.
Vitamin K deficiency	Increased gingival bleeding, lack of blood coagulation after surgery.

IMPORTANT CAUSES OF LYMPHADENOPATHY

Infections		Neoplasms	
Bacterial infections	Oral, tonsil, face and scalp Tuberculosis Syphilis Cat-scratch disease Lyme disease	**Primary**	Hodgkin's disease Non-Hodgkin's lymphoma Leukemia
Viral infection	Herpetic stomatitis Infectious mononucleosis HIV infections	**Secondary**	Carcinoma of oral, salivary gland and nasopharyngeal Malignant melanoma Mesenchymal tissue neoplasms
Parasitic infections	Toxoplasmosis	**Miscellaneous conditions**	Sarcoidosis Drug reactions Connective tissue diseases

BLOOD DYSCRASIAS

Name of the disease	Important oral manifestations
Leukemias	Enlargement, bleeding and necrosis of gingiva, Ecchymosis, necrosis and ulceration of oral mucosa, profuse bleeding upon trauma or following extraction of tooth.
Agranulocytosis	Gangrenous ulceration of the gingiva, buccal mucosa, soft palate and lip. Delayed wound healing. Severe secondary infections.
Polycythemia	Petechiae, ecchymosis, hematoma formation and ulceration of the mucosa, gingiva and tongue. Spontaneous gingival bleeding. Purplish red discoloration of tongue, cheek and lips.
Multiple myeloma	Pain and swelling of the jaw, numbness of the lips, multiple punched-out radiolucencies in the jaw bone, formation of epulis and unexplained mobility of teeth.
Iron deficiency anemia	Mucosal atrophy and pallor, bald tongue with atrophic glossitis. Angular cheilitis, glossodynia and increased risk of candidiasis.
Plummer-Vinson's syndrome	It is a rare condition characterized by Iron deficiency anemia, dysphagia and glossitis. Other features of the disease include atrophy of the tongue papilla with smooth red surface, glossodynia, increased risk of oral precancer and cancer, angular cheilitis and difficulty in wearing prosthesis.
Pernicious anemia	Erythematous oral mucosa with burning sensation, beefy red tongue with depapillation (Hunter's glossitis), focal areas of atypical mucosal erythema.
Folic acid deficiency anemia	Depapillation of tongue with glossitis and glossodynia, aphthous-like ulceration.
Aplastic anemia	Purpura, spontaneous gingival bleeding, ulceration and bad breath, etc. Severe mucosal pallor.

Erythroblastosis fetalis	Black, brown or bluish pigmentations of teeth, protrusion of upper teeth, osteoporosis of bone, thinning of lamina dura.
Thalassemia	Protrusion of upper teeth, osteoporosis of bone, thinning of lamina dura, prominent premaxilla and cheek bone, Mongoloid facies.
Sickle cell anemia	Mucosal pallor, "**stepladder-like**" arrangement of bony trabeculae between the roots of the teeth, pain in the mandible with lip paresthesia. Osteoporosis of the jaw bone including the alveolar bone.
Purpura	Gingival bleeding, petechiae and ecchymosis.
Hemophilia	Petechiae, hemarthrosis, excessive bleeding upon trauma or extraction of tooth.
Hereditary hemorrhagic telangiectasia	Cherry red, pinpoint or large lesions resembling a crushed spider in the mucosa. The lesion blanches on pressure.

METABOLIC DISORDERS

Name of the disease	Important oral manifestations
Diabetes mellitus	Severe periodontitis with loosening of teeth, gingivitis and painful gingiva, burning mouth syndrome, delayed wound healing, mucosal ulceration, acetone breath, increased risk of infection, bilateral non-tendered enlargement of parotids (diabetic sialadenitis), xerostomia, gingival hyperplasia, candidiasis and atrophy of tongue papillae.
Amyloidosis	Macroglossia with smooth, brawny and indurated tongue, localized, yellow, non-ulcerated nodules on the oral mucosa. Hoarseness of voice, dry mouth, claudication of the jaw, petechiae and ecchymosis of the oral mucosa.
Hurler's syndrome	Short and broad mandible, coarse lips, delayed eruption of teeth, multiple radiolucencies in the jawbone, diastema, hyperplastic dental follicles.
Jaundice	Icterus (diffuse yellow pigmentation) of the palatal and sublingual area.
Hypophosphatesia	Premature loss of primary teeth, especially deciduous incisors. Delayed eruption of permanent teeth, premature loss of permanent teeth, thin cortex and lamina-dura of bone, decreased enamel thickness and large pulp size of tooth.
Hypophosphatemia	Bone pain, muscle weakness, poorly formed teeth, large pulp chambers of teeth with pulp horns extending up to the dentino-enamel junction, increased incidences of periodontal and periapical abscess formation with sinus tract. Deformity of tooth enamel with microclefts helps in early pulp exposure.
Protein-energy malnutrition	Oral mucosal pallor, atrophy of the tongue papilla, enamel hypoplasia, glossitis, angular cheilitis, generalized stomatitis, fissuring of lips, delayed wound healing.

Chronic alcoholism	Inflamatory gingival lesion with bleeding tendency.
Chronic steroid therapy	Obesity of the upper part of the body, "**buffalo-hump**" or round shouldered person, mooning of the face, secondary oral infections due to depressed immunity, osteoporosis.
Uremic stomatitis	It occurs due to renal failure and is characterized by development of multiple ragged white plaques on the buccal mucosa, tongue and floor of the mouth. Unpleasant taste in the mouth, oral burning sensation and odor of ammonia or urine in the mouth.

HEAVY METAL POISONING

Name of the metal	Oral manifestations
Arsenic	Vomiting, diarrhea, hyperpigmentation, hyperkeratosis of oral mucosa.
Lead	Excessive salivation, metallic taste and a dark lead line along the gingival margin.
Bismuth	Burning sensations of the oral mucosa, metallic taste and a bismuth line (similar to lead line) along the gingival margin.
Mercury	Stomatitis, increased salivation, glossitis and enlargement of salivary glands.
Phosphorus	Progressive osteomyelitis of the jaws
Silver-amalgam	Gray-black discoloration of the oral mucosa.
Graphite	Gray-black mucosal color change.
Lead-mercury	Gray oral mucosa.

ENDOCRINE DISTURBANCES

Name of the disease	Important oral manifestations
Pituitary gigantism	Enlargement of jaw bone, enlargement of oral soft tissues, increased vertical height of jawbone, macroglossia, true macrodontia, early eruption of teeth and hypercementosis, etc.
Pituitary dwarfism	Underdeveloped face and jaws, delayed shedding of primary teeth and delayed eruption of permanent teeth, delayed root completion of teeth, microdontia and absence of third molars.
Acromegaly	Increased mandibular growth with development of class-III mal-occlusion, diastemas, anterior open bite, increased soft tissue growth with macroglossia, periodontitis, gingivitis and hypercementosis, etc.
Cushing's syndrome	Mooning of the face (face becomes round due to excessive deposition of fat within the facial tissues), osteoporosis of bone, loss of lamina dura, increased risk of infection due to lowered immunity, increased incidences of pathological fractures of bone.
Hypoparathyroidism	Hypocalcemia, tetany, delayed eruption of teeth, pitting enamel hypoplasia, extensive bone resorptions. Positive Chvostek's sign and persistent oral candidiasis.

Hyperparathyroidism	Loosening of teeth, **brown tumors in the jaws**, loss of lamina dura, radiograph shows ground glass appearance of the bone (due to severely decreased bone density) and multicystic jaw lesions, bone and joint pain, peptic ulcer, hypercalcemia, renal calculi. Massive enlargement of jaw.
Imbalance of sex hormones	***Puberty***—Puberty gingivitis ***Menstruation***—Gingivitis, cyclical ulceration of the oral mucosa, gingival bleeding. ***Menopause***—Dry mouth, burning tongue.
Pregnancy	Gingival bleeding, pregnancy tumor (epulis) Aggravated gingivitis, recurrent aphthous ulcer. Vomiting, hypo or hypertension.
Addison's disease	Yellow to brown pigmentations of oral mucous membrane due to increased melanin production.
Hyperthyroidism	Premature eruption of teeth and loss of deciduous dentition, osteoporosis of the jaw bones.
Cretinism	Retarded tooth eruption or complete failure of tooth eruption, delayed exfoliation of deciduous teeth, malocclusion, macroglossia, macrocheilia, drooling of saliva, delayed closure of bony sutures, etc.
Myxedema	Thick lips, macroglossia and swollen face.

GRANULOMATOUS DISEASES

Name of the disease	Important oral manifestations
Syphilis	Oral chancres in primary syphilis, **mucous patches** in secondary syphilis, **gumma** in tertiary syphilis and **Hutchinson's triad** in congenital syphilis.
Tuberculosis	Oral tuberculous ulcer, tuberculous gingivitis and osteomyelitis, scrofula.
Sarcoidosis	Enlargement of salivary glands, circumscribed nodules in the soft palate, gingiva and cheek, etc.
Histoplasmosis	Ulceration and nodular growth on the gingiva, tongue or palate that often simulates a carcinoma.
Candidiasis	White or grayish white "curdled milk"-like patches on the oral mucosa, which leave raw painful, bleeding surfaces upon their removal.
Actinomycosis	Enlargement of mandible with many pus discharging sinuses,the pus contains small yellowish sulfur granules.
Crohn's disease	Recurrent aphthous stomatitis, diffuse nodular swelling of the lips and cheeks, cobble-stone appearance of the oral mucosa. Linear granulomatous ulcer on buccal vestibule.
Ulcerative colitis	Recurrent aphthous ulcer, pyostomatitis vegetans, hemorrhagic ulcers.

Pyostomatitis vegetans	Multiple linear yellow pustules over the buccal and labial mucosa, soft palate and undersurface of the tongue.
Celiac disease	Recurrent aphthous stomatitis.

DERMATOLOGICAL DISEASES

Name of the disease	Important oral manifestations
Ectodermal dysplasia	Anodontia, salivary gland aplasia with xerostomia, depressed nasal bridge, frontal bossing, dry skin, unexplained pyrexia, hoarseness of voice.
Pemphigus	Vesicle or bullae formation in oral mucosa, vesicles rupture with subsequent ulcer formation, Nickolsky's sign is positive, pain with bleeding and secondary infection.
Pemphigoid	Vesicle or bullae formation, desquamation of the gingiva.
Epidermolysis bullosa	Multiple bullae in the area of trauma, hypoplasia of teeth.
Ehlers-Danlos syndrome	Increased fragility of skin, gum bleeding, tooth mobility, delayed wound healing, enamel hypoplasia.
Lichen planus	Patchy white lesions on the oral mucosa that present lace-like radiating striae at the periphery, burning sensations and mucosal pigmentations often develop.
Scleroderma	Atrophy of the oral mucous membrane with stiffening and fixation, depapillation of tongue, difficulty in deglutition, and widening of the periodontal ligament space.
Psoriasis	Erythematous patches with white scaly surface on the oral mucosa.
Lupus erythematous	Multiple white plaques in oral mucosa with dark-reddish purple margins. Erythematous skin rash on the face with a butterfly configuration across the bridge of the nose.
Keratosis follicularis	Multiple small papules on the oral mucosa.

BONE DISEASES

Name of the disease	Important oral manifestations
Paget's disease of bone	Enlargement of the jaws, loosening of teeth and diastema formation, **"cotton-wool"** type radiographic features of the bone, hyercementosis of teeth and pulp calcification, etc.
Osteopetrosis	Delayed tooth eruption, retarded healing of the extraction wound, spontaneous jaw fractures, etc.
Osteogenesis imperfecta	Frequent bone fractures, blue sclera, in case of associated dentinogenesis imperfecta feature like obliteration of pulp chambers, excessive tooth wear and short roots, etc.
Caffey's disease	Sudden jaw swelling that disappears in 3 to 12 months, cortical thickening and bulging of the lower border of mandible.

Fibrous dysplasia	Enlargement of the jaws, hypergonadism in females and café–au–lait spots on the skin, etc. ground-glass radiographic appearance of bone.
Fluorosis	Lustless opaque white teeth with mottling or pitting, opaque hypomineralized areas of tooth which may stain yellow to dark brown, decreased caries incidence.

ACUTE INFECTIVE DISEASES

Rabies	Excessive salivation, facial palsy, hydrophobia, difficulty in deglutition.
Tetanus	Lock jaw, risus sardonicus.
Anthrax	Malignant edema of the lip, oral mucosa, larynx and pharynx. Malignant pustule formations in the labial and palatal mucosa.
Meningitis	Bleeding from the mouth, stomatitis, mouth ulcers, foul breath, loss of taste sensation, coating on the tongue.

HELMINTHIC DISEASES

Tapeworm infections	**Teniasis:** Edematous mucosal ulcerations, gingival bleeding. **Cysticercosis:** Well-defined, painless, fluctuant swelling over the lips, tongue and cheek, which often resembles mucoceles. **Hydatid cyst:** Small, progressively increasing, painless, well-defined, soft fluctuant swelling on the tongue.
Roundworm infections	**Trichinosis:** Bilateral gingival swelling, swelling of the tongue and myelohyoid muscle. **Ascariasis:** Submental swelling, mucosal pigmentations, toxic manifestations from worm by-products, e.g. facial edema and urticaria etc. **Filariasis:** Edematous swelling of the lips and tongue.
Protozoal infections	**Tripanosomiasis:** Unilateral facial edema with crepitations, widening of the transverse diameter of face, salivary gland swelling, cervical and preauricular lymphadenopathy.
Leishmaniasis	Ulcerations of the oral mucosa, progressive destructions of soft palate, uvula and gingiva.
Toxoplasmosis	Aphthous stomatitis, pharyngitis, lymphadenopathy, facial palsy.

RENAL DISEASES

Renal failure	Bad odor or smell of ammonia in the mouth, gingivitis, stomatitis, xerostomia, parotitis, mucosal erythema, oral thrush, bacterial plaques, mucosal ulcerations, purpura, giant-cell lesions (secondary to hyperparathyroidism) mucosal pallor due to anemia.
Renal osteodystrophy	Demineralization of maxillary and mandibular bone, loss of trabeculations, total or partial loss of lamina dura, ground-glass radiolucency of bone.

Kidney transplantation	Xerostomia, metallic taste, mucosal pallor, low grade gingival inflammation, increased bleeding tendency from gingiva and oral mucosa, petechiae or ecchymosis, erosive glossitis, staining of teeth, bone demineralization, gingival hyperplasia.

NEURAL DISEASES

Multiple sclerosis	Anesthesia or paresthesia of all branches of trigeminal nerve, non-specific neuralgia, glossopharyngeal neuralgia.
Epilepsy	Gingival hyperplasia due to intake of phenytoin sodium, hirsutism, lymphadenopathy.
Cerebral palsy	Class II malocclusion with open bite is often seen, severe caries and periodontal diseases, severe tooth erosion, enamel hypoplasia, bruxism, mouth breathing, drooling, delayed tooth eruption, traumatic damage of teeth, disturbance in swallowing.

SEXUALLY TRANSMITTED DISEASES

Syphilis	***Oral chancres***—in primary syphilis. ***Mucous patches***—in secondary syphilis. ***Gumma***— in tertiary syphilis. ***Hutchinson's triad***— in congenital syphilis.
Gonorrhoea	Gonococcal stomatitis with ulcerations of the oral mucosa, gingivostomatitis with red, yellow or greenish discoloration of the tissue.
Granuloma inguinale	Extensive superficial ulcerations in the oral mucosa with ill-defined margins.

CARDIOVASCULAR DISEASES

Congestive cardiac failure	Cyanosis of the lips, tongue and other parts of oral mucosa.
Coarctation of aorta	Enlargement of the mandibular artery and it's branches supplying the teeth, enlargement of the dental pulp, excessive hemorrhage after tooth extractions.
Congenital heart disease	Generalized bluish discoloration of the gingiva, severe marginal gingivitis, bleeding gums, delayed eruption of teeth.
Hypertension	Uncontrolled hemorrhage following oral surgical procedures, gingival hyperplasia due to intake of nifedipine, oral mucosal ulcers due to intake of methyldopa, dryness of mouth due to use of diuretics.
Stroke	Impaired speech, facial paralysis, poor oral hygiene, inability to wear artificial prosthesis.

GENETIC DISORDERS

Down's syndrome	Small mouth, large tongue, conical teeth, high arched palate, microdontia, delayed eruption of teeth.
Apert's syndrome	Cleft palate, cleft uvula, malocclusion, high palatal vault.
Achondroplasia	Hypoplastic maxilla, mandibular prognathism, malocclusion.
Cleidocranial dysplasia	Midfacial hypoplasia, high-arched palate with or without cleft, delayed eruption of teeth, multiple impacted or unerupted supernumerary teeth.
Cruzon's syndrome	Anodontia, peg-shaped teeth, palatal cyst.
Marfan syndrome **Pierre-Robin syndrome**	TMJ-dysarthrosis, high arched palate, cleft palate. Cleft palate, micrognathia, glossoptosis.
Trisomy- 13 syndrome	Cleft lip, cleft palate.

ALLERGIC CONDITIONS

Contact allergy	Multiple vesicles followed by ulcerations, in the oral mucosa, swelling and fissuring of the lips.
Systemic allergy	**Type-I**—Anaphylactic shock. **Type-II, III, IV**—Lichenoid reaction, pemphigus, pemphigoid and erythema multiforme, etc.

GENERAL MANIFESTATIONS OF ORAL DISEASES

Diseases produced	**Oral diseases responsible for such conditions**
Cavernous sinus thrombosis and meningitis	Cavernous sinus thrombosis and meningitis occurs in rare cases, when the infections from the "danger zone" of the face reaches the cavernous sinus and the meninges. ***Clinical features*** Exophthalmos, loss of vision, Photophobia, lacrimation, fever, chills and vomiting.
Septicemia	Extraction of an infected teeth without antibiotic coverage may lead to septicemia or even death.
Oral infections	Fever, malaise, leukocytosis, headache and lymphadenopathy, etc. may develop when there is presence of a dentoalveolar abscess or osteomyelitis of the jaw.
Subacute bacterial endocarditis	In case of careless tooth extraction in a cardiac patient without proper antibiotic therapy, the *streptococcus* beta–hemolyticus group of organisms may spread from the oral cavity to the heart and produce SABE.
Hypovolemic shock	Excessive hemorrhage from the oral cavity following tooth extraction may produce hypovolemic shock.
Malignant oral tumors	Malignant oral tumors, e.g. squamous cell carcinoma, malignant melanoma, osteosarcoma and lymphoma, etc. can metastasize to the distant areas of the body and kill the patient.

Loss of teeth	If the lost teeth in the oral cavity are not replaced by artificial dentures, the patients ability to masticate adequate nutritious food is decreased and nutritional deficiency symptoms develop.
Oral foci of infection	The infected dental pulp, dental abscess, periodontal abscess, inflammed gingiva, etc. harbor microorganisms and hence are called oral foci of infections. The microorganisms from these oral foci may produce secondary infections in the distant parts of the body.
Transitory bacteremia	Extraction, scaling or any other minor oral surgical procedure may cause spread of bacteria from the oral cavity into the circulation. This type of bacteremia lasts for about 30 minutes.

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CHAPTER 22

Syndromes Related to Oral Diseases

A syndrome can be defined as a set of symptoms, which collectively indicate or characterize a disease, a psychological disorder or other abnormal condition. Some investigators state that 'a disease which has more than one identifying features or symptoms is a syndrome'.

A large number of syndromes occur as symptom complexes in association with many oral diseases, some of them are very common while few others are extremely uncommon entities.

It is important to remember that once a single component feature of a syndrome is found in a patient, care should always be taken to look for the other possible symptoms, which might be present elsewhere in the body so that an early and accurate diagnosis of a syndrome could be made whenever it is present. Early diagnosis of a syndrome is always important since severity of a disease can be much more when it is occurring in association with a syndrome rather than when it is occurring as a single entity.

In the following section, salient features of some important 'oral disease related syndromes' will be discussed.

Name of the syndrome	Important features
Aarskog syndrome	Ocular hypertelorism, anteverted nostrils, broad upper lip, defective penis and small hands, etc.
Acquired immunodeficiency syndrome	Severe reduction in T-lymphocytes due to human immunodeficiency virus, breakdown of cell mediated as well as humoral immunity, overwhelming opportunistic infections and neoplasms, etc.
Acute radiation syndrome	A syndrome caused by exposure to a whole body dose of over 1 gray radiation, features include erythema, nausea, vomiting, fatigue, diarrhea, petechiae, bleeding from oral mucosa, hypotension and tachycardia.
Adrenogenital syndrome	Pseudohermaphroditism, sexual precocity, virilism in women or feminization in men, premature eruption of teeth, if the disease begins in early life.
Albright syndrome	Polyostotic fibrous dysplasia of bone, café-au-lait spots on the skin, endocrine disturbances, e.g. precocious puberty.
Aldrich syndrome	Thrombocytopenic purpura eczema, increased susceptibility to infection, otitis media, petechiae, ecchymosis.
Ameloonycho-hypohydrotic syndrome	Severe hypoplastic-hypocalcified enamel, subungual hyperkeratosis, defective nails, hypofunction of the sweat glands, seborrheic dermatitis.
Anderson syndrome	Craniofacial and skelatal anomalies, hyperuricemia, diastolic hypertension, maxillary hypoplasia, mandibular prognathism, malocclusion.
Angio-osteohypertrophy syndrome	Port-wine stains on the face, varices, hypertrophy of bone including jaw bones, facial asymmetry, malocclusion, altered eruption pattern of teeth.

Anorexia-cachexia syndrome	Systemic response to cancer occurring as a result of a poorly understood relationship between anorexia and cachexia, manifested by malnutrition, weight loss, muscular weakness and toxemia.
Apert syndrome	Early synostosis of cranial sutures, triangular facial defects, high arched palate, syndactyl and mandibular prognathism. Shovel-shaped incisors, malocclusion, parrot-beak type nose.
Ascher's syndrome	Acquired double lip, blepharochalasis and non-toxic thyroid enlargement. Recurrent edema of both eyelids.
Baby bottle syndrome	The condition occurs in children those, who drink excessive sugar containing milk or other drinks by feeding bottle for a longer period of time (especially if the milk is kept in mouth overnight). There will be multiple number of caries in several teeth.
Beckwith's hypoglycemic syndrome	Macroglossia, neonatal hypoglycemia, umbilical hernia, post-natal gigantism.
Behcet's syndrome	Oral ulceration, genital ulceration, photophobia, conjunctivitis, uveitis, pyoderma and arthralgia.
Bernard-Soulier syndrome	It's a bleeding disorder due to some platelet defect and is characterized by normal platelet aggregation to ADP and collagen but an abnormal response to fibrinogen. Increased BT and decreased platelet count.
Bing-Neel syndrome	Hyperglobulinemia with CNS involvement on a toxic infectious basis. Encephalopathy, hemorrhage, stroke and convulsions.
Baelz syndrome	A rare disease of children or adolescents, characterized by enlargement, hardening and finally eversion of the lip leading to exposure of the opening of accessory salivary glands.
Berry's syndrome	Mandibulofacial dysostosis evident at birth.
Book's syndrome	Premature whitening of hair, hyperhydrosis of palms and soles, aplasia of premolars and third molars.
B-K Mole syndrome	A hereditary condition characterized by the presence of large pigmented nevi. It often carries a very high risk for development of melanoma.
Bloch-Sulzberger syndrome	Erythematous, vesiculobullous lesion on the trunk and extremities. The initial lesion disappears, following which a lichenoid, papillary or verrucous lesion develops. Finally, a brownish-gray macule develops over the skin. Delayed tooth eruptions, conical tooth crowns, extra cusp, anodontia.
Blepharonasofacial syndrome	Mental retardation, microcephaly, joint disorders, hypoplastic maxilla and protruding lips.
Bowen syndrome	Craniofacial anomalies, hypotonia, hepatomegaly, micrognathia, protruding tongue, high arched palate, increased serum iron level.
Brittle bone syndrome	Fragile bones, clear blue sclera, deafness, loose ligaments, open fontanelles, repeated fractures of bone, opalescent teeth with short roots and obliterated pulp chambers.
Brocq-Pautrier syndrome	A rhomboid shaped, shiny lesion on the middle of the base of the tongue.
Borjeson's syndrome	Mental retardation, epilepsy, swelling of the subcutaneous tissue of face, large ears and marked obesity.
Burning mouth syndrome	Acute intense pain and burning sensation in the mouth, altered taste sensation and xerostomia, no clinically detectable lesion in the mouth, middle-aged women are commonly affected.

Caffey-Silverman syndrome	Development of a tender, deeply placed-soft tissue swelling in bone especially mandible, increased cortical thickening of bone, severe malocclusion, fever, pseudo-paralysis, dysphagia, anemia, leukocytosis
Candidiasis endocrinopathy syndrome	Chronic oral candidiasis, hypoparathyroidism, hypothyroidism, hypoadrenocorticism, diabetes mellitus, enamel hypoplasia
Carotid artery syndrome	Pressure or impingement on the external or internal carotid artery by elongated or deviated styloid process or calcified stylohyoid ligament. It often causes pain in the pharyngeal region.
Cerebrocostomandibular syndrome	Thoracic deformity with barking cough, mandibular micrognathia, palatal defects, absence of uvula or even soft palate, mental retardation,
Chinese restaurant syndrome	Throbbing headache, lightness of the jaw, neck and shoulders, lightheadedness, etc. after taking Chinese foods. These symptoms occur as a result of transient arterial dilatation due to ingestion of 'monosodium glutamate' which is sometimes used liberally for seasoning the Chinese foods.
Coffin-Lowry syndrome	Incapability of speech, severe mental deficiency, muscle, ligament and skeletal abnormality.
Coffin-Siris syndrome	Coarse facies, microcephaly, hypoplasia of fifth finger and toenails, mental deficiency, mental deficiency and laxity of joints.
Cri-dui-chat syndrome	Hypertelorism, microcephaly, mental retardation and a plaintive cat-like cry.
Chediak-Higashi syndrome	It is a progressive systemic disorder with oculo-cutaneous albinism, photophobia, nystagmus, severe gingivitis, oral ulcer, glossitis, pancytopenia and histiocytic inclusions in different organs.
Costen's syndrome	Intermittent or continuous impairment of hearing, stuffy sensation in the ear, tinnitus, otalgia, dizziness, headache, glissodynia.
Cowden's syndrome	Multiple papules on the lips and gingiva, papillomatosis of the oral mucosa resulting in a "cobble-stone" appearance, follicular keratosis of the perioral, perinasal and periorbital skin, variety of neoplastic changes in many organs.
CREST syndrome	This phenomenon is a variant of progressive systemic sclerosis characterized by calcinosis cutis, raynaud's phenomenon, esophageal dysfunction, sclerodactyly, telangiectasia.
Cushing syndrome	It occurs due to hyperadrenocortism with development of adiposity, mooning of the face, buffalo hump, abnormal hair distribution in the body, vascular hypertension, glycosuria, osteoporosis, hypertrichosis
Cross syndrome	Microphthalmia, gingival enlargement, corneal clouding, hypopigmentations, white hair, blond skin.
Cracked tooth syndrome	This syndrome is characterized by development of a crack in a restored or an unrestored tooth due to excessive occlusal forces. There will be sharp pain on biting, the pain can mimic trigeminal neuralgia and the crack can't be detected by the radiograph.
Crouzon syndrome	Craniosynostosis without syndactyly, early synostosis of bone, triangular frontal defect, mandibular prognathism and high-arched palate, nasomaxillary retrusion with mouth breathing.
Down syndrome	Small slanting eyes with epicanthral folds, mongoloid facies, flat face, large anterior fontanel, open sutures, sexual underdevelopment, open mouth with macroglossia, mental retardation and cardiac abnormalities.

Dejerine-Roussy syndrome	Tumors of the pons or occlusion of the posterior cerebral artery with sensory or motor abnormality on the contralateral side, severe episodes of pain including orofacial pain, dysgeusia.
Eagle's syndrome	Elongation of the styloid process of temporal bone or ossificaton of styloid ligament causing dysphagia, glossodynia, sore throat and pain along the distribution of the external carotid artery. The pain starts at the tonsillar area during mandibular movements, radiates to the TMJ or base of the tongue and interestingly it subsides as the jaws are closed.
Edwards syndrome	Mental retardation, small eyes, prominent occiput, micrognathia, cleft palate and uvula, the index finger overlaps the third finger and fifth finger overlaps the fourth.
Ehler's-Danlos syndrome	Hyperelasticity of skin, hyperextensibility of joints. Increased capillary fragility, easy bruising of the skin and mucosa, delayed wound healing, increased bleeding tendency.
Ellis-Van Creveld syndrome	Dwarfism, polydactyly, cardiac malfunction, dysplasia of hair and nails, hypodontia, fusion of the mid-portion of the upper lip to the anterior maxillary alveolar ridge and hypoplasia of teeth.
Epidermal nevus syndrome	Cutaneous nevi extending upto oral mucosa and gingiva, mental deficiency, skeletal abnormality, hypoplastic teeth.
Elashy-Waters syndrome	Mental retardation, brachycephaly, ocular hypertelorism, cleft palate(submucous) and uvula, multiple jaw cysts.
EEC syndrome	Ectodermal dysplasia, hypopigmentation of skin and hair, cleft palate, cleft lip and tooth abnormality.
Fanconi's syndrome	Aplastic anemia, bone abnormality, microcephaly, hypogenitalism, generalized olive brown pigmentation of skin.
Favre-Racouchot syndrome	Extensive sun damage of the facial skin. Numerous open, dialated and cystic comedones, dermis shows solar elastosis characterized by dialated pilosebaceous openings with distended, horn-filled hair follicles.
Fetal-alcohol syndrome	This abnormal condition occurs in children born of women, who were chronically alcoholic during pregnancy. The features include maxillary hypoplasia, prominent forehead and mandible, short palpebral fissures, microcephaly and mental retardation.
Fragile X syndrome	X-linked mental retardation, macro-orchidism, large ears, long narrow face, cleft palate, mitral valve prolapse.
Floppy infant syndrome	Hypotonia, generalized muscle weakness, reduced tendon reflexes, inability to sit, stand or walk due to generalized weakness.
Focal dermal hypoplasia syndrome	Focal absence of dermis with herneation of the subcutaneous fat into the defect, atrophy and pigmentation of skin, telangiectasias, papillomatosis, syndactyly. Microdontia, enamel hypoplasia, cleft lip and palate.
Frey's syndrome	It occurs as a result of damage to the auriculotemporal nerve with subsequent reinnervations of sweat glands by parasympathetic salivary fibers. The feature include flushing and sweating of the temporal area during taking foods.
Gardner's syndrome	Multiple polyposis of large intestine (colon), osteomas of bone, multiple epidermoid or sebaceous cysts of the skin, desmoid tumor, multiple impacted supernumerary and permanent teeth.

Gorlin-Goltz syndrome	Basal cell carcinoma of the skin, multiple odontogenic kerocysts, bifid-ribs, hypertelorism, mental retardation, hypogonadism, multiple basal cell nevi.
Goldenhar syndrome	Unilateral microstomia, mental retardation,hypoplastic zygomatic arch, downward slanting of palpebral fissures, malformed pinna,high arched palate, cleft-palate and uvula.
Gorham syndrome	Osteolysis of single or multiple bones followed by replacement with fibrous tissue, pain in the bone, pathological fractures. Cavernous angioma-like permeation of the affected bone.
Grinspan syndrome	It occurs in association with lichen planus and consists of lichen planus of skin and mucosa, vascular hypertension, diabetes mellitus.
Gorlin-Chaudhry-Moss syndrome	Craniofacial dysostosis, patent ductus arteriosus, hypertrichosis, hypotonia, hypoplasia of labia majora.
Gunn's syndrome	Unilateral ptosis of the eyelid with movement of the affected eyelid.
Giles de la Tourette syndrome	Spontaneous erratic behavior of the patient, incoherent facial expression and verbalizations, tendency for self-mutilation (often the oral tissues) by the use of teeth and finger nails along with movement of the jaw.
Heerfordt's syndrome	Painless, firm enlargement of the parotid and other glands due to sarcoidosis, uveitis of the eye, fever, vomiting, facial palsy, xerostomia, malaise, GI disturbances.
Horner's syndrome	It occurs due to ipsilateral brainstem lesion causing miosis or contraction of pupil, ptosis of the upper eye lid, anhidrosis and vasodilatation over the facial or periorbital skin causing flushing.
Horton's syndrome	Unilateral paroxysm of intense pain in the eye, maxilla, ear,mastoid region, base of the nose and beneath the zygoma. Absence of trigger zone, occurence of pain everyday exactly at the same time.
Hurler's syndrome	Inherited mucopolysaccharide metabolism effect characterized by prominent forehead, saddle nose, hypertelorism, macroglossia, puffy eyelids, corneal clouding, short broad mandible, gingival hyperplasias, multiple cystlike osteolytic lesions of the jaws, dwarfism, deafness.
Hunter syndrome	Mild but similar features like hurler's syndrome but without corneal clouding, death usually occurs before age of 15 years.
Hutchinson-Gilford syndrome	Alopecia, atrophic skin with areas of pigmentation, Prominent veins with loss of subcutaneous fat, high pitched squeaky voice, young boys with wizened old man like look. Small mandible, delayed eruption of teeth, excessive secondary dentin formation.
Hand-Schuller-Christian syndrome	Punched-out bone destruction in the skull, exophthalmos, diabetes insipidus, premature exfoliation of teeth.
Hajadu-Cheney syndrome	Short stature, long nose, low frontal hairline, disintegration of the terminal phalanges of fingers and toes. Premature loss of teeth, susceptibility to multiple fractures of bone.
Hallermann-Streiff syndrome	Small face, microphthalmia, beak like nose, strabismus, double cutaneous chin with central furrow, hypodontia, microstomia, retained deciduous teeth.
Hanhart syndrome	Peromelia, micrognathia, syndactyly, microglossia, hypodontia.

Hetch-Beals-Wilson syndrome	Limited mandibular opening, campylodactyly, shortened leg and hamstring muscles, club foot.
Hyoid syndrome	Elongation of the greater cornu of hyoid bone with impingement on adjacent laryngeal tissue, pain in the lateral neck and carotid area when the neck is turned to one side, pain during swallowing. Ipsilateral referred pain in the ear, syncope, patient always feels as if a foreign body is lodged in the throat.
Happy Puppet syndrome	Jerky puppet-like movements of the body, peculiar open mouthed appearance, frequent laughter, mental and motor retardation and seizures.
Hay-Wells syndrome	Inherited syndrome of ectodermal dysplasia, cleft lip and palate, adhesions of the margins of eyelids—tooth, skin and hair defects.
Jaffe-Lichtenstein syndrome	Multiple bone lesions of fibrous dysplasia, skin pigmentations.
Jugular foramen syndrome	Dysphagia, hoarseness of voice, glossopharyngeal neuralgia like pain, palatal weakness, vocal cord paralysis.
Jadassohn-Lewandowsky syndrome	Bilateral oral white lesions involving the tongue and buccal mucosa, laminated thickening of the finger and toenails.
Jaw Winking syndrome	Exaggerated opening of the eye on moving of the mandible in a contralateral direction, ptosis of the affected eye at rest, normal pupilar reflexes.
Klinefelter's syndrome	This syndrome occurs in males, whose sex chromosome constitution includes one or more extra chromosomes. The patient may develop taurodontism. Small testes, azoospermia and infertility.
K B G syndrome	Macrodontia, mental retardation, unusual facies, short stature.
Lacrimal-auricular-dental and digital syndrome	Lacrimal duct obstruction with overflow of tears, cup-shaped deformed ear with loss of hearing, peg-shaped teeth, enamel hypoplasia and medial/lateral deviation of fingers.
Larsen syndrome	Prominent forehead with frontal bossing, flat midface, depressed nasal bridge, hypertelorism, congenital (bilateral) dislocation of tibia or femur with displaced patella, cleft palate.
Laugier-Hunziker syndrome	Acquired pigmented macules in the lips, oral cavity and fingers.
Lesch-Nyhan syndrome	Hyperuricemia, spastic cerebral palsy with mental retardation, compulsive aggressive behavior with self-mutilation of fingers and lips by constant chewing or self biting. Teeth are often lost due to prophylactic extractions to avoid self mutilation or injury.
Marfan's syndrome	Disproportionately long thin extremities, spidery fingers, long and narrow face, hyperextensibility of joints, kyphosis or scoliosis, recurrent joint dislocations.
Morquio's syndrome	Severe enamel hypoplasia with gray and pitted enamel , severe bone changes, mild corneal clouding, aortic regurgitation, pigeon breast.
Marin-Amat syndrome	This condition occurs usually after peripheral facial paralysis and is characterized by automatic closing of the eye during forceful wide mouth opening like—chewing, etc. Tears may also flow.
Myofacial pain dysfunction syndrome	This condition occurs in relation to the temporomandibular joint and is characterized by the following features—pain, muscle tenderness,

	clicking sound in TMJ, limitation of jaw movements, but no pain in the joint when palpated through the external auditory meatus.
Median cleft face syndrome	Hereditary defect of abnormal midline development of face and head characterized by hypertelorism, median cleft of the lip, premaxilla and palate, cranium bifidum occultum, malocclusion.
Melkersson-Rosenthal syndrome	Cheilitis granulomatosa, facial paralysis and scrotal tongue, persistent unlilateral edema of the orbit and eyelid.
Multiple endocrine nesplasia syndrome (MEN-I)	Tumors or hyperplasia of the pituitary, parathyroids, adrenal cortex and pancreatic islets. Peptic ulcer or gastric oversecretion.
Meniere's syndrome	Tinnitus, vertigo, deafness, nausea and vomiting.
Migraine syndrome	Severe periodic headache, nausea, irritability, sleep disturbance, photophobia.
Miescher's syndrome	Diffuse swelling of the lip. Scaling, fissuring, vesicle or pustule formation on the vermillion border. It is a monosymptomatic form of Melkersson-Rosenthal syndrome.
Mikulicz's syndrome	Painless, chronic bilateral hypertrophy of the parotid or lacrimal glands accompanied by enlargement of the lymph nodes, xerostomia. The syndrome represents some generalized septic disease, e.g. lymphomas and tuberculosis.
Mobius syndrome	Congenital facial diplegia, expressionless face due to facial paralysis, inability to close the eyes due to paralysis of the abducens, swollen lips, deafness, epilepsy, etc.
Mucocutaneous lymph node syndrome	Fever, bilateral congestion of ocular conjunctiva, edema of the extremities, dryness and fissuring of the lips, strawberry-like redness and swelling of the tongue, acute nonpurulent swelling of the lymph node.
Myxoma syndrome	Perioral pigmented macules, soft tissue myxomas and endocrinopathies.
Murray-Puretic-Drescher syndrome	Gingival fibromatosis, tumors of the head, trunk and extremities, mental retardation, suppurative skin lesions, flexon contractures.
Melnick-Needles syndrome	Exophthalmos, full cheeks, large ears, micrognathia, transversely long mouth, delayed closure of fontanels, defect in clavicles, ribs, vertebrae, etc. Two unrelated patients may look like siblings.
Mohr syndrome	Short stature, digital deformities, midline cleft lip, bifid tip of nose, high arched palate, hypodontia. Lingual, facial and mandibular deformity.
Middle fossa syndrome	The condition occurs due to a tumor in the region of the gasserian ganglion and causes hypesthesia, paresthesia, paralysis of the ocular muscles, deviated mandibular opening, unilateral soft palate paralysis.
Muir-Torre syndrome	Multiple sebaceous neoplasms, keratoacanthoma.
Magic syndrome	Mouth and genital ulcers with inflammed cartilage.
Munchausen syndrome	A factitious disorder with habitual seeking of hospital admission for apparent acute illness, patient often gives a plausible and dramatic history of the disease which is entirely false.
Myelodysplastic syndrome	A group of bone marrow disorder preceding to development of acute myelogenous leukemia, characterized by abnormal hematopoietic stem cells, anemia, neutropenia and thrombocytopenia.

Miller syndrome	An inherited disorder characterized by extensive facial and limb defects, hearing loss and heart disease.
MEN-III syndrome	Medullary carcinoma of thyroid, pheochromocytoma, café-au-lait pigmentation of skin, neurofibromatosis.
Maffucci's syndrome	Multiple hemangiomas of the skin and oral mucosa, multiple chondromas of the jaw bone.
Nagar syndrome	Hypoplasia of malar bones, antimongoloid obliquity, palpebral fissures, defective hearing, cleft palate, micrognathia,
Neck-Tongue syndrome	Unilateral upper nuchal or occipital pain with or without numbness in the area, simultaneous numbness of the tongue on the same side. malocclusion.
Noonan syndrome	Congenital heart disease, chest deformity, mental retardation, short stature, facial bone anomalies, cryptorchidism.
Occipital condyle syndrome	Occipital pain, which is exacerbated by neck fixation, weakness of the hypoglossal nerve.
Oculoglandular syndrome of parinaud	Localized granuloma of the eye, preauricular lymphadenopathy. It occurs in association with Cat-scratch disease.
Olmsted syndrome	Rare congenital condition characterized by severe palmo-plantar keratosis, peri-orofacial keratosis and hypertrichosis.
Oral facial digital syndrome	Cleft of the tongue, upper lip, palate and mandibular alveolar process, micrognathia, depressed nasal bridge, frontal bossing, digital malformation, thick fibrous bands in the lower mucobuccal fold eliminating the sulcus, supernumerary canines and premolars, small hands and feet.
Oromandibular-Limb hypogenesis syndrome	Ocular hypotelorism, cranial nerve palsy, hypodactyly of hands and feet, hypoglossia, cleft palate, conical shaped mandibular incisors.
Otopalatodigital syndrome	Deafness, cleft palate, generalized bone dysplasia, prominent supraorbital ridge, frontal bossing.
Orbital syndrome	It occurs due to malignant disease of the orbit, supraorbital pain and hyperesthesia, blurred vision or diplopia, ptosis, ophthalmoplegia.
Paraneoplastic syndrome	A symptom complex arising in a cancer bearing patient that can't be explained by local or distant spread of the tumor.
Parasellar syndrome	It occurs due to encroachment of the cavernus sinus by any tumor, frontal pain, ophthalmoplegia.
Patau syndrome	Microcephaly, microphthalmia, ocular hypertelorism, deafness, polydactyly, heart anomalies, cleft lip and cleft palate.
Pfeiffer syndrome	Craniosynostosis, turribrachycephaly, broad thumbs, halluces, midface hypoplasia, mandibular prognathism, high arched palate.
Papillon-Lefevre syndrome	Hyperkeratosis palmoplantaris, generalized hyperhydrosis, fine body hair, peculiar dirty-colored skin, aggressive periodontitis with severe destruction of alveolar bone, gingival hyperplasia.
Paratrigeminal syndrome	Severe pain or headache in the area of trigeminal distribution with sign of ocular sympathetic paralysis. Onset of pain is sudden, middle aged males are frequently affected.

Paray-Romberg syndrome	Atrophy of the skin, subcutaneous tissue, bone and cartilage causing hemifacial deformity, trigeminal neuralgia, loss of hair and vitiligo on the affected side. Contralateral jacksonian epilepsy.
Plummer-Vinson syndrome (Paterson-Kelly syndrome)	Dysphagia, smooth, red, depapillated painful tongue. Lemon tinted pallor of skin, cracks and fissures on the corner of the mouth, atrophy of the filiform and fungiform papillae of tongue.
Portsmouth syndrome	Bleeding disorder due to defective platelet aggregation. The condition shows normal ADP-induced platelet aggregation but an abnormal or absent collagen induced aggregation. Severe bleeding tendency, easy bruisability, epistaxis.
PFAPA syndrome	Periodic fever, aphthous- stomatitis, pharyngitis and adenitis.
Pierre Robin syndrome	Cleft-palate, micrognathia, glossoptosis and congenital heart disease. Absent gag-reflex, airway obstruction due to falling back of tongue on the posterior pharyngeal wall due to micrognathia.
Peutz-Jeghers syndrome	Recurrent abdominal pain due to familial intestinal polyposis, cutaneous pigmentation in perioral region, precocious puberty, GI bleeding and pigmentation of the buccal mucosa.
Pickwickian syndrome	Morbid obesity, hypersomnolence, periodic breathing with hypo-ventilation, corpulmonale, difficult patients for dental treatments.
Ramon syndrome	Hypertrichosis, gingival fibromatosis, cherubism, epilepsy, mental retardation.
Raley- day syndrome	Congenital absence of tongue papilla, vasomotor dysfunctions, loss of reflexes, feeding problems, lack of pain and taste sensations.
Reiter's syndrome	Urethritis, arthritis, conjunctivitis, keratotic macules and papules on the skin.
Ramsay-Hunt syndrome	Facial paralysis, pain in the external auditory meatus and pinna of the ear, vesicular eruptions in the oral cavity and oropharynx, hoarseness of voice, tinnitus, vertigo.
Rubinstein-Tyabi syndrome	Developmental retardation, broad thumbs and great toes, delayed or incomplete descent of testes in males.
Rieger's syndrome	Hypodontia, enamel hypoplasia, protruding lower lip, maxillary hypo-plasia, blue sclera, coloboma, malformed anterior teeth, microdontia.
Rutherford syndrome	Congenitally enlarged gingiva, delayed tooth eruption, curtain-like superior corneal opacities and mental retardation.
Scheie syndrome	Stiff joints, corneal clouding, aortic regurgitation, normal intelligence.
Sipple's syndrome (MEN-II)	Parathyroid hyperplasia or adenoma, pheochromocytomas of the adrenal medulla, medullay carcinoma of thyroid, no peptic ulcer, no pancreatic tumor.
Sjogren's syndrome:	Dry eyes, keratoconjunctivitis sicca, xerostomia**,** parotid swelling, burning pain in the oral, nasal and pharyngeal mucosa, rheumatoid arthritis.
Scheuthauer-Marie-Sainton syndrome	Open fontanel of the skull, partial or complete absence of clavicles, underdeveloped maxilla, multiple impacted or unerupted permanent or supernumerary teeth.
Senear-Usher syndrome	Occurence of vesicles or bullae on the skin and mucosa simultaneous with appearance of crusted patches.

Stevens-Johnson's syndrome	It's a severe expression of erythema multiforme characterized by widespread vesiculation, denudation, sloughing and necrosis involving the skin, oral mucous membrane, eyes and genitalia.
Sturge-Weber syndrome	Orofacial and meningeal angiomatosis with secondary mental deficiency, intracranial calcifications, seizures, hemiplegia, nevus, gingival enlargement.
Saethre-Chotzen syndrome	Short stature, mild mental retardation, facial asymmetry, ptosis of eyelids, prognathism, high arched palate.
Sanfillipo's syndrome	Severe CNS defects, mild somatic disturbances, enamel hypoplasia, excessive dentinogenesis with obliteration of pulp chambers.
Sweet's syndrome	Acute onset of fever, leukocytosis, erythematous papules and plaques in the skin, predominantly neutrophilic infiltrates in the dermis without leukocytoclastic vasculitis, internal malignancy.
Sweat retention syndrome	Extravassation of sweat or saliva in the tissue with subsequent inflammation, keratin plug formation in sweat glands and accessory salivary glands.
Syndrome of crocodile tears	This abnormal condition occurs following facial nerve paralysis, herpes zoster and operative trauma in the cranium. It seems to occur due to straying of the regenerating autonomic nerve fibers, some of those destined for salivary glands go to the lacrimal gland instead, resulting in a salivary-lacrimal reflex. It is characterized by spontaneous lacrimation occurring parallel with normal salivation during meals.
Treacher Collin's syndrome	Anti-mongoloid palpebral fissures with coloboma. Hypoplasia of the facial, especially malar and mandibular bones. Microstomia and oral fistulas, etc.
Turner syndrome	Short stature, cubitus vulgus, webbed neck, sexual infantalism, renal disorders, micrognathia, premature eruption of teeth.
Trotter's syndrome	Nasopharyngeal tumor often producing trigeminal neuralgia-like pain, in the mandible, tongue and side of the head in association with middle ear deafness.
Trichodento-osseous syndrome	Tightly curled and kinky hair, osteosclerosis, hypoplastic hypocalcified enamel, many unerupted teeth and taurodontism, diastema, microdontia.
Urbach-Wiethe syndrome	Pathologic accumulation of glycoprotein in most bodily tissues, hoarseness of voice, multiple papules and nodules in the body, intracranial calcifications, hypodontia.
Van Buchem syndrome	Excessive deposition of endosteal bone throughout the skeliton, facial swelling, visual acuity, occasional facial paralysis and deafness.
Vander Woude's syndrome	The simultaneous occurence of pits of the lower lip, cleft lip or cleft palate.
Von-Recklinghausen's syndrome	Multiple neurofibromatosis in the body including oral cavity, pigmentation and hirsutism, risk of malignant transformation of one or more lesions.
Velocardiofacial syndrome	Elongated face, almond-shaped eyes, wide nose, cleft palate, nasal regurgitation of foods, heart defect.
Von-Hippel-Lindau syndrome	Hemangioblastomas in retina and cerebellum, pancreatic and renal cysts, renal adenomas, hepatic hemangiomas, multiple endocrine neoplasia.

Waterhouse-Friderichsen syndrome	This syndrome occurs due to acute adrenal cortical insufficiency and is characterized by acute meningitis, septicemia, pronounced purpura, bilateral adrenal hemorrhage fever, coma , etc. death usually occurs within 48 to 72 hours.
Waber-Cockayne syndrome	It is a localized form of epidermolysis bullosa characterized by recurrant bullous eruptions of hands and feet.
Whistling face syndrome	Sunken eyes, true ocular hypertelorism, antimongoloid obliquity of palpebral fissures, small nose, micrognathia, protruding lips as seen during whistling, high arched palate.
Wolf-Hirschhorn syndrome	Microcephaly, ocular hyperlelorism, cleft palate, micrognathia and lowly placed ear.
XXXXY syndrome	Hypoplastic midface, short stature, mental retardation, taurodontism, cleft uvula, hypertelorism.
Zimmerman-Laband syndrome	Gingival fibromatosis with defects in ear, nose, bone and nails, frog-like fingers and nails, hyperextensible joints and hepatosplenomegaly.
Zinssner syndrome	Oral leukoplakia, dystrophic nails, hyperpigmentation of skin, pancytopenia, aplastic anemia.
Zinc deficiency syndrome	Defective taste bud function secondary to zinc deficiency.

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CHAPTER 23

Important Classifications of Oral Diseases

Classifications of diseases are important, since they not only help in understanding the disease in a better way, but also provide guidelines regarding the diagnosis and prognosis of a particular disease belonging to a specific group or category. In a sense, classification of diseases are as useful as the classifications of the animals and the plants made in the field of biology. While making the classification, some diseases are categorized from others and put into certain specific groups on the basis of their clinical features or radiological features or biological behavior, etc. However, the most important criteria in this regard will be the histopathological nature of diseased tissue that can determine finally regarding which category a particular disease will belong to while making their classification. In the following section some important classifications of oral diseases are discussed.

WHITE LESIONS OF THE ORAL CAVITY

HEREDITARY CONDITIONS

- Leukoedema
- White sponge nevus
- Hereditary benign
- Intraepithelial dyskeratosis
- Keratosis follicularis
- Pachyonychia congenita
- Dyskeratosis congenita
- Incontinentia pigmenti
- Ptylosis syndrome.

LEUKOPLAKIA AND MALIGNANCIES

- Chronic cheek biting
- Friction or trauma associated leukoplakia
- Idiopathic leukoplakia
- Tobacco associated leukoplakia
  - Homogeneous leukoplakia
  - Ulcerative leukoplakia
  - Nodular or speckeled leukoplakia
- Leukoplakia associated with smokeless
  - Tobacco
  - Hairy leukoplakia
- Actinic cheillitis
- Carcinoma-in-*situ*
- Squamous cell carcinoma
- Verrucous carcinoma
- Stomatitis nicotina palati
- Verruciform xanthoma.

DERMATOSIS

- Lichen planus
- Lupus erythematosus.

INFLAMMATION

- Koplik spots of measles
- Mucous patches of syphilis
- Chemical burns
- Candidiasis
- Dentifrice associated slough.

MISCELLANEOUS CONDITIONS

- Fordyce's granules
- Dental lamina cyst
- Bohn's nodules
- Epstein's pearls
- Oral submucous fibrosis
- Ectopic lymphoid nodules
- Geographic tongue
- Papilloma
- Parulis
- Lipoma
- Systemic sclerosis
- Hairy tongue
- Heck's disease
- Oral lesions of chronic renal failure
- Paterson-Kelly syndrome.

RED-BLUE LESIONS OF THE ORAL CAVITY

DEVELOPMENTAL LESIONS

- Hemangioma
- Median rhomboid glossitis.

REACTIVE LESIONS

- Pyogenic granuloma
- Peripheral giant cell granuloma.

NEOPLASTIC LESIONS

- Erythroplakia
- Kaposi's sarcoma
- Squamous cell carcinoma
- Field cancerization
- Angiosarcoma.

METABOLIC CONDITIONS

- Vitamin C deficiency
- Vitamin B deficiency
- Pernicious anemia
- Iron-deficiency anemia
- Burning mouth syndrome.

INFECTIVE CONDITIONS

- Scarlet fever
- Atrophic candidiasis
- Lymphonodular pharyngitis
- Infectious mononucleosis
- Herpetic ulcers
- Aphthous ulcer.

IMMUNOLOGICAL ABNORMALITIES

- Plasma cell gingivitis
- Drug reactions
- Allergic mucositis.

PETECHIAE OR ECCHYMOSIS

- Suction petechiae
- Thrombocyte disorders
- Hereditary hemorrhagic telangiectasia
- Ecchymosis.

MISCELLANEOUS CONDITIONS

- Bullous and erosive mucosal disorders.
- Radiation mucositis
- Xerostomic mucositis
- Traumatic wound
- Dermatitis herpitiformis
- Mucosal burns
- Nonspecific mucositis
- Hematoma
- Mucocele.

PIGMENTED LESIONS OF THE ORAL CAVITY

BENIGN MELANOCYTIC LESIONS

- Racial pigmentations
- Physiologic pigmentations
- Smoking associated pigmentations
- Ephelis
- Lentigo
- Oral melanotic macules
- Nevi
- Hematoma.

NEOPLASTIC CONDITIONS

- Melanoma
- Multiple neurofibromatosis
- Neuroectodermal tumor of infancy
- Hemangioma
- Kaposi's sarcoma.

PIGMENTATIONS DUE TO EXOGENOUS DEPOSITS

- Amalgam tattoo
- Graphite tattoo
- Heavy metal pigmentations
- Drug-induced pigmentations.

MISCELLANEOUS CONDITIONS

- Peutz-Jeghers syndrome
- Addison's disease
- Pigmented lichen planus
- Hairy tongue
- HIV-associated oral pigmentations
- Mucocele
- Endocrinopathic pigmentations
- Café-au-lait pigmentations.

CLASSIFICATION OF VESICULO-BULLOUS DISEASES

VIRAL DISEASE

- Herpetic gingivostomatitis
- Herpetic labialis
- Recurrent herpitic stomatitis
- Herpangina
- Hand foot and mouth disease
- Primary vericella zoster
- Secondary vericella zoster
- Measles.

IMMUNOLOGIC CONDITIONS

- Pemphigus vulgaris
- Pemphigus vegetens
- Pemphigus foliaceous
- Bullous pemphigoid
- Cicatricial pemphigoid
- Erythema multiforme
- Dermatitis herpetiformis
- Linear IgA disease
- Epidermolysis bullosa aquisita
- Bullous lichen planus
- Contact vesicular stomatitis.

HEREDITARY CONDITIONS

- Epidermolysis bullosa(inherited form)
- Hailey-Hailey disease
- Darier's disease.

MISCELLANEOUS CONDITIONS

- Impetigo
- Oral blood blisters.

CLASSIFICATION OF ULCERATIVE CONDITIONS

INFECTIVE LESIONS

Bacterial diseases	Viral diseases	Fungal diseases
Syphilis	Acute herpitic gingivostomatitis	Sporotrichosis
		Histoplasmosis
Gonorrhea	Herpes labialis	Cryptococcosis
Tuberculosis	Herpangina	Mucormycosis
Leprosy	HIV infections	
Actinomycosis	Infectious mononucleosis	
Noma	Herpes zoster	
ANUG	Measles	
Nonspecific mixed bacterial infections		

TRAUMATIC CONDITIONS

- Mechanical
- Thermal
- Chemical
- Factitious injury
- Radiation.

IMMUNOLOGIC DISORDERS

- Aphthous ulcer
- Behcet's syndrome
- Reiter's syndrome
- Erythema multiforme
- Pemphigus
- Pemphigoid
- Contact allergy
- Ulcerative lichen planus
- Discoid lupus erythematosus.

SYSTEMIC DISEASES

- Leukemia
- Agranulocytosis
- Cyclic neutropenia
- Pernicious anemia
- Gluten enteropathy
- Crohn's disease
- Uremic stomatitis.

NECROTIC CONDITIONS

- Midline lethal granuloma
- Wegner's granulomatosis
- Malignant reticulosis
- Osteoradionecrosis.

MALIGNANT CONDITIONS

- Squamous cell carcinoma
- Antral carcinoma
- Verrucous carcinoma.

MISCELLANEOUS LESIONS

- Angular cheilitis
- Congenital lip pits
- Commissural pits
- Necrotizing sialometaplasia
- Oroantral fistula.

CLASSIFICATION OF DISCOLORATION OF TOOTH

EXTRINSIC STAINS

- Substances in the diet
- Smoking
- Habitual chewing of tobacco, betel nut, etc.
- Medicaments, e.g. chlorhexidines or dentifrices
- Chromogenic microorganisms.

INTRINSIC STAINS

- *Changes in structure or thickness of dental tissues*
  - Enamel hypoplasias.
  - Fluorosis.
  - Amelogenesis imperfecta.
  - Enamel opacities
  - Enamel caries.
  - Dentinogenesis imperfecta.
  - Dentin dysplasia. (Type II)
  - Age changes in dental tissues.
- *Diffusion of pigments into dental tissues after their formation*
  - Extrinsic stains.
  - Endodontic materials.
  - Products of pulp necrosis.
- *Pigments incorporated during formation of dental tissues*
  - Bile pigments in biliary atresia.
  - Hemosiderin pigments in erythroblastosis fetalis.
  - Porphyrines in porphyria.
  - Tetracycline stains.
  - Postmortem pink tooth.

CLASSIFICATION OF CYSTS OF THE ORAL REGION

ODONTOGENIC

Developmental

- Gingival cyst of infants
- Odontogenic keratocyst (primordial cyst)
- Dentigerous (follicular) cyst
- Eruption cyst
- Lateral periodontal cyst
- Gingival cyst of adults
- Botryoid odontogenic cyst
- Glandular odontogenic (sialo odontogenic; mucoepidermoid odontogenic) cyst
- Calcifying epithelial odontogenic cyst.

Inflammatory

- Radicular cyst, apical and lateral
- Residual cyst.
- Paradental cyst and mandibular infected buccal cyst.
- Inflammatory collateral cyst.

NONODONTOGENIC

- Nasopalatine duct (incisive canal) cyst.
- Nasolabial (nasoalveolar) cyst.
- Midpalatal raphe cyst of infants.
- Median palatine, median alveolar and median mandibular cysts.
- Globulomaxillary cyst.

Nonepithelial

- Solitary bone cyst (traumatic, simple, hemorrrhagic bone cyst)
- Aneurysmal bone cyst.

CYSTS ASSOCIATED WITH THE MAXILLARY ANTRUM

- Benign mucosal cyst of the maxillary antrum
- Postoperative maxillary cyst (surgical ciliated cyst of the maxilla).

CYST OF THE TISSUE OF THE MOUTH, FACE AND NECK

- Dermoid and epidermoid cysts
- Lymphoepithelial (branchial cleft) cyst
- Thyroglossal duct cyst
- Anterior median lingual cyst (intralingual cyst of foregut origin)
- Oral cysts with gastric or intestinal epithelium (oral alimentary tract cyst)
- Cystic hygroma
- Nasopharyngeal cysts
- Thymic cyst
- Cysts of the salivary glands—Mucous extravasation cyst, mucous retention cyst, ranula, polycystic (dysgenetic) disease of the parotid.
- Parasitic cysts—Hydatid cyst, cysticercus cellulosae, trichinosis.

CLASSIFICATION OF ODONTOGENIC NEOPLASMS

BENIGN TUMORS

- Tumors of the epithelial tissue origin
  - Ameloblastoma
  - Squamous odontogenic tumor
  - Calcifying epithelial odontogenic tumor (CEOT)
- Tumors of mixed tissue origin (made by both epithelium and mesenchyme)
  - Adenomatoid odontogenic tumor (AOT)
  - Ameloblastic fibroma
  - Ameloblastic fibro–odontoma
  - Complex odontoma
  - Compound odontoma
- Tumors of the mesenchymal tissue origin
  - Odontogenic fibroma
  - Odontogenic myxoma
  - Cementoma
  - Cementifying fibroma
  - Benign cementoblastoma

MALIGNANT TUMORS

- Odontogenic carcinomas
  - Malignant ameloblastoma
  - Primary intra-alveolar carcinoma
- Odontogenic sarcomas
  - Ameloblastic fibrosarcoma
  - Ameloblastic carcinosarcoma

CLASSIFICATION OF GIANT CELL LESIONS

NEOPLASMS

- Giant cell tumor of the bone
- Central giant cell granuloma
- Peripheral giant cell granuloma
- Giant cell epulis
- Brown tumor of hyperparathyroidism
- Giant cell fibroma
- Malignant fibrous histiocytoma.

OTHER LESIONS WHERE GIANT CELLS MAY BE PRESENT

- Osteoblastoma
- Chondroblastoma
- Aneurysmal bone cyst
- Fibrous dysplasia of bone
- Cherubism
- Tuberculosis
- Fibrous histiocytoma
- Sarcoidosis
- Hodgkin's disease
- Calcifying epithelial odontogenic cyst
- Eosinophilic granuloma
- Letterrer Siwe disease
- Giant cell arteritis
- Pulse granuloma
- Histoplasmosis.

CLASSIFICATION OF VERRUCAL–PAPILLARY LESIONS OF ORAL CAVITY

REACTIVE LESIONS

- Papillary hyperplasia of palate
- Condyloma latum
- Squamous papilloma
- Oral warts
- Oral papillomatosis
- Condyloma acuminatum
- Heck's disease.

NEOPLASMS

- Keratoacanthoma
- Verrucous carcinoma
- Unknown etiology
- Pyostomatitis vegetans
- Verruciform xanthoma.

CLASSIFICATION OF DISEASES OF SALIVARY GLANDS

NON-NEOPLASTIC DISORDERS

DEVELOPMENTAL ANOMALIES

- Agenesis (Aplasia)
- Hypoplasia
- Atresia
- Ectopia.

REACTIVE LESIONS

- Mucus retention cyst
- Mucus extravasation cyst .

- Sialolithiasis
- Post-radiation sialadenitis
- Chronic sclerosing sialometaplasia.

INFECTIVE LESIONS

Bacterial Sialadenitis

- Acute
- Chronic
- Recurrent.

Viral Sialadenitis

- Mumps.
- Cytomegalic inclusion disease.

IMMUNE-MEDIATED DISEASE

- Mikulicz's disease
- Sjogren's syndrome.

MISCELLANEOUS DISEASES

- Heerfordt's syndrome
- Sialosis
- Ptyalism and aptyalism
- HIV associated salivary gland disease.

NEOPLASTIC DISORDERS

A. Epithelial Tissue Neoplasms

Adenomas

- Pleomorphic adenoma (mixed tumor)
- Monomorphic adenoma
- Adenolymphoma
- Oxyphil adenoma
- Other types
- Mucoepidermoid tumor
- Acinic cell tumor
- Carcinomas
- Adenoid cystic carcinoma
- Adenocarcinoma
- Epidermoid carcinoma
- Undifferentiated carcinoma
- Carcinoma in pleomorphic (malignant mixed tumor).

B. Connective Tissue Neoplasms

- Fibroma
- Fibrosarcoma
- Lipoma
- Neurilemoma
- Hemangioma
- Melanoma
- Lymphoma.

CLASSIFICATION OF FIBRO-OSSEOUS LESIONS

- Fibrous dysplasia of bone
  - polyostotic
  - monostotic
- Ossifying fibroma
- Cementing fibroma
- Central giant cell granuloma
- Brown tumor of hyperparathyroidism
- Paget's disease of bone
- Cherubism
- Aneurysmal bone cyst
- Hemorrhagic bone cyst
- Focal condensing osteitis
- Exostoses
  - Torus palatinus
  - Torus mandibularis
- Focal osteoporotic bone marrow defect (FOBMD)
- Fibrous defect (non-ossifying fibroma) of the mandible
- Osteogenesis imperfecta
- Osteoporosis
- Vanishing bone disease (massive osteolysis)
- Histiocytosis-X
- Condylar hypertrophy
- Acromegaly
- Infantile cortical hyperostosis
- Fragile-X syndrome
- Cleidocranial dysplasia
- Achondroplasia
- Rickets
- Scurvy
- Hurler's syndrome
- Garres' osteomyelitis.

CLASSIFICATION OF VASCULAR TISSUE DISEASES

- The arteritides
  - Polyarteritis nodosa
- Midfacial granuloma syndrome
  - Wegner's granulomatosis

- Stewart-type midfacial granuloma
- Giant cell arteritis
- Radiation arteritis

- Vascular hamartomas
  - Hemangiomas
  - Lymphangiomas
- Telangiectases
  - Hereditary hemorrhagic telangiectasia
  - Radiation telangiectasia
- Vascular tumors
  - Leiomyoma
  - Leiomyosarcoma
  - Hemangiopericytoma
  - Hemangioendothelioma
  - Kaposi's sarcoma
  - Angiolymphoid hyperplasia with eosinophils and Kimura's disease.

CLASSIFICATION OF DISEASES OF THE HEMOPOIETIC TISSUES AND LYMPHORETICULAR SYSTEM

- Anemia
- Sickle cell disease
- Thalassemia
- Leukopenia
- Acquired immunodeficiency syndrome (lymph node changes)
- Purpura
- Leukemias
  - Acute lymphocytic leukemia
  - Acute myelocytic leukemia
  - Chronic lymphocytic leukemia
  - Chronic myeloid leukemia
  - Granulocytic sarcoma
- Lymphomas
  - Hodgkin's lymphoma
  - Non-Hodgkin's lymphoma
  - Burkitt's lymphona
- Pseudolymphoma
- Mycosis fungoides
- Lymphomatoid granulomatosis
- Multiple myeloma
- Solitary plasmacytoma
- Amyloidosis
- Lymphoma and leukemia like reactions
- Infectious mononucleosis
- Angiofollicular lymphoid hyperplasia

CLASSIFICATION OF STOMATITIS

- Infective stomatitis
  - Primary herpetic stomatitis
  - Herpes labialis
  - Chicken pox
  - Infectious mononucleosis
  - Hand-Foot-and-Mouth disease
  - Herpangina
  - Candidiasis
  - Tuberculosis
  - Syphilis
- Stomatitis immunologically mediated or of dubious origin
  - Aphthous stomatitis
  - Behcet's syndrome
  - Lichen planus
  - Lupus erythematosus
  - Pemphigus vulgaris
  - Pemphigus vegetans
  - Pyostomatitis vegetans
  - Cicatricial pemphigoid
  - Desquamative gingivitis
  - Bullous erythema multiform
  - Epidermolysis bullosa
  - Dermatitis herpetiformis
  - Reiter's syndrome
  - Cowden's syndrome
  - Acanthosis nigricans

CLASSIFICATION OF SEVERE INFECTIONS OF THE OROFACIAL TISSUES

- Acute cellulitis
- Ludwig's angina
- Space infections
- Cavernous sinus thrombosis
- Actinomycosis
- Histoplasmosis
- Phycomycosis
- Cryptococcosis
- Aspergillosis
- Blastomycosis
- Cat scratch disease
- Cancrum oris
- Midline lethal granuloma
- Suppurative parotitis
- Acute osteomyelitis of maxilla

- Acute osteomyelitis of mandible
- Acute infections in AIDS patients and other immunocompromised conditions.

CLASSIFICATION OF CHRONIC OROFACIAL PAIN

NEURALGIAS

- Primary trigeminal neuralgia (tic douloureux)
- Secondary trigeminal neuralgia (CNS lesions or facial trauma)
- Herpes zoster
- Postherpetic neuralgia
- Geniculate neuralgia
- Glossopharyngeal neuralgia
- Superior laryngeal neuralgia
- Occipital neuralgia.

PAIN OF MUSCULAR ORIGIN

- Cervical osteoarthritis
- TMJ disorders
  - TMJ rheumatoid arthritis
  - TMJ osteoarthritis
  - Myofacial pain dysfunction syndrome
- Fibromyalgia
- Cervical sprain or hyperextension
- Eagle's syndrome.

PRIMARY VASCULAR DISORDERS

- Migraine with aura
- Migraine without aura
- Cluster headache
- Tension–type headache
- Hypertensive vascular changes
- Mixed headache
- Cranial arteritis
- Carotodynia
- Thrombophlebitis.

PSYCHOGENIC PAINS

- Delusional/hallucinatory
- Hysterical/hypochondriac.

GENERALIZED PAIN SYNDROME

- Post-traumatic pain
- Sympathetically maintained pain (Causalgia)
- Phantom pain
- Central pain.

LESION OF THE EAR, NOSE AND ORAL CAVITY

- Maxillary sinusitis
- Otitis media
- Odontalgia
  - Dentin defects
  - Pulpitis
  - Periapical pathology
  - Periapical abscess
  - Periodontal pathology
  - Cracked tooth syndrome
  - Occlusal trauma
- Atypical odontalgia
- Cyst and tumors
- Osteitits
- Mucocutaneous diseases
- Salivary gland diseases
- Atypical facial pain
- Glossodynia.

CLASSIFICATION OF DISEASES OF TONGUE

DEVELOPMENTAL DISORDERS

- Aglossia
- Hypoglossia
- Cleft tongue
- Ankyloglossia
- Fissured tongue
- Scrotal tongue
- Median rhomboid glossitis
- Benign migratory glossitis
- Hairy tongue
- Lingual thyroid
- Thyroglossal duct cyst
- Microglossia
- Macroglossia
- Bald tongue.

DISORDERS IN LINGUAL PAPILLAE

- Hairy tongue
- Oral thrush
- Chemicals burns
- White sponge nevus
- Vesiculobullous lesions
- Lichen planus
- Leukoplakia
- Hairy leukoplakia

- Vitamin deficiency
- Hunter's glossitis
- Atrophic glossitis in Plummer-Vinson's syndrome or Paterson-Kelly syndrome.
- Glossitis due to syphilis
- Pigmentations
- Traumatic ulcers
- Infectious diseases
- Lingual varicosities
- Lingual hematoma.

DISEASES AFFECTING BODY OF THE TONGUE

- Amyloidosis
- Lingual abscess
- Muscular dystrophy
- Hypoglossal nerve palsy
- Actinomycosis
- Cysticercosis
- Trichinosis
- Neck-tongue syndrome
- Glossoptosis
- Glossophyrosis
- Glossodynia
- Intracts in the tongue
- Angioneurotic edema.

BENIGN TUMORS

- Traumatic fibroma
- Pyogenic granuloma
- Granular cell myoblastoma
- Hemangioma
- Lymphangioma
- Neurofibroma
- Salivary gland tumor.

MALIGNANT TUMORS

- Squamous cell carcinoma
- Verrucous carcinoma
- Malignant fibrous histiocytoma.

CLASSIFICATION OF GINGIVAL ENLARGEMENTS

FOCAL GINGIVAL ENLARGEMENTS

- Pyogenic granuloma
- Fibroepithelial polyp
- Parulis
- Denture irritation
- Peripheral giant cell granuloma
- Peripheral fibroma
- Giant cell fibroma
- Fibrous histiocytoma
- Malignant fibrous histiocytoma
- Fibrosarcoma
- Nodular fascitis
- Localized fibromatosis
- Exostosis
- Gingival cyst
- Eruption cyst
- Congental epulis of newborn

GENERALIZED GINGIVAL ENLARGEMENTS

- Inflammatory enlargements
  - Scurvy
  - Puberty
  - Pregnancy
  - Oral contraception
  - Acute leukemias
  - Hormonal imbalance
  - Crohn's disease
  - Wegeners' granulomatosis
- Fibrous overgrowths of the gingiva
  - Hereditary gingival fibromatosis
  - Drug induced gingival fibromatosis
    - Phenytoin sodium
    - Cyclosporine
    - Nifedipine and verapamil
  - Chronic hyperplastic gingivitis
  - Orofacial angoiomatosis
  - Idiopathic
- Syndrome associated gingival enlargements
  - Rutherford syndrome
  - Limmerman-Laband syndrome
  - Cowden syndrome
  - Tuberous sclerosis syndrome
  - Gorlin-Goltz syndrome
  - Murry-Puretic-Drescher syndrome
  - Cross syndrome
  - Ramon syndrome
  - Lysosomal storage disease
  - Acanthosis nigricans
  - Epidermal nevus syndrome

CLASSIFICATION OF SKIN DISEASES

MACULES AND PATCHES

- Hypopigmented vitiligo,
- Hyperpigmented ephelides
  - Café –au –lait macules
  - Solar lentigo
  - Melasma
- Erythematous
  - Erysipelas
  - Telangiectasia
  - Petechiae
  - Purpura
  - Ecchymosis
  - Splinter hemorrhage

PAPULES AND PLAQUE

- Flesh colored or yellow
  - Acrochordon
  - Fibrous papule
  - Adenoma sebaceum
  - Neurofibroma
  - Syringoma
  - Molluscum contagiosum
  - Sebaceous hyperplasia
  - Xanthelasma
  - Milia
  - Favre-Racouchot syndrome
- Hyperpigmented
  - Nevus
  - Melanoma
  - Seborrheic keratitis
- Erythematous
  - Acne
  - Perioral dermatitis
  - Folliculitis
  - Furuncle
  - Miliaria
  - Granuloma faciale
  - Cherry hemangioma
  - Spitz Nevus
  - Acute febrile neutrophilic dermatosis (Sweet's Syndrome)
  - Morbilliform drug eruptions
  - Violaceous (Blue or Purple)
  - Lichen planus
  - Venous lake
  - Blue nevous
  - Angiosarcoma.

NODULES

- Basal cell carcinoma
- Keratoacanthoma
- Squamous cell carcinoma.

WHEALS

- Urticaria (Hives)
- Angioedema.

PAPULOSQUAMOUS DERMATOSIS

- Actinic keratosis (solar keratosis)
- Seborrheic dermatitis
- Psoriasis
- Atopic dermatitis
- Keratosis pilaris
- Pityriasis Rosea
- Verruca vulgaris (Warts)
- Flat wart (Verruca Plana).

VESICLES/BULLAE/PUSTULES

- Herpes simplex infection
- Varicella-zoster infection
- Contact dermatitis
- Impetigo
- Rosacea
- Erythema multiforme
- Pemphigus vulgaris/foliaceous/ erythematosus.

EROSIONS/FISSURES/ULCERS/SCARS

- Perleche
- Pyoderma gangrenosum
- Burns
- Keloid
- Radiodermatitis.

CONNECTIVE TISSUE DISEASE

- Dermatomyositis
- Lupus erythematosus
- Scleroderma
- Temporal arteritis.

CLASSIFICATION OF TASTE DISORDERS

- Gustatory-Olfactory confusion in patients with hyposmia.
- Post-upper respiratory tract infection.
- Any of the multiple causes of olfactory loss
- Secondary dysgeusias and parageusias.
- Retained food, heavy dental plaque, calculus caries, defective dental restorations, acute gingivitis, periodontitis, poorly cleaned bridges or dentures, poor oral hygiene.
- Abnormal compounds in saliva and nasal mucus sialadenitis, sialolithiasis, salivary hypofunction, Sjogren's syndrome, post–therapeutic radiation, medications.
- Metabolic byproducts of ingested foods and medications.
- Crevicular fluid and inflammatory transudates.
- Gingivitis periondontitis, mucositis, extraction socket and wounds.
- Bacterial or fungal metabolic products.
- Cryptic tonsillitis, tonsilloliths.
- Abnormal metabolic products circulating in the blood stream (intravascular taste).
- Metallic cations.
- Corrosion of metallic restorations, prosthesis.
- Electric stimulation of taste receptors.
- Transport disorders.
- Salivary hypofunction and xerostomia.
- Sjogren's syndrome, other sialadenitis, post–therapeutic radiation, medications affecting salivary flow.
- Blocking of taste bud pores by bacteria or other debris.
- Blocking of taste bud pores by bacteria or dental prosthesis.
- Idiopathic taste abnormality
- Age-related changes of gustatory function.
- Disorders affecting sensorineural structures for taste inherited disorders.
- Loss of taste buds or taste bud function.
- Glossitis, lichen planus, leukoplakia, leprosy, therapeutic radiation, chemotherapy, medications toxins, and other substances affecting taste bud cell function or turnover rate (e.g., captopril, penicillamine, gymnemic acid, cholinergic acid and cynarin), smokeless tobacco bulimic purging.
- Damage to taste nerves (facial and glossopharyngeal).
- Surgical trauma to lingual V, chorda tympani, or facial nerve (third molar extraction, middle ear surgery).
- Surgery trauma to glossopharyngeal nerve (tonsillectomy).
- Viral or bacterial infection of facial nerve (Bell's palsy) otitis media diphtheritic neuritis of seventh and ninth cranial nerves.
- Head trauma.
- Lesions affecting central taste pathways.
- Head trauma.
- Brain tumors, cerebrovascular lesions, tertiary neurosyphilis, and other neurodegenerative disease.
- Epilepsy.
- Multiple sclerosis and demyelinating diseases.
- Metabolic disorders.
- Diabetes mellitus.
- Hypothyroidism and hyperthyroidism.
- Adrenal insufficiency.
- Hepatic disease.
- Pregnancy.

CLASSIFICATION OF ORAL SWELLINGS

SWELLING ON THE FLOOR OF THE MOUTH

- Mucous retention cyst
- Mucous extravasations cyst
- Dermoid cyst
- Lymphoepithelial cyst
- Salivary gland tumor
- Sialolithiasis
- Benign and malignant tumors

SWELLING OF THE LIP AND BUCCAL MUCOSA

- Upper lip
  - Salivary gland tumor
  - Mucocele
- Lower lip
  - Traumatic fibroma
  - Mucoceles
  - Salivary gland tumor
  - Benign and malignant tumors

- Buccal mucosa swelling
  - Traumatic fibroma
  - Mucoceles
  - Salivary gland tumor
  - Benign and malignant tumors
- Palatal swellings
  - Mucoceles
  - Salivary gland tumor
  - Palatal abscess from periapical lesions
  - Lymphoma
  - Metastatic tumor
  - Torus
  - Neoplasms of maxilla
  - Neoplasms of maxillary sinus

CLASSIFICATION OF NECK SWELLINGS

- Lateral neck swelling
  - Lymphadenitis—(nonspecific, bacterial , viral, fungal)
  - Metastatic carcinoma to lymph nodes
  - Lymphoma
  - Parotid lesion (neoplasms, mumps, Sjogren's syndrome).
  - Metabolic diseases
  - Carotid body tumor
  - Epidermoid cyst
  - Cystic hygroma
- Midline neck swelling
  - Thyroglossal duct cyst
  - Thyroid tumor
  - Dermoid cyst

CLASSIFICATION OF ORAL SOFT TISSUE

- Lymph nodes
  - Chronic infections (tuberculosis)
  - Calcification following necrosis
  - Calcification in metastatic tumor
- Sialoliths
  - In submandibular gland
  - In other major salivary glands
  - In minor salivary glands
- Antroliths
  - In maxillary antrum
- Calcified ligaments
  - Eagle's syndrome
- Osteomas
  - Osteoma cutis (skin)
  - Osteoma of the tongue
  - Miliary osteoma
- Calcified blood vessels
  - Arteriosclerosis of facial artery
  - Sturge-Weber syndrome
  - Phleboliths (dystrophic calcification in veins)
- Myositis ossificans
  - Localized (traumatic)
  - Progressive myositis ossificans.
- Cysticercosis
  - Calcification of worm larvae (in the muscles of mastication)
- Neoplasms
  - Ossifying fibroma
  - CEOT
  - CEOC
  - Cementifying fibroma
  - Calcifying fibroma
- Miscellaneous
  - Pulp calcifications
  - Hypervitaminosis A
  - Chronic osteomyelitis
  - CEOT
  - CEOC
  - Systemic sclerosis
  - Dystrophic calcifications in areas of tissue necrosis.

CLASSIFICATION OF YELLOW CONDITIONS OF ORAL MUCOSA

- Fordyces' granules
- Superficial abscess
- Superficial nodules of tonsillar tissue.
- Acute lymphonodular pharyngitis
- Lipoma
- Lymphoepithelial cyst
- Epidermoid and dermoid cysts
- Pyostomatitis vegetans
- Jaundice or icterus
- Lipoid proteinosis
- Carotenemia
- Pseudoxansthoma clasticum.

ANATOMIC RADIOLUCENCIES OF JAWBONES

- **Structures related to mandible**
  - Mandibular foramen
  - Mandibular canal
  - Mental foramen
  - Lingual foramen
  - Airway shadow
  - Mental fossa
  - Midline symphysis
  - Medial sigmoid depression.
- **Structures related to maxilla**
  - Intermaxillary suture
  - Incisive canal
  - Incisive foramen
  - Nasal cavity
  - Naris
  - Nasolacrimal duct or canal
  - Maxillary sinus
  - Greater palatine foramen.
- **Structures common to the jaw**
  - Pulp chamber
  - Root canals
  - Periodontal ligament space
  - Marrow space
  - Nutrient canals
  - Developing root crypt.

RADIOLUCENT LESIONS OF THE PERIAPICAL REGION

- Periapical granuloma
- Periapical cyst
- Periapical abscess
- Periapical scar
- Surgical defect
- Dentigerous cyst
- Cementoma stage I
- Periodontal pathology
- Traumatic bone cyst
- Benign nonodontogenic tumor
- Malignant nonodontogenic tumor
- Ameloblastoma
- Aneurysmal bone cyst
- Ameloblastic fibroma
- Hemorrhagic bone cyst
- Buccal cyst
- Cementifying fibroma (early stage)
- Ossifying fibroma (early stage)
- Osteoblastoma
- Cementoblastoma
- Gaucher's disease
- Central giant cell granuloma
- Hemangioma
- Brown tumor of hyperparathyroidism
- Histiocytosis-X
- Leukemic cell invasion
- Lingual mandibular salivary gland depression
- Mandibular infected buccal cyst
- Odontoma (early stage)
- Periodontal cyst
- Solitary/multiple myeloma
- Metastatic tumor.

CLASSIFICATION OF PERICORONAL RADIOLUCENT LESIONS

- Dentigerous cyst
- Follicular space around the crown of an impacted tooth
- Ameloblastoma
- Calcifying epithelial odontogenic cyst
- Adenomatoid odontogenic tumor
- Ameloblastic fibroma
- Calcifying epithelial odontogenic tumor
- Envelopmental odontogenic keratocyst
- Ewing's sarcoma
- Histiocytosis-X
- Teratoma
- Odontogenic carcinoma
- Odontogenic fibroma
- Squamous odontogenic tumor
- Odontogenic myxoma
- Odontoma in pericoronal area
- Ossifying fibroma
- Paradental cyst
- Pseudotumor of hemophilia
- Nonodontogenic malignant tumors
- Salivary gland tumors

CLASSIFICATION OF INTER-RADICULAR RADIOLUCENT LESIONS

- Periodontal pocket
- Lateral radicular cyst
- Lateral periodontal cyst
- Furcation involvement

- Odontogenic keratocyst(collateral type)
- Traumatic bone cyst
- Globulomaxillary cyst
- Odontogenic tumors
- Nasopalatine duct cyst
- Benign nonodontogenic tumors
- Median mandibular cyst
- Paradental cyst

CLASSIFICATION OF MULTILOCULAR RADIOLUCENT LESIONS OF THE JAWS

- Odontogenic keratocyst
- Ameloblastoma
- Central giant cell granuloma
- Central hemangioma
- Neurilemmoma
- Giant cell tumor of hyperparathyroidism
- Cherubism
- Odontogenic myxoma
- Aneurysmal bone cyst
- Calcifying epithelial odontogenic tumor
- Calcifying epithelial odontogenic cyst
- Ameloblastic fibroma
- Lymphoma
- Central ossifying fibroma
- Central mucoepidermoid tumor
- Central odontogenic and nonodontogenic fibroma
- Chondroma
- Chondrosarcoma
- Eosinophilic granuloma
- Immature odontoma
- Neuroectodermal tumor of infancy osteomylitis

MIXED RADIOLUCENT-RADIOPAQUE LESIONS ASSOCIATED WITH TEETH

- Rarefying and condensing osteitis
- Periapical cementoma—intermediate stage
- Cementifying and ossifying fibroma
- Calcifying and keratinizing odontogenic cyst
- Cementoblastoma—intermediate stage
- Foreign bodies
- Generalized (nodular cemental masses) Paget's disease
- Odontoma—intermediate stage
- Osteomyelitis—chronic
- Adenomatoid odontogenic tumor
- Keratinizing and calcifying odontogenic cyst
- Ameloblastic fibro-odontoma
- Calcifying epithelial odontogenic tumor
- Odontogenic fibroma
- Eruption sequestrum

MIXED RADIOLUCENT-RADIOPAQUE LESIONS NOT NECESSARILY ASSOCIATED WITH TEETH

- Chronic osteomyelitis
- Osteoradionecrosis
- Fibrous dysplasia
- Paget's disease–intermediate stage
- Cementifying and ossifying fibromas
- Osteogenic sarcoma
- Osteoblastic metastatic carcinoma
- Chondroma and chondrosarcoma
- Ossifying subperiosteal hematoma
- Adenomatoid odontogenic tumor
- Ameloblastic fibrodentinoma
- Ameloblastic fibro-odontoma
- Calcifying epithelial odontogenic tumor
- Central hemangioma
- Ewing's sarcoma
- Intrabony hamartoma
- Keratinizing and calcifying odontogenic cyst
- Lymphoma of bone
- Malignant tumors with superimposed osteomyelitis
- Sclerosing cemental masses
- Osteoblastoma (intermediate)
- Osteoid osteoma.

MULTIPLE SEPARATE RADIOPAQUE LESIONS OF THE JAWS

- Tori and exostosis
- Multiple retained roots
- Multiple socket sclerosis
- Multiple mature cementomas
- Multiple periapical condensing osteitis
- Multiple embedded or impacted teeth
- Cleidocranial dysplasia
- Multiple hypercementosis
- Rarities
- Calcinosis cutis

- Cretinism (unerupted teeth)
- Cysticercosis
- Gardner's syndrome (osteomas)
- Idiopathic hypoparathyroidism
- Maffucci's syndrome
- Multiple calcified nodes
- Multiple chondromas (Ollier's disease)
- Multiple odontomas
- Multiple osteochondromas
- Multiple osteomas of skin
- Multiple phleboliths
- Multiple sialoliths
- Myositis ossificans
- Oral contraceptive sclerosis
- Paget's disease—intermediate stage
- Sickle cell sclerosis.

GENERALIZED RADIOPACITIES OF THE JAWS

- Sclerotic cemental masses
- Paget's disease—mature stage
- Osteopetrosis
- Rarities
- Albright's syndrome
- Caffy's disease (infantile cortical hyperostosis)
- Camurati-Engelmann disease
- Craniometaphyseal dysplasia
- Craniodiaphyseal dysplasia
- Fluorosis
- Gardner's syndrome
- Hyperostosis deformans juvenilis
- Melorheostosis
- Metastatic carcinoma of prostate
- Multiple large exostoses and tori
- Osteogenesis imperfecta
- Osteopathia striata
- Pyknodysostosis
- Van Buchem's disease.

CLASSIFICATION OF CAUSES OF TRISMUS

INTRA-ARTICULAR

- Traumatic arthritis
- Infective arthritis
- Rheumatoid arthritis
- Dislocation
- Intracapsular fracture
- Fibrous or bony ankylosis following trauma or infection

EXTRA-ARTICULAR

- Adjacent infection, inflammation, and abscesses (e.g. mumps, pericoronitis, submasseteric abscess impacted 3rd, molar tonsil or peritonsillar infection)
- Extracapsular fractures (mandible, zygoma, middle third)
- Overgrowth (neoplasia) of the coronoid process
- Fibrosis from burns or irradiation
- Hematoma/fibrosis of medial pterygoid (e.g. following inferior dental block)
- Myofascial pain-dysfunction syndrome
- Drug-associated dyskinesia and psychotic disturbances
- Tetanus
- Tetany
- Parotitis, osteomyelitis of jaw, fractures of jawbone, rabies, hysteria, poliomyelitis and strychnine poisoining.

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