Oral Pathology

Lec.1

Biopsy (Principles and techniques)

Oral and maxillofacial pathology: is the specialty of dentistry and the discipline of pathology that addresses the nature, identification and management of diseases affecting the oral and maxillofacial regions.

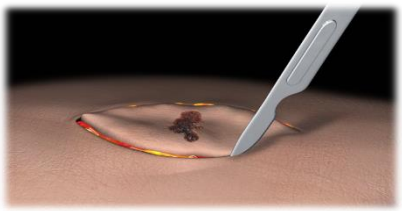
Surgical Pathology: is that specialty of pathology which deals with the diagnosis of diseases by microscopical examination of tissues taking by a surgeon ((Biopsy)).

Interpreting biopsies is one of the most important duties of the surgical pathologist, having taken a careful history and completed the clinical examination; the clinician is often in a position to formulate the diagnosis, or at least a list of differential diagnosis. In the latter case, the diagnosis is provisional and another opinion (consultation and referral) or investigation may be necessary to reach a firm diagnosis.

- **Biopsy:** is the removal of tissue from a living individual for a diagnosis by histopathological examination. The use of biopsy is not restricted to the diagnosis of the tumors, but is invaluable in determining the nature of any unusual lesion.' However not all lesions present a specific microscopic appearance and for this reason a definitive diagnosis cannot always be made. The need for special techniques in surgical pathology is sometimes needed to reach a final diagnosis.

Types of biopsy according to the size of tissue that to be biopsied: -

1- Incisional biopsies: only a portion of the lesion are sampled, and therefore the procedure is strictly of a diagnostic nature.



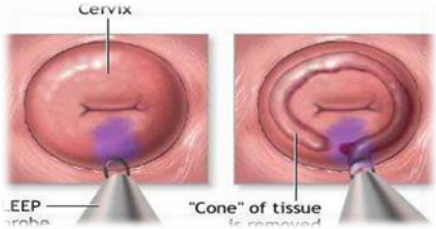
2- Excisional biopsy: the entire lesion is removed, usually with a rim of normal tissue, and therefore the procedure serves both a diagnostic and a therapeutic function.

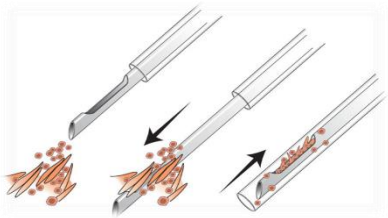
Types of biopsy according to the instruments used to obtain them: -

- **Cautery biopsy.**
- **Cone biopsy.**
- **Core needle biopsy.**
- **Vacuum assisted biopsy.**
- **Endoscopic biopsy.**
- **Punch biopsy.**
- **Surface biopsy.**

1-Cautery : the one usually least suitable for microscopic interpretation is that obtained with a cautery, because this instrument chars and distorts tissues.

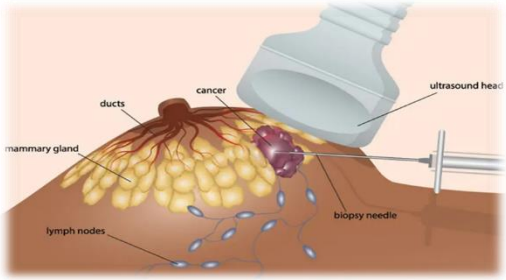
2-Cone biopsy Cone Biopsy removes a piece of tissue which is cylindrical or cone shaped. Cone biopsy is performed to diagnose **cervical cancer**. Cone biopsy is often done following a pap smear, colposcopy (examination of the cervix under illuminated magnification), and a punch biopsy.

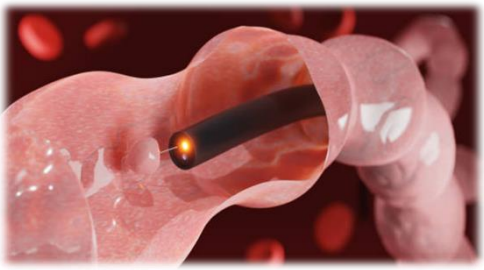




3-Core needle biopsy Core needle biopsy (or core biopsy) is performed by inserting a small hollow needle through the skin and into the organ or abnormality to be investigated. The needle is then advanced within the cell layers to remove a sample or core. Needle biopsy is also a type of percutaneous (through the skin) biopsy. The needle may be designed with a cutting tip to help remove the sample of tissue. Core biopsy is often performed with the use of spring loaded gun to help remove the tissue sample.

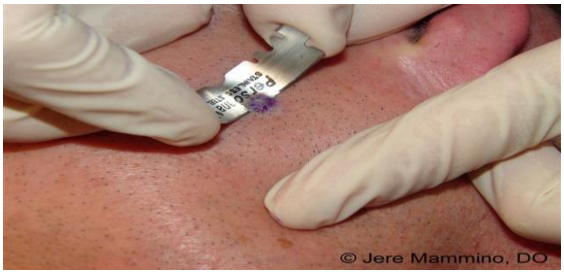
4-Vacuum Assisted Biopsy : Core biopsy is sometimes suction assisted with a vacuum device. This method enables to removal of multiple samples with only one needle insertion. Vacuum assisted core biopsy is being used more and more in breast biopsy procedures.





5-Endoscopic Biopsy: Endoscopic biopsy is a very common type of biopsy that is done through an endoscope (a fiber optic cable for viewing inside the body) which is inserted into the body along with sampling instruments.

6-Punch Biopsy: Punch biopsy is typically used by dermatologists to sample skin rashes, moles and other small masses. After a local anesthetic is injected.



7-Surface Biopsy: Surface biopsy involves sampling or scraping the surface of a sore or tumor to remove cells for pathologic testing. Surface biopsy is often performed by dermatologists to remove a small piece of skin to test for carcinoma (cancerous tissue).

General rules for the biopsy procedure.

The fact that they are so obvious makes it particularly bothersome that they are so often violated or ignored.

1. The larger the lesion, the more numerous the biopsies that should be taken from it because of the variability in pattern that may exist and the fact that the diagnostic areas may be present only focally.

2. In ulcerated tumors, biopsy of the central ulcerated area may show only necrosis and inflammation. The most informative biopsy is likely to be one taken from the periphery that includes both normal and diseased tissue; however, the biopsy should not be so peripheral

that only normal tissue is obtained.
3. The biopsy should be deep enough that the relationship between tumor and stroma can be properly assessed. Epithelia involved by carcinoma have a tendency to detach from the underlying stroma. This should be avoided whenever possible by careful handling of the tissue.
4. Deeply seated lesions are sometimes accompanied by a prominent peripheral tissue reaction, which may be characterized by chronic inflammation, hyperemia, fibrosis, calcification, and metaplastic bone formation. If the biopsy is too peripheral, this may be the only tissue obtained. Similarly, in a mass of lymph nodes, a deep-seated node may show involvement by a malignant tumor, whereas a superficial node may show only nonspecific hyperplasia.
5. When several fragments of tissue are obtained, they should all be sent to the pathology department and all of them submitted for microscopic examination. Sometimes the smaller or grossly less impressive fragment is the only one that contains the diagnostic elements.
6. Crushing or squeezing of the tissue with forceps at the time of performance of the biopsy by the surgeon, at the time of the gross examination by the pathologist, or at the time of embedding by the histotechnologist should be carefully avoided. The artifacts resulting from it often renders a biopsy impossible to interpret.
7. Once the biopsy is obtained, it should be placed immediately into a container with an adequate volume of fixative. The temptation on the part of the surgeon or the pathologist to turn it around, wash it, or scrape the surface should be resisted, since it will not provide any information of diagnostic significance but only create artifacts.
8. Depending on the presumed or known nature of the lesion, consideration should be given at the time of the biopsy to the possible need for special studies, such as touch preparations, electron microscopy, cytogenetics, molecular genetics, flow cytometry, or others.

For the above points to be fulfilled the following technical points to be considered by the surgeon in a biopsy procedure
1- Do not paint the surface of the area to be biopsied with iodine or a highly colored antiseptic
2- Local anesthesia should not be injected directly into the lesion but around the peripheries
3- Use a sharp scalpel to avoid tearing tissue.
4- Use care not to mutilation the specimen when holding it with forceps.
5- Remove a border of normal tissue if possible.
6- Fix immediately with 10% buffered formalin or 70% alcohol.
7- Put a land marks on tissue to indicate direction (e.g. sutures).
8- Labeling by name.

Indications for biopsy

- Any lesion that persist for more than 2 weeks with no apparent etiologic basis.
- Any inflammatory lesion that does not respond to local treatment after 10-14 days.
- Persistent hyperkeratotic changes in surface tissue.
- Any persistent tumescence, either visible or palpable beneath relatively normal tissue.
- Lesion that interfere with local function.
- Bone lesions not specifically identified by clinical and radiographic findings.
- Any lesion that has the characteristics of malignancy.
- Erythroplasia-lesion is totally red or has speckled red appearance.
- Ulceration-lesion is ulcerated or present as an ulcer persisted for more than 2 weeks.

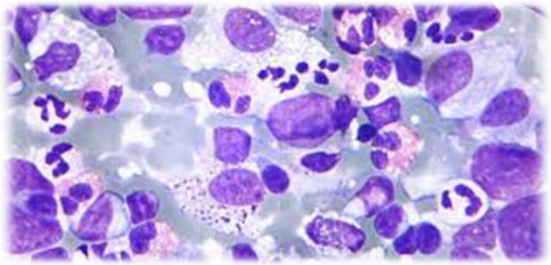
- Growth rate-lesion exhibits rapid growth.
- Bleeding-lesion bleeds on gentle manipulation.
- Induration-lesion and surrounding tissue is firm to the touch.
- Fixation-lesion feels attached to adjacent structures.

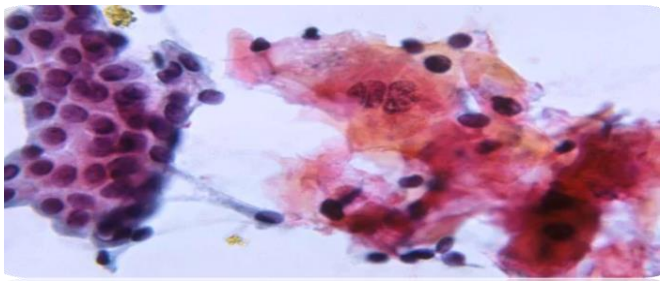
Indications for incisional and excisional biopsy

Interpreting biopsies is one of the most important duties of the surgical pathologist.
In ***incisional biopsies*****,** only a portion of the lesion is sampled, and therefore the procedure is strictly of a diagnostic nature.
In ***excisional biopsies***, the entire lesion is removed, usually with a rim of normal tissue, and therefore the procedure serves both a diagnostic and a therapeutic function.
The decision whether to perform an incisional or an excisional biopsy depends **primarily on the size of the lesion**; the smaller it is, the more logical to take it out completely when first encountered. For large lesions, particularly those of deep soft tissues, an incisional biopsy is usually preferable because of the fact that the type and extent of excision vary considerably depending on the tumor type.

Diagnostic cytology

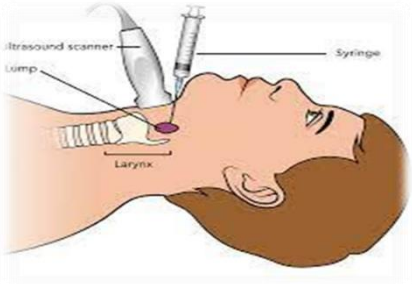
Diagnostic cytology, when performed by well-trained, experienced individuals, offers an extremely high degree of reliability. A positive cytological diagnosis of malignancy made under these circumstances should be given the same weight as one obtained from a surgical biopsy. The cytologist will make a certain number of false-negative diagnoses depending on the source of the material, but false-positive diagnoses should practically never occur, for they will in themselves invalidate the method.

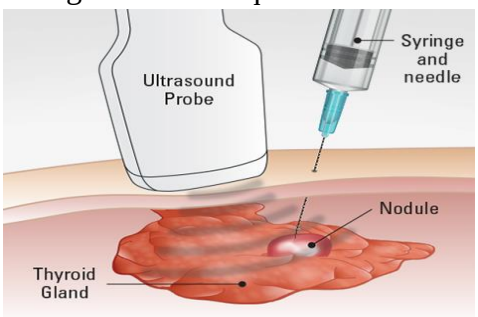




Fine needle aspiration (FNA)

The technique of fine-needle aspiration (FNA) was developed at Memorial Hospital in New York City in the 1920s. It is generally carried out with a ‘fine’ needle (OD 0.6–0.9 mm), sometimes under image guidance. There is no question that the procedure is, in most instances, inexpensive, safe, quick, and – when performed by experienced workers – quite accurate. It has contributed a great deal to transform cytology from a primarily screening tool to a powerful diagnostic technique**.**

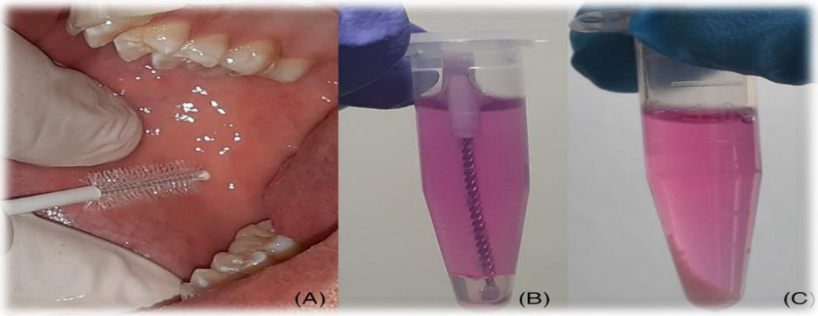




Abrasive cytology (exfoliating cytology):

This method has provided very accurate results over the years for symptomatic patients, as good as or better than with the use of mucolytic agents or abrasive methods, this rather involved procedure precludes its use as a general screening method for unselected patients.

1. Cytology is not a substitute but an adjunct to the surgical biopsy.
2. It is quick, simple, painless and bloodless procedure.
3. It helps as a check against false – negative biopsies.
4. It is especially helpful in follow-up detection of recurrent carcinoma in previously treated cases.
5. It is valuable for screening lesions whose gross appearance is such that biopsy is not warranted.



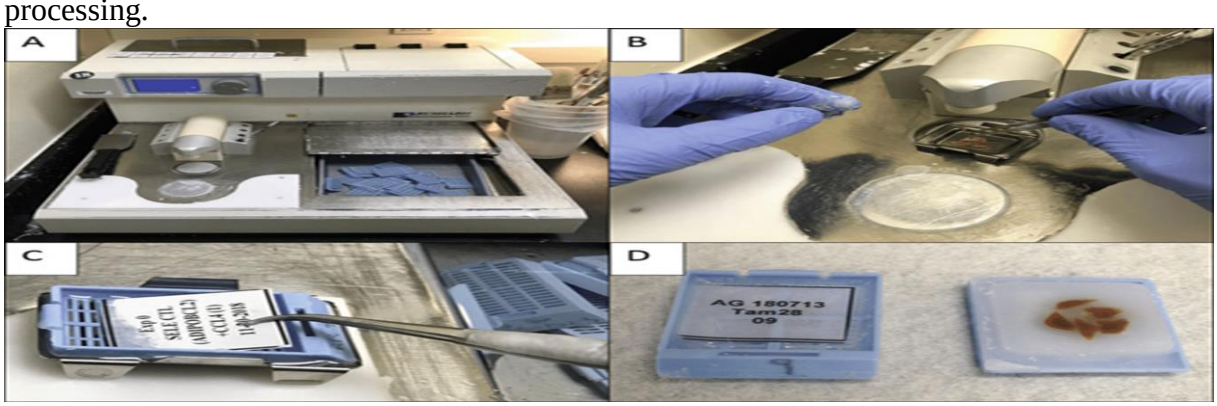
Laboratory techniques in histopathology

1-Fixation. Of the many fixatives that have been proposed, **10% buffered formalin** remains the best compromise under most circumstances. It is inexpensive, the tissue can remain in it for prolonged periods without deterioration, and it is compatible with most special stains, including immunehistochemical techniques, as long as the tissue is placed in fixative shortly (<30 min) after surgical removal, and over fixation (>24–48 hours) is avoided. Other fixative solutions are as follows:
Zenker fluid (which incorporates mercuric chloride) is an excellent fixative, one of the best that has ever been devised for light microscopic work, but it is expensive, requires careful disposal of the mercury
Bouin fixative (which contains picric acid) has been especially recommended for testicular biopsies, but Zenker fluid results in almost identical preparations. Bouin, Zenker, and B-5 are excellent fixatives for routine work and for most immunohistochemical stains, but the preservation of nucleic acids are very poor.

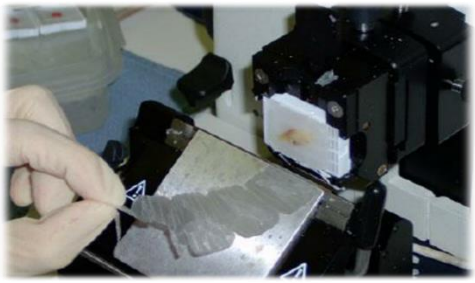
2-Laboratory tissue processing These refer to any treatment of tissues necessary to impregnate them with a solid medium to facilitate the production of sections for microscopy.
1- labeling of tissue
2- completion of fixation process
3- gentle and complete dehydration to remove aqueous fixative and any tissue water (e.g. **Ethanol and alcohol)**

4- Clearing with a substance which is totally miscible with both the dehydrating agent which precedes it and the embedding agent which follows it. (e.g. **Xylene**) .

5- Embedding e.g. wax, resins and agar. we have two types of tissue processing. Manual and automated tissue processing.



6- Microtomy-is the sectioning of tissue blocks by microtome.



7- Staining either by ordinary stains (**hematoxylin and eosin** [H&E]) or **(special stains).**

Special stains

Of the hundreds of ‘special’ stains listed in the classic texts dealing with histologic techniques, the surgical pathologist will find a relatively small minority to be of real diagnostic utility at present. This is especially true since the advent of immunohistochemistry, which has rendered many of them obsolete. Those most commonly used at present are the following:

1. Periodic acid–Schiff (PAS) stain. This is an extremely useful and esthetically pleasing technique,and makes evident most types of fungi and parasites.

2. Stains for microorganisms. These include techniques for gram-positive and gram-negative bacteria, acid-fast mycobacteria, fungi, and parasites.

3. Argentaffin and argyrophilic stains. Silver stains are mainly used for the identification of neuroendocrine cells and their tumors, but also for the demonstration of reticulin fibers, melanin, and calcium.

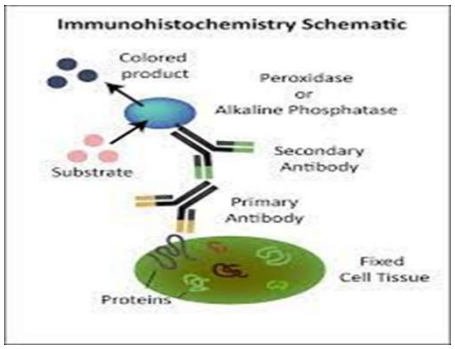
4. Amyloid stains. The mysteriously named Congo red followed by examination with both standard and polarized light (the notorious apple green birefringence) is regarded as the most reliable and practical technique to detect amyloid.

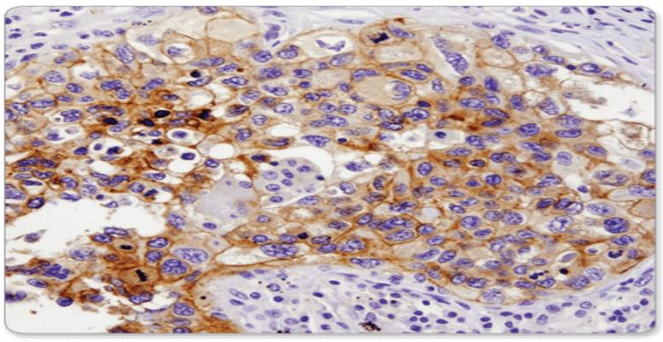
5. Reticulin stains. Reticulin stains demonstrate both ‘reticular fibers’ and basement membrane material.

6. Trichrome stain. The main value of this group of stains is in the evaluation of the type and amount of extracellular material**.**
7. Phosphotungstic acid–hematoxylin (PTAH) stain.
8. Stains for hemosiderin (Perls), melanin (Fontana–Masson), and calcium (von Kossa).
9. Stains for neutral lipids.
10. Mucin stains. since it demonstrates mucosubstances of neutral, slightly acidic, and highly acidic types

Immunohistochemistry

Briefly stated, immunohistochemistry is the application of immunologic principles and techniques to demonstrate molecules in cells and tissues. The original method, brilliantly conceived by Coons, consisted of labeling with a fluorescent probe an antibody raised in rabbits and searching for it (and therefore, for the antigen against which the antibody was directed) in tissue sections examined under a fluorescent microscope following incubation. The technical improvements that supervened in subsequent years have been responsible for these methods becoming a staple of the histopathology laboratory.





The most important diagnostic applications of immunohistochemical marker that have been applied widely to surgical pathology problems, whether as diagnostic aids, prognostic or predictive indicators, or as histogenetic probes are listed as follows: -
Actin. It is an extremely useful marker for the identification of smooth muscle cells and myofibroblasts
Albumin. Albumin comprises about one half of the blood serum proteins. It is potentially a good marker for hepatocellular and hepatoid carcinomas,
P53. Mutations of the *TP53* tumor-suppressor gene represent the most common genetic alteration in human tumors
S-100 protein. This is a family of acidic, dimeric, calcium-binding proteinsIts main use is in the evaluation of peripheral nerve sheath and melanocytic tumors
Desmin. This muscle-type intermediate filament (MW 55?000) is found in cells of smooth and striated muscle and in a lesser amount in myofibroblasts. Therefore, it has been primarily used for the identification of smooth muscle and skeletal muscle tumors.
CD34. This marker stains normal and neoplastic endothelial cells, as well as a variety of soft tissue neoplasms, including dermatofibrosarcomaprotuberans, solitary fibrous tumor.

Digital pathology and Telepathology

The era of digital pathology has arrived to surgical pathology. It has done so mainly through the many anatomic pathology information systems now on the market and the various devices that exist to capture digital images of gross and microscopic specimens, which can be integrated with the respective pathology reports. This has also allowed for these images to be transmitted electronically to any part of the globe. The latter, in short, is what is meant by *telepathology*. This can be done at various levels, from the e-mail attachment of a few static photographs to sophisticated systems that

duplicate almost to perfection the examination of slides under the microscope and are, therefore, accurately referred to as *virtual microscopy*. These instruments allow the remote user to move the microscopic field in any direction, to change magnifications, and even to change the focus, the latter function being particularly useful for cytologic preparations. This can be achieved by moving the components of a microscope located elsewhere by remote control or by scanning the desired images and performing the above operations on those images.

Surgical pathology report

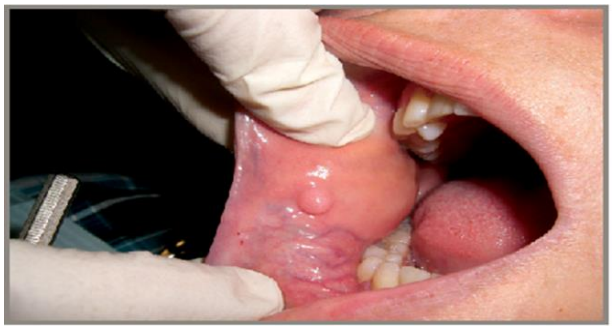
The delivery of a specimen to the surgical pathology laboratory initiates a complex series of events that culminates in the issuance of the final pathology report. The surgical pathology report should describe, as thoroughly but also as concisely as possible, all the relevant gross and microscopic features of a case, and should also interpret their significance for the clinician. It should be accurate, prompt, and brief.

The usual surgical pathology report is composed of five major fields:

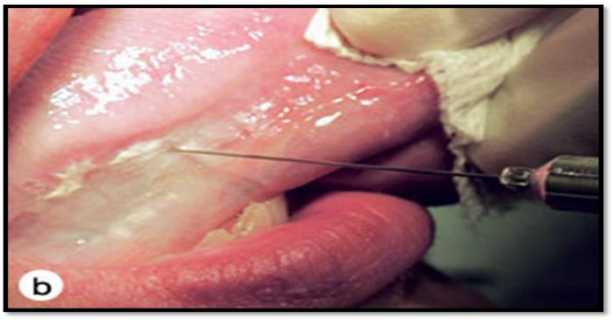
* **The first**, which follows the demographics information, is designated as **'History'**, and contains the essential clinical data known to the pathologist at the time he dictates a description of the gross specimen(s), such as sex and age of the patient, symptoms, surgical findings, and type of surgery. It should also list previous biopsies on the same patient, if any had been taken.
* **The second field**, designated as **'Gross'**, contains the gross description of the specimen(s). This should be precise and thorough, because once the gross specimen is discarded, and unless a picture has been taken, this description remains the only document by which the gross features of the case can be evaluated.
* **The third field** is termed '**Microscopic**'. We regard this as an optional feature of the report, which in many cases is unnecessary. When included, it should be short and to the point.
* **The fourth** and most important field of the report is the '**Diagnosis'**. Each specimen received should have a separate diagnosis. It is preferable to divide each diagnosis into two parts, separated by a dash. The first lists the organ, specific site in that organ, and operation; the second gives the morphologic diagnosis (e.g., Bone, femur, biopsy – Osteosarcoma).
* **The fifth field**, which is optional, is a '**Note'** or **'Comment'**. Here, the pathologist may mention the differential diagnosis, give the reasons for his diagnostic interpretation, make some prognostic and therapeutic considerations about the entity, clarify some aspects of the case, and include selected references.

If a frozen section has been performed, the information regarding the organ biopsied, the diagnosis given, the names of the pathologist(s) who performed the procedure, and the final diagnosis corresponding to *the frozen sample* should be included in the report, either as a separate field (which we prefer) or incorporated into the History or Gross fields.

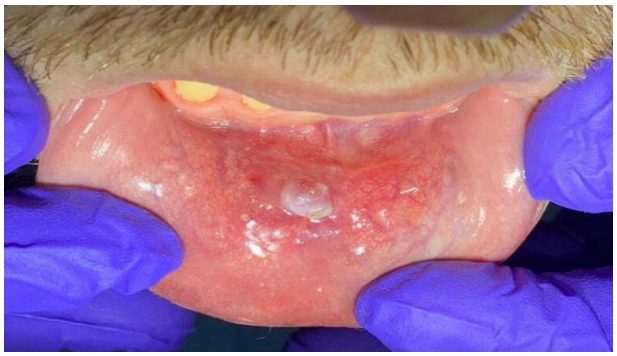
Lab.1 **Biopsy**



Excisional biopsy

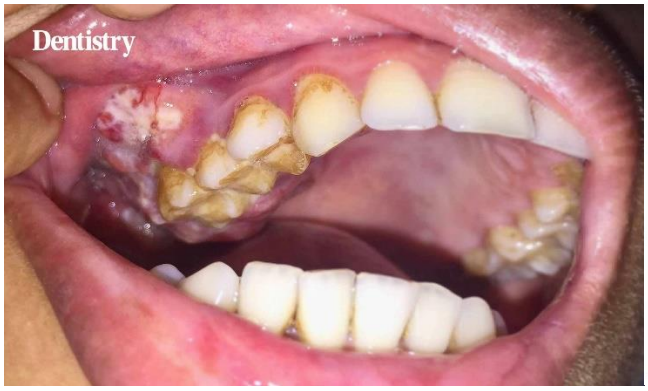


Incisional biopsy

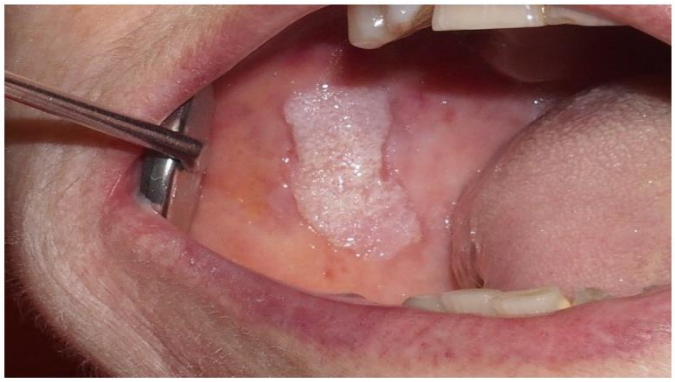


Excisional biopsy

Incisional Biopsy



Incisional biopsy



Excisional biopsy

Oral pathology

Lec.2

Dental caries

Dental caries is a multifaceted disease involving interplay among the teeth, the oral host factors of saliva and microflora, and the external factor of diet. The disease is a unique form of infection in which specific strains of bacteria accumulate on the enamel surface, where they elaborate acidic and proteolytic products that demineralize the surface and digest its organic matrix. Once penetration of the enamel has occurred, the disease progress through the dentin to the pulp. If the process is not stopped, the tooth becomes destroyed.

Epidemiology of dental caries

The prevalence and severity of dental caries differs among various populations throughout the world. The caries activity in a particular society or geographic area is closely correlated with the amount of sugar consumed per capita. In the more industrialized countries, where diets have traditionally had a high content of refined carbohydrates, the caries rate has been considerably higher than in less-developed countries. In recent years with the trend toward preventive measures such as fluoridated water, greater access to dental care and better oral hygiene in industrialized countries, and the concurrent rapid increase in caries activity in the less-developed societies, the large difference in caries rate has decreased.

Factors affecting caries prevalence: -

1- race: people living in same geographical area but belonging to different race have differing caries incidence. Generally, chinese, blacks, indians have lesser caries incidence than the caucasian whites.

2. Age: dental caries more prevalent in children up to 12 years. Incidence decreases somewhat in younger and middle age group. Incidence increases again by the older age.

3. Gender: incidence of caries is significantly higher in females than males. This may be due to the fact that teeth in females erupt earlier compared to males.

4. Familial: there appears to be heredity involved. Children of parents with low caries experience also show lesser caries incidence and vice versa.

- Loss of tooth substance may result from the action of oral microorganism in dental caries (bacterial causes), or may be due to non- bacterial causes, which include:

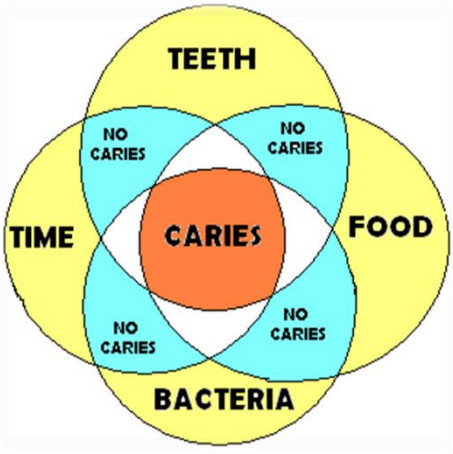
A- Mechanical factors associated with attrition and abrasion.
B- Chemical erosion.
C- Pathological resorption.

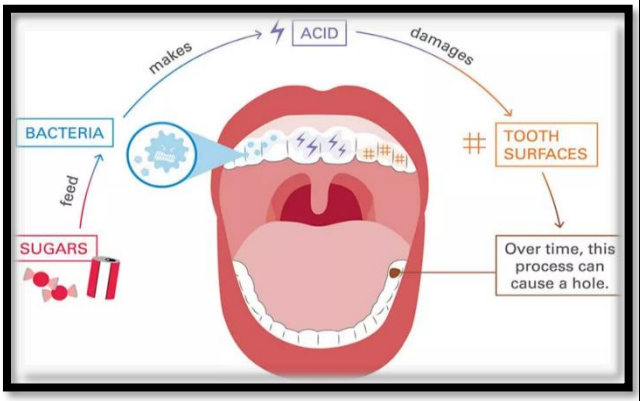
Primary causes of dental caries

Dental plaque, dietary carbohydrates, tooth (susceptible tooth surface) and time.

The carious process: bacteria in dental plaque fermentable carbohydrates such as sugars (sucrose & glucose). production of acids causing the plaque Ph to fall below 5. Repeated fall in Ph in time may result in the demineralization of susceptible site on the tooth surface initiating the carious process.

Dental caries follows the interaction of four main factors, the host, bacteria, food (diet) and time for the process to develop.





Food + bacteria acid +tooth D.C.

Caries is one of the most common of all diseases and still a major cause of loss of teeth. Dental caries is the most prevalent chronic disease in man throughout the world, 95% of the population have decay or will have it before they die. The only way to control the disease is through the use of systemic and topical fluoride, furthermore dental cry caries can be controlled by controlling the four main factors that are related to it: -

1- Host (tooth): administration of fluoride (as tables, or fluoride-containing diet), and fissure sealant (seal deep fissures in tooth surface to prevent accumulation of plaque).

2- Microorganism (bacterial flora): their action is hindered by active and passive immunization, and reduces the intake of sugars.

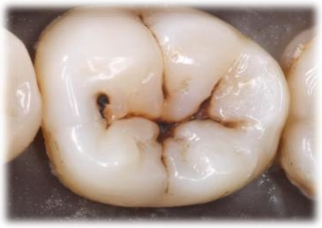
3- Diet (food):- reduction in consumption of cariogenic sugar like sucrose, fructose, maltose, glucose, both intrinsic sugar (from fruits and vegetables) and extrinsic sugars (added sugars, milk, fruit juices).

Sucrose is considered as the most cariogenic type of sugar because **(1)** it is readily fermented by bacterial plaque, and **(2)** its easily converted to extracellular glucans by bacterial glucosyltransferase. Glucans act as glue for bacteria helping their adherence to tooth surface.

4- time: frequent sugar intake between primary meals, as well as stopping teeth brushing for 12-14 hours will permit formation of bacterial plaque.

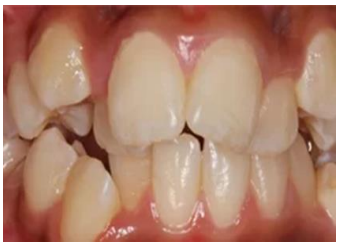
- There are other indirect factors that have a role in the development of dental caries, such as: -

Tooth: regarding its



- Composition; (less fluoride, iron, zinc, magnesium make tooth more susceptible to dental caries).
- Morphology; (deep pits and fissures can seat more bacterial plaque).
- Position; (malposed tooth can hold more bacterial plaque).

Saliva: regarding its:



- Composition; inorganic constituents are more beneficial than organic constituents.
- Ph; the higher the Ph the less the action of bacteria.
- Quantity; the more the best washing action of plaque out of embrasures, fissures and pits.
- Viscosity; the more watery the best for the removal of plaque.
- Other antibacterial factors that prevent the proliferation of bacterial flora.

Diet (food): regarding its: Physical factors: quantity of diet.

Local factors: carbohydrate content, fluoride content, vitamin content. Soft sticky food enhances the formation of plaque, and consequently caries. Refined carbohydrates, especially sucrose, are more likely to cause caries than raw products.

Vitamin content of diet: -

Of all vitamins, only V. D and V.K appear to have some role in the caries process. V. D may have an indirect effect on caries process. Its deficiency can cause enamel hypoplasia which can make the tooth more susceptible to caries. V. K has enzyme inhibiting action in carbohydrate degradation cycle can be utilized as an anticariogenic agent.

Calcium &phoshorus content:-

Available evidence indicates that there is no relation between dietary calcium and phosphorus and dental caries.

Fluorine content: - while topical and water fluoridation has been known to be effective in caries control, dietary fluorine may have no role as it is unavailable metabolically.

Systemic factors

Heredity: - racial tendency for high or low caries may be explained by heredity. However, local factors like change in dietary habits can change this tendency. Possible that caries tendency may be inherited through tooth form & structure

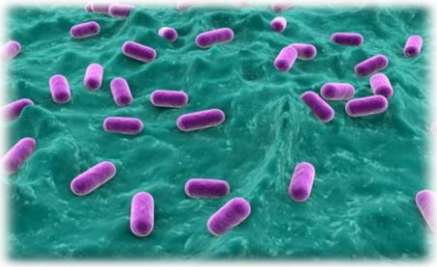
Pregnancy & lactation: - commonly observed that during pregnancy, women tend to neglect their oral health owing to all her attention being diverted to that of care for the newborn. Thus increased caries incidence during pregnancy & lactation is more a problem of neglect.

The mouth:

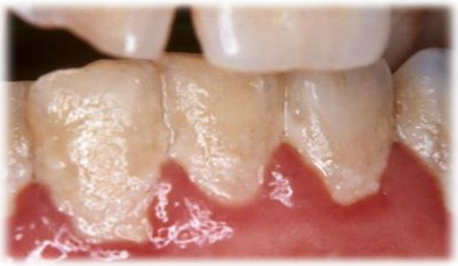
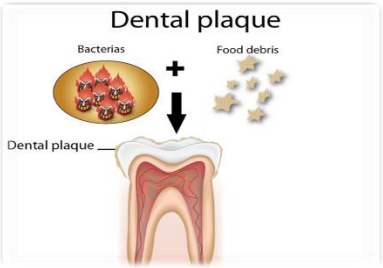
The mouth is the beginning of the digestive system chewing (masticating) not only grinds foods but degrades it with enzymes in the saliva. Saliva is a complex mixture of salts, carbohydrates, and enzymes. Some of these enzymes (amylases) break down carbohydrates into sugars that are important for the initiation of dental caries. There are many bacteria in the mouth there are really only a few species of bacteria, each bacterial species has a unique habitat in the mouth mainly streptococci are found in the mouth. *Streptococcus Salivarius*, S*streptococcus Sanguis*, *streptococcus mitis*, streptococcus *mutans*.

The streptococci are gram positive (and have a sticky cell wall) and facultative anaerobes. Facultative organisms can live in both aerobic and anaerobic environments. Lactobacilli and actinomyces are also important oral micro flora.





Role of dental plaque: - plaque defined as a soft, unmineralized, bacterial deposit or biofilm which forms on teeth and dental prostheses that are not adequately cleaned. Resists cleansing by physiological oral forces like salivary washing and tongue movements but is removable by tooth brushing. Considered as a contributing factor for at least initiation of caries. However mere presence of dental plaque doesn't necessarily mean caries will occur.

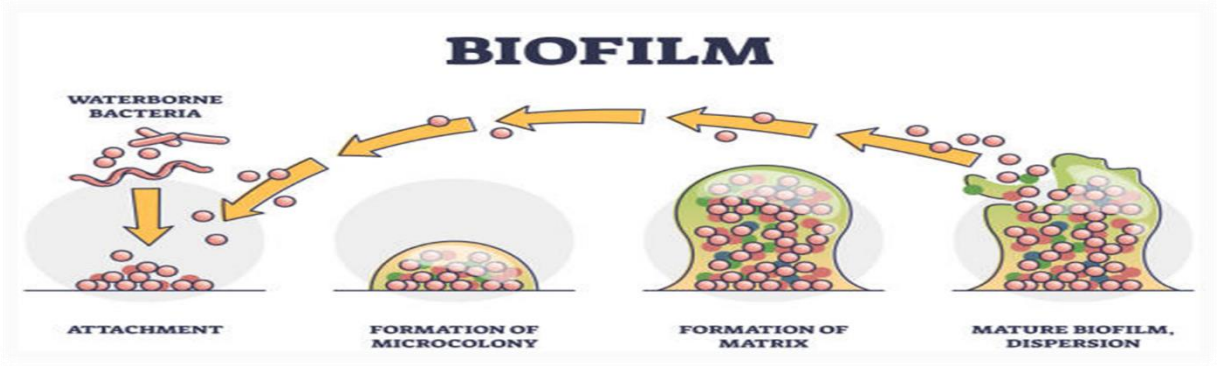



Composition of dental plaque => water – 80% solids – 20% dry weight of plaque composed of bacterial & salivary proteins – 50% carbohydrates & lipids - 25% inorganic ions, mainly Ca++ &PO4--- - 10%.

Classification of dental plaque => plaque classified as – supragingival & subgingival. Supragingival plaque – essential role in causing caries, while subgingival plaque – role in periodontal diseases.

Mechanism of formation =>

1- Plaque formation proceeds through following stages deposition of a cell free layer, acquired pellicle which is derived from salivary glycoproteins. This layer acts as nutrient for plaque bacteria.
2. Colonization of pellicle by gram positive bacteria like S.Sanguis and S.Mutans within 24 hours.
3. Maturation of plaque by further colonization with filamentous and other bacteria. Also there is buildup of plaque substance by polysaccharides produced by plaque bacteria.



Etiology and pathogenesis:

Etiology is still controversial and not clear, due to its being complicated by many direct and indirect factors. Many theories were postulated in order to explain dental caries. Most noticed theories are:

1) Acidogeneic theory ***(miller s chemoparasitic theory 1890):*** **-** it is the most accepted and supported theory, because it is based on experimental studies; made later by Orland and his workers in 1954, showed that in germ free oral hygiene in some laboratory animals, even with administration of sugar; there is no dental caries in these animals. Thus, dental caries is produced by chemical action of acids produced by micro flora.

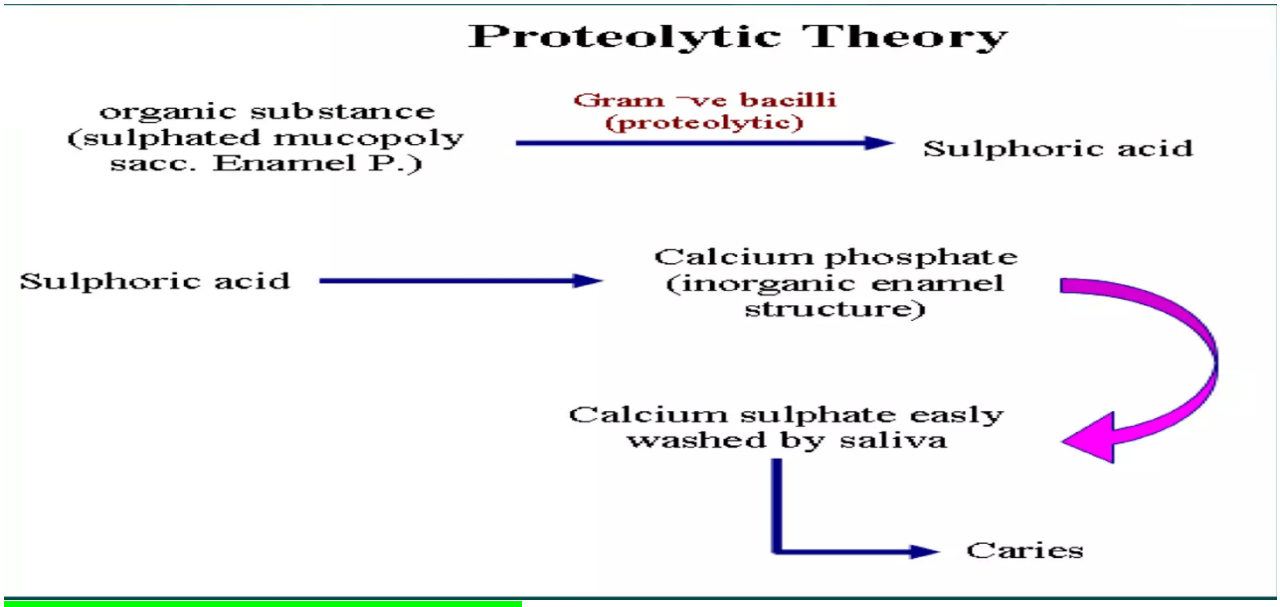
Miller s theory suggests that dental caries develop in two phases. In the **first phase**, microflora attack the inorganic structure, where decalcification of enamel and dentin is carried out by means of acids produced as a result of fermented sugar accumulating in retaining spots on tooth surface. In the **second phase**, dissolution of the soft organic part is carried out. Miller isolated numerous microorganisms from the oral cavity; most important species are lactobacillus acidophilus, streptococcus mutans, streptococcus sanguis, and streptococcus salivarius.

Objections to the hypothesis: - unable to explain predilection of specific sites on tooth to caries. Initiation of smooth surface caries not explained. Unable to explain why some populations are caries free and some are caries prone. However, this theory is accepted by majority in unchanged form. Also, bulk of evidence does implicate carbohydrates, acids and microorganisms.

2) proteolytic theory (bodecker 1878) :-

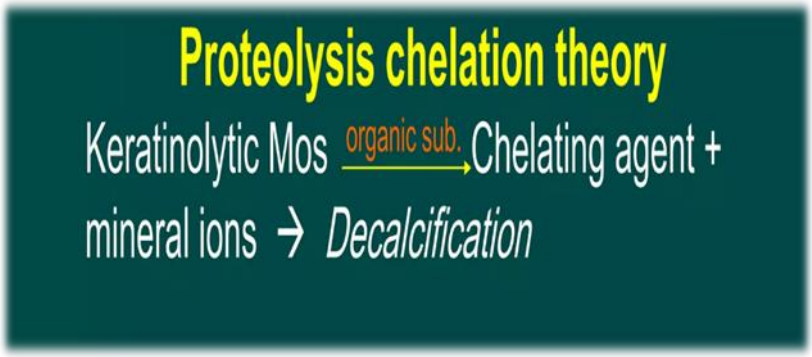
Main suggestion of this theory is that microorganism attack the organic part of enamel, leaving the generated acid responsible for further decalcification of inorganic part. Bodecker suggested that bacteria could penetrate into enamel through lamellae and interprismatic substance.

Objections to the theory: - out of 0.56% of organic matrix, 0.18% is keratin. However, no enzyme systems capable of attacking keratins have been isolated so far. Studies in germ free rats have shown that caries can occur in the absence of proteolytic organisms. However, even though proteolysis may not play any role in initiation of caries, their role in progression of more advanced carious lesions cannot be ruled out.



3-proteolysis – chelation theory: -

Schatz et al in 1955 proposed that caries occurred as a result of simultaneous degradation of organic substances (proteolysis) and dissolution of tooth minerals by a process called chelation. According to this theory, the initial attack on the tooth is on the organic components of enamel. Breakdown products of the proteolysis have chelating properties which form chelates with mineralized components of enamel and thereby decalcify the enamel even in neutral or even alkaline ph.



Objections to this theory: - direct evidence for proteolysis – chelation as a mechanism for causing caries is lacking. Recent studies have shown that saliva as well as plaque does not contain substances in sufficient concentrations to chelate calcium from enamel. However, although chelation may not be actually responsible for initiating caries, it may still have some role to play in advanced carious lesion where the ph levels return to neutral.

The last two theories are disregarded, simply because they lack support by experimental studies.

Clinical classification of dental caries: -

It is classified either

- **According to whether lesion is new or under previous restoration: -**

1. Primary (virgin) caries
2. Secondary (recurrent) caries

- **According to site of attack, it is classified as follows:**

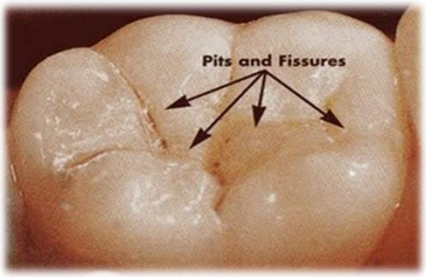
1. Pit and fissure caries.
2. Smooth surface caries.
3. Cemental or root caries.

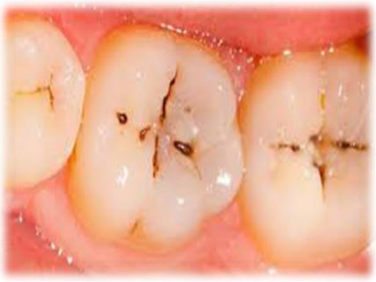
- **According to rate of attack**

1. Rampant or acute caries.
2. Slow progressive or chronic caries.
3. Arrested caries.

Pit and fissure caries: this is frequent in occlusal surfaces of molars and premolars, buccal surface of molars, lingual and palatal pits of incisors.

Early caries appears as brown or black discoloration in fissures and pits, and when inspected with dental probe, probe stick to it. In some caries in occlusal surface, where caries extends laterally in to dentin, enamel above it appears chalky white in color, because of undermined caries.





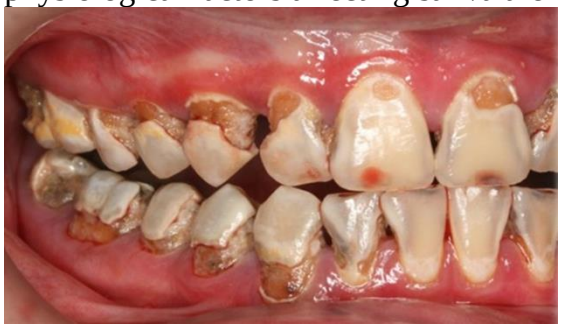
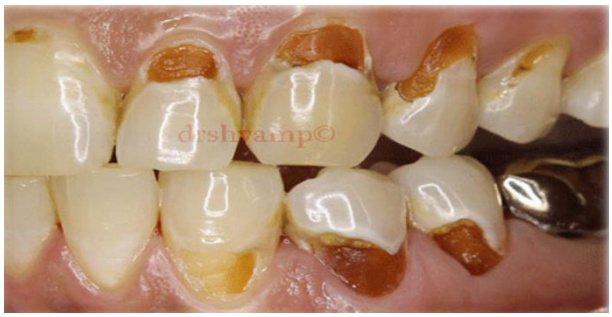
Smooth surface caries: this caries is frequent on proximal surface and gingival third of buccal and lingual surfaces (class v). Proximal caries occurs just below contact point and appear as a well-demarcated chalky white opacity of enamel.

- According to rate of attack, dental caries is classified in to:

1- Acute dental caries it is that form of caries that follows a rapid clinical course and results in early pulpal involvement by carious process. Predominantly affects children and young adults probably because their dentinal tubules are larger and show no sclerosis. The point of entry of caries is small even though there is rapid spread of caries at DEJ, producing large internal cavitation. The small point of opening doesn't allow the buffering ions of saliva to neutralize acids formed within the cavity. The affected dentin is usually stained light yellow compared to deep brown / black of chronic caries. Pain is more likely to be seen in acute dental caries than chronic caries.

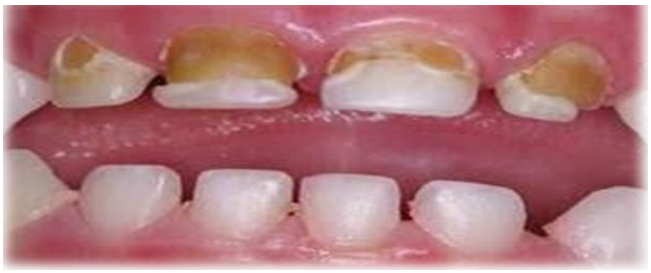
Rampant dental caries characterized by sudden, rapid destruction of teeth affecting even relatively caries free surfaces like proximal and cervical surfaces of mandibular teeth. 10 or more carious lesions over a one-year period are characteristic of rampant caries. Prominently observed in deciduous dentition of young

children and permanent dentition of teenagers. Dietary factors like high carbohydrate intake as well as physiological factors affecting saliva are major contributors to etiology of rampant caries.

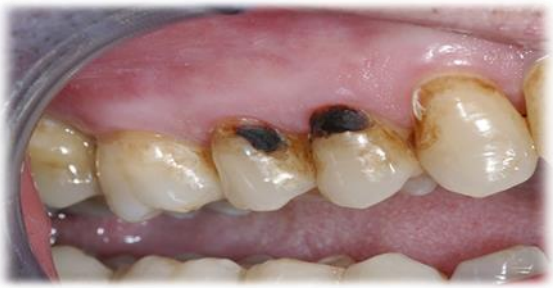
Nursing bottle caries also called baby bottle syndrome and bottle mouth syndrome. It is a type of rampant caries and occurs due to – nursing bottle containing milk, milk formula or sweetened water. Usually, the above aids are used at sleeping time after one year of age.

Clinically seen as widespread caries of the 4 maxillary incisors followed by 1st molars and then canines. Absence of caries in mandibular teeth distinguishes it from ordinary rampant caries. If milk or other carbohydrates are rapidly cleared from mouth, they aren't cariogenic, but if they pool in the mouth, then they can cause rampant caries.

2- Chronic caries: ordinary caries that develops slowly, and appears fully damaging in old ages, because it requires time.

3- Arrested caries: is type of caries where a reminalization of dentin occurred, thus hindering further caries. Reminalization is achieved by fluoride in saliva, and if the caries is in a self – cleansing area. This happen in case of badly carious teeth, where enamel is grossly damaged and fractured, thus dentin is reminalized. Also in proximal surfaces caries, after one of the teeth is extracted, the spot of caries will be in self – cleansing area and get reminalized by fluoride in saliva.



4.Recurrent caries:


Histopathology of caries:

Histopathology of caries of enamel

Enamel forms the main protective covering of the grown. Enamel is composed of 96% inorganic material, and 4%organic material and water. Enamel structure is constructed by enamel rods or prisms, rod sheath and interprismatic substance. Enamel rods appear as a body and tail directed from dentinoenamel junction; DEJ, outward to root surface.

Enamel consists of crystals of hydroxyapatite packed tightly together in orderly arrangement. Each crystal is separated from its neighbors by tiny intercrystalline spaces or pores. The spaces are filled with water and organic material. When enamel is exposed to acids produced by dental plaque, minerals is removed from the surface of the crystals which shrinks in size. The intercrystalline spaces enlarge and the tissue becomes more porous. "At this stage the carious lesion can be detected clinically and called white spot lesion ".

White spot lesion

The earliest microscopic evidence of caries in enamel best seen on dried tooth as a small, opaque, white area. Sometime the lesion may appear brown in color due to exogenous materials absorbed into its porosities. If the early enamel lesion progress, the intact surface breaks down (cavity formation). The carious lesions in smooth surface are slightly different when compared to that in pits and fissure caries.

Microscopic appearance of the white spot lesion on a smooth surface:

Usually cone shaped: the apex of the cone pointing toward the dentino enamel junction (DEJ). The lesion takes this shape because it follows the direction of the enamel prisms. Several zones can be distinguished before complete destruction of the enamel.

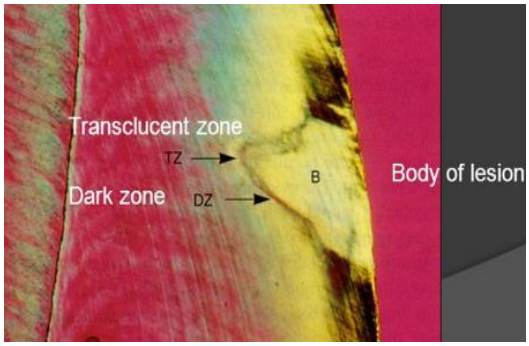
Zone i: translucent zone: In this zone, demineralization has taken place (magnesium and carbonates are dissolved) not seen in all lesions lies at the advancing front of the lesion More porous than sound enamel. Pores have been created by the demineralization process.

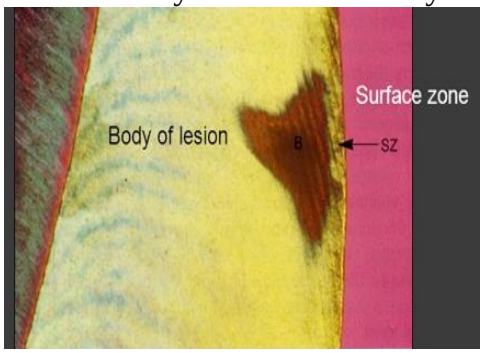
Zone ii: dark Zone: Some remineralization happens due to reprecipetation of minerals, lost from the translucent zone just superficial to the translucent zone. More porous than the translucent zone.

Zone iii: body of the lesion: It is the area of greatest demineralization and having a higher fluoride level and lower magnesium level. The largest portion of the lesion superficial to the dark zone. Increase in porosity from the peripheries to the center.

Zone iv: the surface zone unaffected surface layer that cover the small lesion. High degree of mineralization than subsurface enamel.

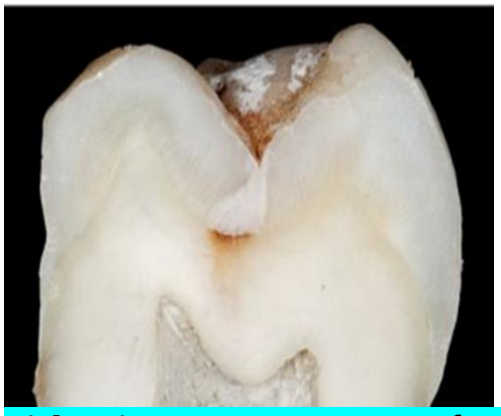
If the lesion progress the surface layer will be destroyed. Leads to cavity formation.

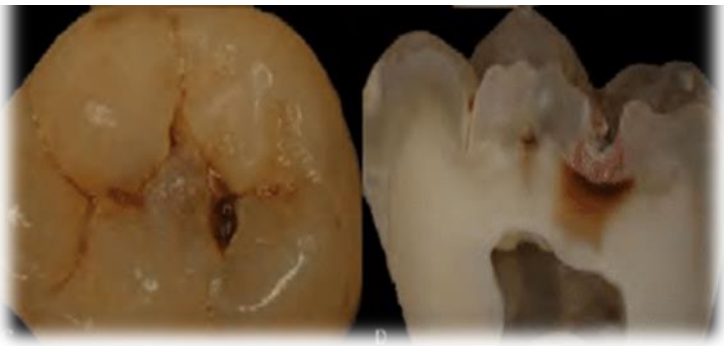




Pit and fissure caries (occlusal caries):-

The caries follows the direction of the enamel rod, and a triangular or cone shaped lesions with the apex at the outer surface, and its base toward the dentino-enamel junction.





Light microscope appearance of occlusal caries: -

The lesion forms around the fissure walls. As the lesion increases in size, it coalesces at the fissures. The enamel lesion enlarges as it approaches the underlying dentin guided by prism direction. The lesion takes the shape of a cone with its base toward the enamel-dentin. junction. The tooth enamel (outer layer of crown) is very hard and doesn't dissolve easily even with acids, but the underlying dentin dissolves easily with lactic acid eventually a cavity is formed in the dentin below the enamel , when the cavity is large enough, the enamel will crack, exposing the dentin, bacteria find the dentin a rich environment for growth and quickly eat through the dentin into the underlying pulp(where the blood vessels and nerves are) this is now a rampant carries and the tooth will likely be removed.

Fluoride makes the tooth mineral harder to dissolve, this is why fluoride treatment is effective in preventing dental caries.

Note: - more cavitations in pits and fissure than smooth surface caries. Why? Because: -

1- The enamel at the bottom of the pit and fissure may be very thin, so caries reach Faster.

2- In pits and fissure, the enamel rods are directly directed laterally (diverge), when caries occur it follows the direction of these roads leading to the formation of cone shaped or triangle.

3- The enamel at the surface become undermined and starts to collapse under the stress of mastication and to fragment around the edge of the cavity. By this stage, bacterial attack on the dentin is well established. Cavitations are greater than that of the proximal surface.

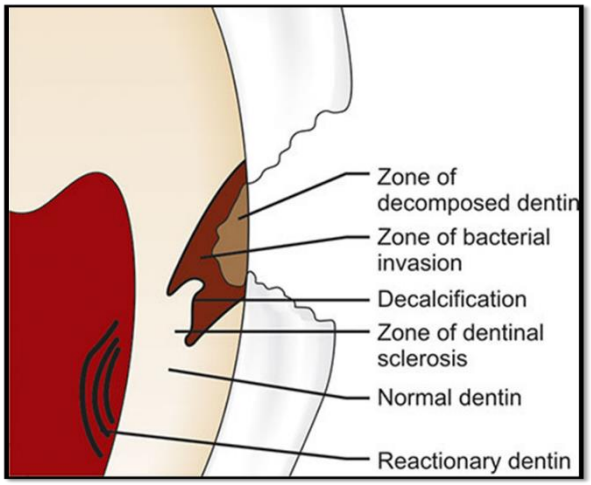
Caries of dentin

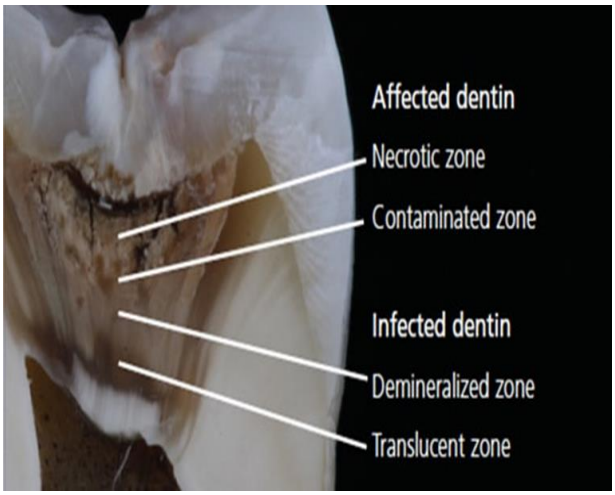
Dentin composed of 30% organic material and water, 70% inorganic material. Dentin is composed of dentinal tubules, inside which is the odontoblastic process. Odontoblastic process is the extension of odontoblas inside the dentin, these process have lateral branches anatomizing with each other, and form a network. As caries reaches the enamel-dentin junction, caries spread laterally along the junction. Sound enamel appears to be undermined by the carious process in dentin. Undermined enamel is brittle and can be fractured producing a large cavity.

When caries reached the dentin, there is a lateral spread of the lesion, involve more tubule which act as pathway or tract along which the microorganism will spread to the deeper areas and then to the pulp in a conical or triangular pattern with the apex toward the pulp and the base to the dentine.

At the first, the decalcified dentin retains its normal morphology and no bacteria can be seen. Once the dentine has been reached, pioneer bacteria extend down the tubule, soon fill them and spread along any lateral branches. The tubules become distended into spindle shapes by the expanding masses of bacteria and their product, as a result, adjacent tubule which are less heavily infected become bent, later the intervening tubule wall are destroyed and collections of bacteria in adjacent tubule coalesce (united) to form irregular liquefaction foci (these are ovoid areas of dentinal destruction and it is parallel to the

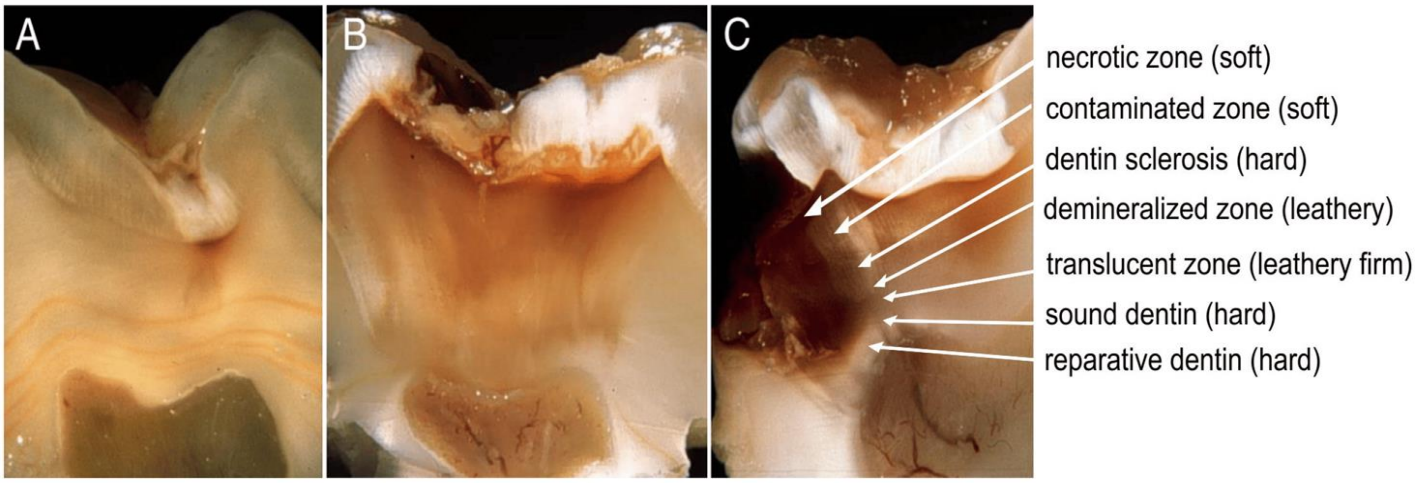
direction of dentinal tubule. It is filled with necrotic debris which increases gradually in size by expansion; in some areas, bacteria also spread laterally and occasionally large bacteria filled, clefts formed right angles to the tubules. Clinically, these clefts may allow carious dentin to be excavated easily.
We can summaries dentin carious lesion from the pulpal aspect outward into following zones: -
1- Zone of dentinal sclerosis (translucent zone): regarded as vital reaction of odontoblast to irritation (deposition of calcifying salts from the demineralized zone).
2- Zone of decalcification: soft dentin due to the action of bacterial enzyme
3- Zone of bacterial invasion.
4- Zone of decomposition of dentin: cavitation (become no mineralized remain and the organic component dissolved by the bacteria).





Protection reaction of dentin and pulp under caries:

The reaction in dentin are mainly due to odontoblast activity, these reactions are not specific to dental caries, but may be occur as a result of other irritant cause such as attrition, abrasion and restorative procedure. At early stage of dentin caries, a defensive mechanism of dentinal tubule and the vital pulp occur by:
1- Development of dentinal sclerosis or translucent dentin which mean calcification of dentinal tubules which will seal them to prevent bacterial penetration, this form in a band about half way between the pulp and adj. This process is minimal in rapidly advancing caries and prominent in slow dentin caries.
2- the odontoblast in the pulp react to changes in dentin by formation of reparative dentin (tertiary dentin – a tubular dentin) this dentin is localized to the irritant odontoblast irregular or a tubular dentin.
3- Secondary dentin: tubular dentin separated from primary dentin by hyperchromatic line or demarcated zone. It is formed following eruption throughout the life of the tooth.



Root surface caries:

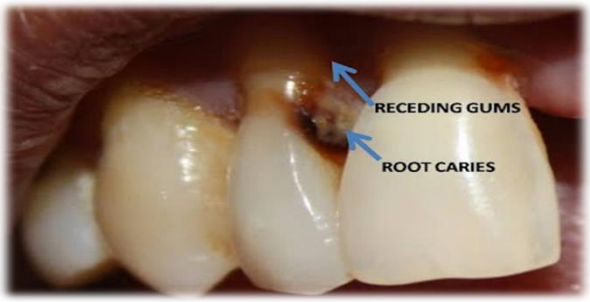
Cemental caries:

Cementum, hard tissue covering dentin in root region. It is composed of 45-50% inorganic material, and50-55% organic material. Cementum is of two types:

A- Cellular cementum , covering root from CEJ to apical one third of the root. Cells are termed cementocytes and are spider shaped cells.

B- A cellular: Occur chiefly in old people in whom the gingiva has retracted.

At first, plaque forms in the cemental surfaces, then the microorganism penetrate the cementum along or across calcified sharpies fibers. Then the bacteria seem to spread vertically in layers following the pattern of cementum formation. The cementums soften beneath the plaque over a wide area producing a saucer-shaped cavity. The decalcification of the cementum is formed by further destruction as in dentin.

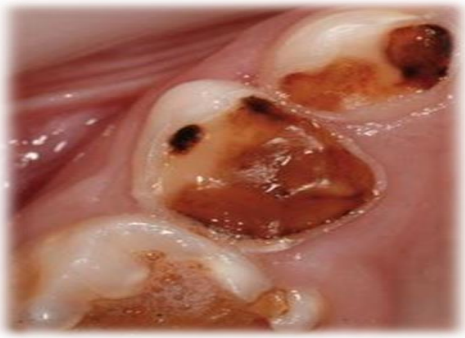


Arrest of lesions:

Inactive or arrested white spot lesions have a shiny surface and may be brown in color, having picked up exogenous stains from the mouth. These lesions cannot be detected by gently drawing a sharp probe across them because they feel the same as normal enamel. Histologically these lesions show wide, well-developed dark zones at the front of the lesion within the body of the lesion and at the surface of the lesion.

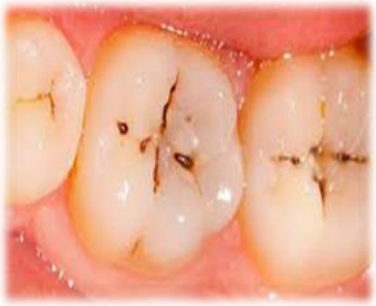
It is very important to realize that the carious process can be arrested by simple clinical measures such as improved plaque control with fluoride toothpaste and altered diet. It is therefore the clinician's responsibility to detect enamel caries in its earliest form by careful visual inspection of teeth after cleaning and drying. The clinician can now help the patient tip the balance in favor of arrest rather than progression of lesions. An arrested white spot is more resistant to acid attack than sound enamel. It may be regarded as scar tissue and should not be attacked with a dental drill.

Arrested caries and remineralization precavity (white spot) may become arrested when the adjacent tooth is removed so that the stagnation area is removed, the lesion may become remineralized by mineral from the saliva. Dentin caries may occasionally be arrested as a result of destruction of so much enamel, that a wide area of dentin become exposed, if this surface is then subject to attrition, plaque deposition may be prevented by use of fluoride and consumption of a less cariogenic diet may cause a surface lesion in enamel to heal entirely.

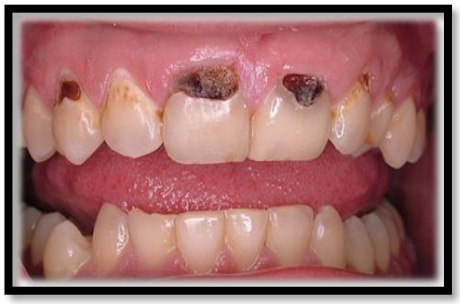


Lab.2

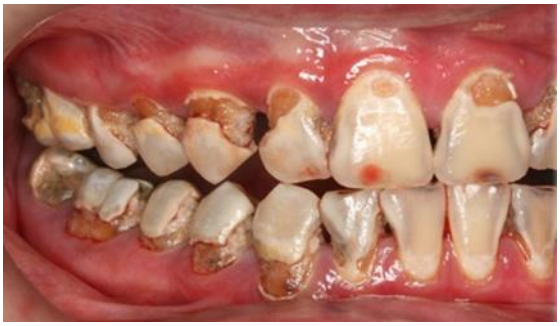
Dental caries

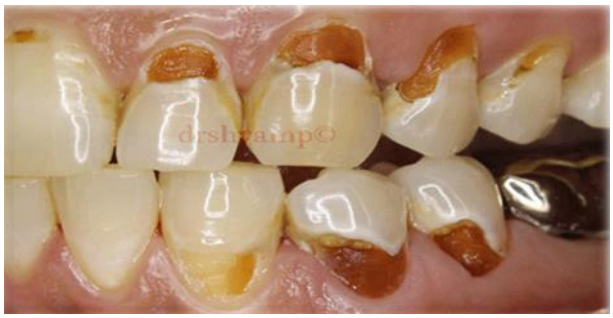


Pit and fissure caries

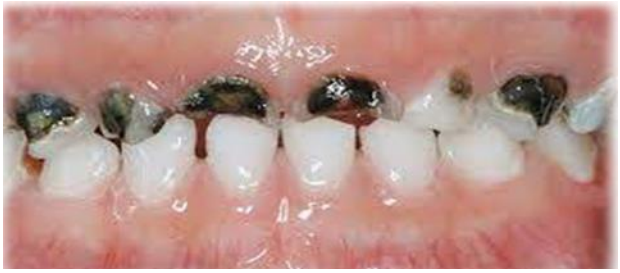


Smooth surface caries



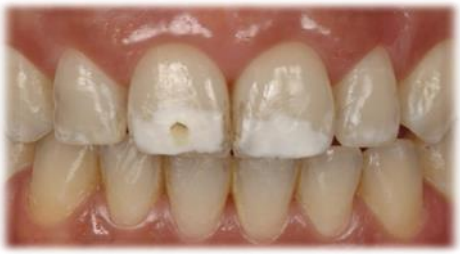


Rampant caries

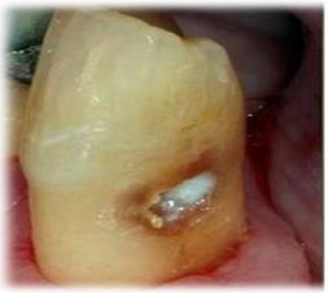


Nursing bottle caries

Recurrent caries



White spot lesion



Root surface caries

Arrested caries

Oral pathology

Lec.3

Pulp diseases (Pulpitis)

The most significant diagnostic problem that the dentists may face in their practice is to determine the extent of the pulp disease that has taken place within a symptomatic (painful) tooth. An evaluation of the damage to the pulpal tissue is essential, since the pulp can neither be seen nor touched, an indirect assessment is required. Inflammation is the single most important disease process affecting the dental pulp and accounts for virtually all pulpal of any clinical significance. The decision to be made by the dentist based on clinical assessment of the pattern of pulp inflammation (pulpitis) is one of three: -

1- To restore the defective tooth structure ((conservative)).
2- To remove the pulp tissue ((endodontic)).
3- To remove the entire tooth.

In making such a decision, the clinician should decide whether the pulp damage ((pulpitis)) is reversible or irreversible pulpitis.

Pulpitis

The dental pulp is a delicate connective tissue, containing tiny blood vessels, lymphatic, myelinated, unmyelinated nerves, and undifferentiated mesenchymal cells like other connective tissues throughout the body; it reacts to noxious stimuli by an inflammatory response. This response is not significantly different from that seen in other tissues, the final result can be different because of certain peculiar (anatomical) features of the pulp which includes: -

1-The pulp is enclosed within the calcified walls of the dentin, which precludes the excessive swelling of the tissue that occurs in hyperemic and edematous phases of inflammation in other tissues.

2-The blood vessels supplying the pulp tissues must enter the tooth through a tiny apical foramen, this precludes the development of an extensive collateral blood supply to the inflamed part.

Causes of pulpitis: -

1- Bacterial-caries in crown, periodontal pockets.
2- Traumatic-crown fractures, root fractures, partial avulsion, bruxism, abrasion.
3- Iatrogenic - Chemical -Thermal.

Heat generation, depth of preparation, dehydration of tubules, pulp exposure, and volatile/toxic disinfectant filling materials. Of these causes, the bacterial effects are the most important. Bacteria can damage the pulp through toxins or directly after extension from caries or transportation via the vasculature ((this is a debatable issue))

Barotrauma (Aerodontalgia)

Dental pain has been described by air crew flying at high altitudes in unpressurized aircraft. And in divers subjected to too rapid decompression following deep sea diving. This pain has been attributed to the formation of nitrogen bubbles in the pulp tissues or vessels, similar to the decompression syndrome elsewhere in the body, however, gas bubbles are seldom found in decompressed organs and the possibility of fat emboli from altered lipoproteins and platelet thrombi around the fat is suggested by some investigators. Aerodontalgia is really a marker of

inadequate pulp protection from the atmosphere and this usually means caries. It is not a direct cause of pulpitis, rather an exacerbating factor.

Pulpitis can be classified as

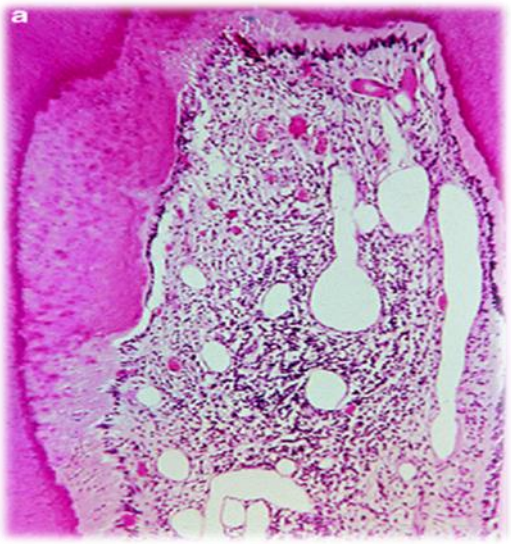
- Acute or chronic
- Subtotal or generalized
- Infected or sterile
- Reversible or irreversible

The best classification system is one that guides the appropriate treatment ((1 of the 3 choices))
Reversible pulpitis denotes a level of pulpal inflammation in which the tissue is capable of returning to a normal state of health if the noxious stimuli are removed. Irreversible pulpitis implies that a higher level of inflammation has developed in which the dental pulp has been damaged beyond the point of recovery When external stimuli reach a noxious level, degranulation of mast cells, decreased nutrient flow and cellular damage occur. Numerous inflammatory mediators (histamine, bradykinin, and prostaglandins) are released. These mediators cause vasodilation, increased blood flow, and vascular leakage with edema. Normally this should promote healing through removal of inflammatory mediators. However, the dental pulp exists in a very confined area. If the inflammatory process continued for an extended period of time can lead to increased pulp injury or even death of the pulp. Previous studies suggested that the associated increased vascular pulpal pressures could compress venous return and lead to (self-strangulation) and pulp necrosis.
Recent studies recognize that the associated increased vascular pulpal pressures could compress venous return and lead to (self-strangulation) and pulp necrosis. Recent studies recognize that the increased fluid pressure usually is localized to the area of inflamed pulp immediately adjacent to the affected dentin, increased interstitial pressure in area of inflammation leads to increased flow of fluid back into capillaries of adjacent un inflamed tissue and increased drainage. In this manner, the increased fluid pressure from inflammation is counteracted and typically does not lead to generalized increase in pulp fluid pressure, effectively preventing (self-strangulation).
According to the above mentioned explanation of the pulp response to injury, it seems that the pulp defense mechanisms may work well with many mild-moderate injuries and rarely result in widespread necrosis. Localized pulp abscesses may heal after eliminating the injury and formation of reparative dentin, however sever localized pulpal damage can overwhelm the system, leading to pulp necrosis.

1-Reversible pulpitis (focal reversible pulpitis)

This denotes that the pulp is capable of full recovery if the irritating factors subside or removed. The symptoms reflect an irritated pulp tissue that reacts with the mildest and earliest forms of the inflammatory response, consisting of vasodilation, transudation, a slight infiltrate of acute inflammatory cells underlying the area of affected dentinal tubules. Tertiary dentin may be noted in the adjacent wall. On clinical examination the pain is mild-moderate in intensity and responds to sudden change in temperature. The pain or discomfort resolves within a few seconds after elimination of the stimulus may remain for 5 minutes and seldom lasts longer than 20 minutes. The tooth remains symptomless until it is stimulated again. Changing body positions do not affect the pattern of pain, or duration of pain. The pain is mostly provoked by cold, although hot, sweet, or sour food may also cause pain.
The tooth responds to electric pulp testing at lower levels of current than normal tooth. Percussion and mobility tests are negative. If the tooth is treated, the condition is reversible and the pulp will heal, if pulpitis is allowed to progress, then irreversible pulp damage will occur.

2-Irreversible pulpitis



The patient with early irreversible pulpitis presented with sharp, sever pain on thermal stimulation, and the pain continues after removal of the stimulus. Cold is the most uncomfortable, although heat or sweet and acidic food can cause pain. The pain may be spontaneous or continuous and may be exacerbated when the patient lies down. The tooth responds to electric pulp testing at lower levels of current. At this stage (early), the pain often can be localized easily to the individual affected tooth. With time the patient discomfort is increasing and can no more be able to identify the offending tooth

In the later stages of irreversible pulpitis, the Pain increases in intensity and experienced as throbbing, which keeps the patient awake at night. At this point heat increases the pain, while cold may produce relief. The tooth responds to electric pulp testing at higher levels of current or demonstrates no response. Mobility and sensitivity to percussion are negative.

Histopathological features of irreversible pulpitis

Irreversible pulpitis often demonstrates congestion of the venules that results in focal necrosis. This necrotic zone contains polymorphonuclear leukocytes and histiocytes. The surrounding pulp exhibits fibrosis and a mixture of plasma cells, lymphocytes and histiocytic.

3-Chronic hyperplastic pulpitis

This is a unique pattern of pulpal inflammation, it occurs in children and young adults who have large exposures of the pulp in which the entire dentinal roof often is missing. The most frequently involved teeth are the deciduous or permanent molars, which have large pulp chambers in these age groups. Mechanical irritation and bacterial result in a level of chronic inflammation that produces hyperplastic granulation tissue that extrudes from pulp chamber and often fills the associated dentinal defect. The apex may be open and reduces the chance of pulp necrosis secondary to venous compression. The tooth is asymptomatic except for a feeling of pressure on mastication.

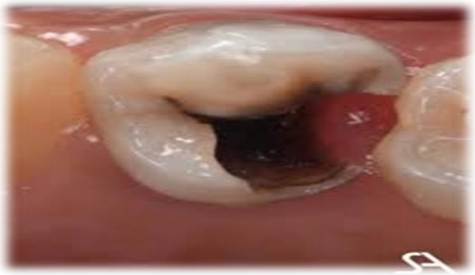
Histopathological features of chronic hyperplastic pulpitis

This demonstrates a cap of sub acutely inflamed granulation tissue that fills the entire space of the original pulp chamber. The surface of the polyp may or may not be covered with stratified squamous epithelium, which migrates from the adjacent gingiva or arise from sloughed epithelium within the oral fluids. The deeper pulp tissue within the canals typically demonstrates fibrosis and chronic inflammation.

Pulp necrosis

Pulp necrosis may follow either pulpitis or a traumatic injury to the apical blood vessels cutting off the blood supply to the pulp. A coagulative type of necrosis is seen after ischemia; trauma and the patient usually have no symptoms. If the necrosis follows pulpitis then

breakdown of the inflammatory cells may lead to liquefactive type of necrosis which may become infected by bacteria from caries, this type is usually associated with foul odor when opened with endodontic treatment.



Diagnosis of pulp pain

The diagnostic procedures that are commonly used to assess the status of a symptomatic tooth and pulp are as follows.

1-History and nature of pain.
2-Visual clinical examination.
3-Reaction to thermal changes.
4-Reaction to electric stimulation.
5-Reaction to tooth percussion.
6-Radiographic examination.
7-Palpation of the surrounding area.

The diagnosis of pulp pain (Pulpalgia) is made from a combination of all the above mentioned points. The value of these tests is sometimes less than optimal for e.g. when the procedures demonstrate that the pulp is disease free, the results are highly reliable. However, when a pulp appears to test positive for irreversible pulpitis, the histopathological examination may demonstrate no obvious evidence of pulp disease.

For this reason, the entire test available should be used to reach a diagnosis aided by the personal judgment and experience of the dentist. If no correlation is existed between the symptoms present and the clinical examination, then this should raise the suspicion that these symptoms may not be of pulp origin, or the tooth that is the source of pain may be difficult to identify.Although pulpal pain never crosses the midline, it can be referred from arch to arch making pulp testing of both arches a necessity in difficult cases. Numerous disorders have been reported to mimic pulpalgia, e.g. migraine, headache, myofacial pain and angina pectoris. If these conditions are not considered, then the results would be sequential extractions or endodontic treatment which is all not needed and inappropriate.

Treatment and prognosis: -

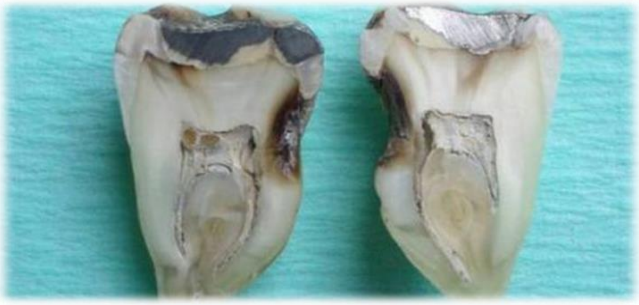
Reversible pulpitis--- removal and elimination of the cause, on occasion analgesics are required. Prognosis is good if action taken early. Pulp testing is essential periodically to ensure that irreversible damage has not occurred.

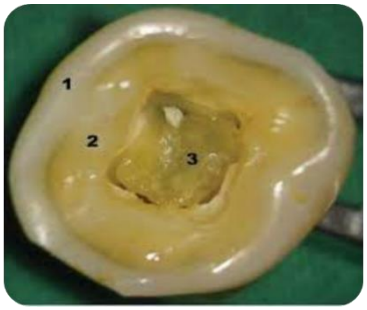
Irreversible pulpitis---both acute, chronic, chronic hyperplastic are treated by endodontic treatment or extraction.

Pulp calcification

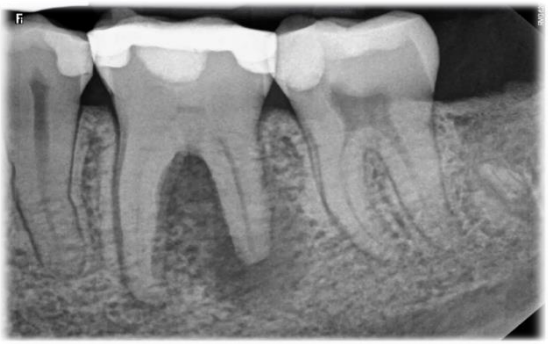
Pulp stones (Denticles) are calcified bodies with an organic matrix and occur most frequently in the coronal pulp, true pulp stones contain tubules (albeit scanty and irregular). And may have an outer layer of predentine and adjacent odontoblasts. False pulp stones are composed of concentric layers of calcified material with no tubular structure. According to their location in the

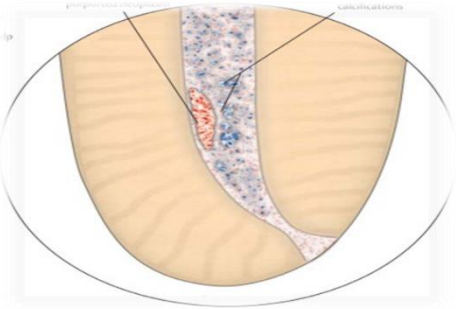
pulp stones may be described as free, adherent, or interstitial when they have become surrounded by reactionary or secondary dentine, pulp stones increases in number and size with age and are apparently more numerous after operative procedures on the tooth, when large they may be recognized on radiographs. They do not cause symptoms. Although neuralgic pain has sometimes been attributed to their presence.





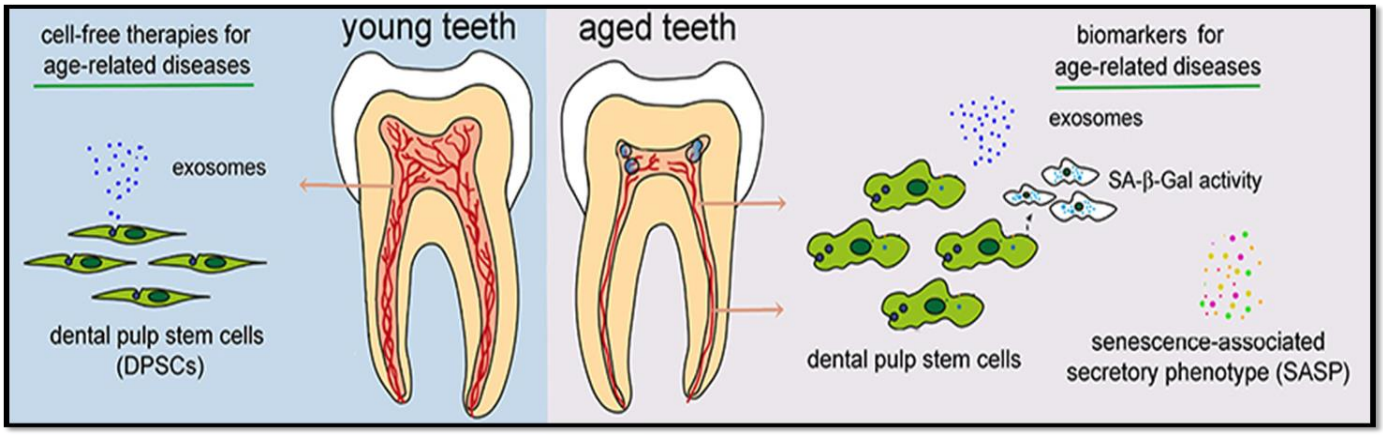
Dystrophic calcifications in the pulp consist of granules of amorphous calcific material which may be scattered along collagen fibers or aggregated into larger masses. They are most commonly found in the root canals. Dystrophic calcifications and pulp stones may obstruct endodontic therapy. Pulp calcification may follow traumatic injury to the apical blood vessels which are not sufficient to cause pulp necrosis. Large quantities of irregular dentine form in the pulp chamber and root canals which become obliterated. Pulp obliteration is also seen in dentinogenesis imperfect and dentinal dysplasia.





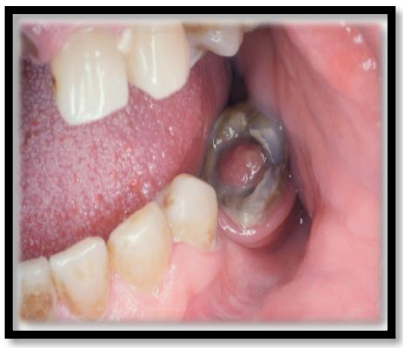
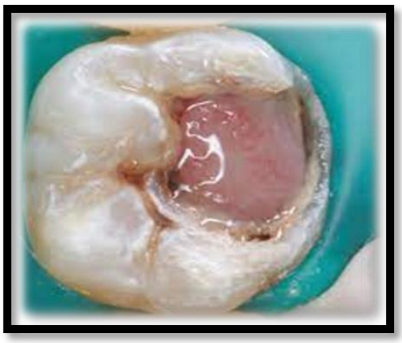
Age changes in the pulp

The volume of the pulp gradually decreases with the age due to the continued production of secondary dentine, decreased vascularity, reduction in cellularity and increase in collagen fiber content have been reported, and these changes may impair the response of the tissue to injury and its healing potential. It is generally accepted that the prevalence of the pulp stones and diffuse calcification increase with age but the evidence for this is inconclusive.

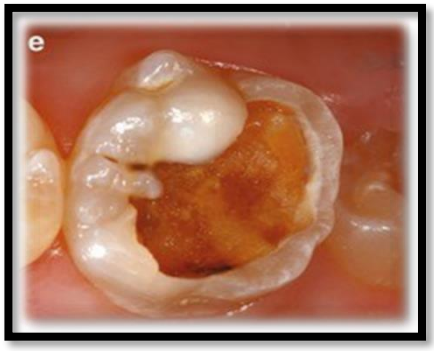
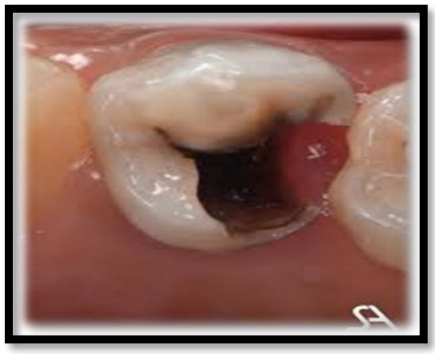


Lab.3

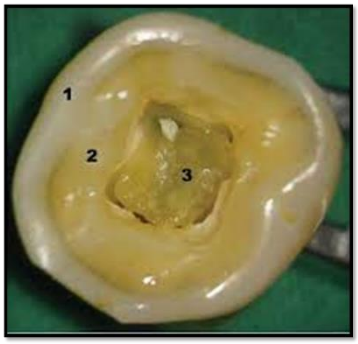
Pulp diseases

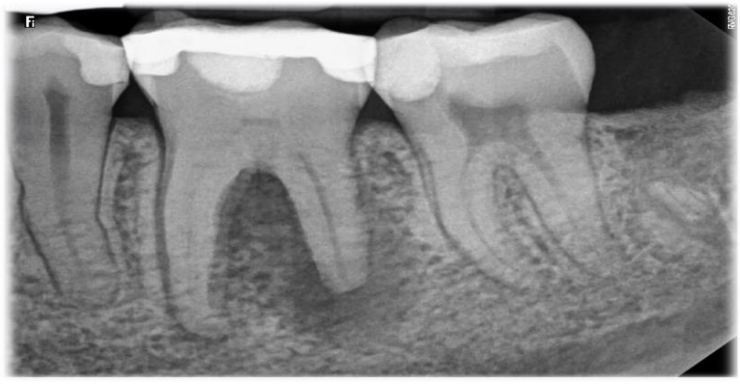

Chronic hyperplastic pulpitis

Pulp necrosis


Pulp stone



Dystrophic calcifications

Oral pathology

Lec.4

Periapical Pathology

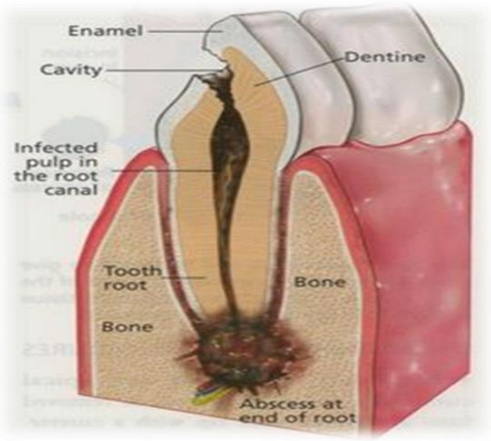
Inflammation in the periapical part of the periodontal ligament is similar to occurring elsewhere in the body, but, because of the confined space within which the process develops; a particular feature of inflammation in this site is that the adjacent bone and occasionally the root apex may resorb. However, the periapical tissue heals, if the cause of inflammation is removed.

The periapical periodontitis is different from pulpitis in the following:

1 -The periapical periodontitis differs markedly from pulpits where the potential for healing is very limited.

2 -The symptoms are also different in that they are generally well located by the patient to a particular tooth, due to the presence of the properioceptive nerve ending in the periodontal ligament.

The factors which may affect these lesions are :



1- The presence of open or closed pulpitis.

2- Virulence of the involved micro organisms .

3- Extent of sclerosis of the dentinal tubules.

4- Competency of the host immune response of the individual.

Where these factors are optimal e.g. the presence of an open chronic pulpitis, bacteria of few virulence, and an older tooth with sclerotic dentinal tubules in a healthy ((immune component)) individual, the changes at the apex of the tooth are mild and chronic.

Where the conditions are mostly adverse e.g. the presence of a closed acute pulpitis, large numbers of highly virulent bacteria, and open dentinal tubules of young teeth, the inflammation at the apex of the tooth will rapidly intensify and large amounts of bacterial toxins and autolytic enzymes will be produced and disseminated leading to rapid destruction of the periapical tissue and the surrounding bone ((e.g. acute periapical abscess).

An etiology of periapical periodontitis

1 -Pulpitis and pulp necrosis If pulpitis is untreated, bacteria, bacterial toxins and the product of inflammation will extend down the root canal and through the apical foramina to cause periodontitis.

2 -Trauma :Occlusal trauma either from a high restoration or less frequently associated with bruxism, may result in periapical periodontitis under **pressure during orthodontic treatment**, a **direct blow** on tooth insufficient to cause pulp necrosis and **biting unexpectedly on a hard body** in food may all cause minor damage to the periodontal ligament and localized inflammation .

3- Endodontic treatment Mechanical instrument through the apex during endodontic treatment as well as chemical irritation from root filling material may result in inflammation in the periapical periodontium. Instrumentation of an infected root canal may be followed by periapical inflammation, due to bacterial proliferation in the root canal or due to bacteria being forced into the periapical tissues .

1-Acute periapical periodontitis

Spread of infection through the apex brings the causative bacteria from a protected site into an environment where the host can mount an effective host response . Acute inflammation and an immune reaction are trigger.

Clinically: Pain is intense when external pressure is applied to the tooth, as the pressure is transmitted through the fluid exudates to the sensory nerve endings. Even light load may be sufficient to induce pain, as the fluid is not compressible; the tooth feels elevated in its socket. Hot and cold stimulation does not cause pain.

Histopathological findings: Vascular dilatation, exudates of neutrophils, and oedema, in the periodontal ligament situated in the confined space between the root apex and the alveolar bone. The findings are often normal as there is generally insufficient time for bone resorption to occur between the time of injury to the periodontal ligament and the onset of symptoms. If radiological changes are present, they consist of slight widening of periodontal ligament and the lamina dura around the apex.

Sequela and prognosis The inflammation may transient if it is due to acute trauma rather than infection and the condition seen resolves. If the irritant persist the inflammation becomes chronic and may be associated with resorption of the surrounding bone. Suppuration may occur associated with necrosis and bacterial infection with continued exudation of neutrophils leading to abscess formation, called acute periapical abscess.

2- Chronic apical periodentitis (periapical granuloma)

The term periapical granuloma refers to a mass of chronically or sub acutely inflamed granulation tissue at the apex of a non-vital tooth. The formation of the periapical granuloma represents a definitive reaction secondary to the presence of microbial infection in the root canal with spread of related toxic products into the apical zone .

In the early stages of infection, neutrophils predominate, and radiographic changes are not present, this phase of periapical inflammation is termed acute periapical periodontitis. The neutrophils release prostaglandins which activate osteoclaststo resorb the surrounding bone leading to detectable periapical radiolucency. With time, chronic inflammatory cells begin to dominate the host response. Mediators released by lymphocytes reduce further osteoclastic acivity while also stimulating fibroblast and microvasculature .For this reason, chronic periapical granuloma is often asymptomatic and demonstrates little additional changes radiographically.

Clinical features:

1-Most of periapical granulomas are asymptomatic.

2 -Pain may develop if acute exacerbation occurs.

3 -Typically the involved tooth does not demonstrate mobility or significant sensitivity to percussion.

5 -The soft tissue overlying the apex may or may not be tender

5- The tooth does not respond to thermal or electric pulp tests unless the pulp necrosis is limited are limited to a single canal in a multirooted tooth.

Radiographic features

Most lesions are discovered on routine radiographic examination which may show:

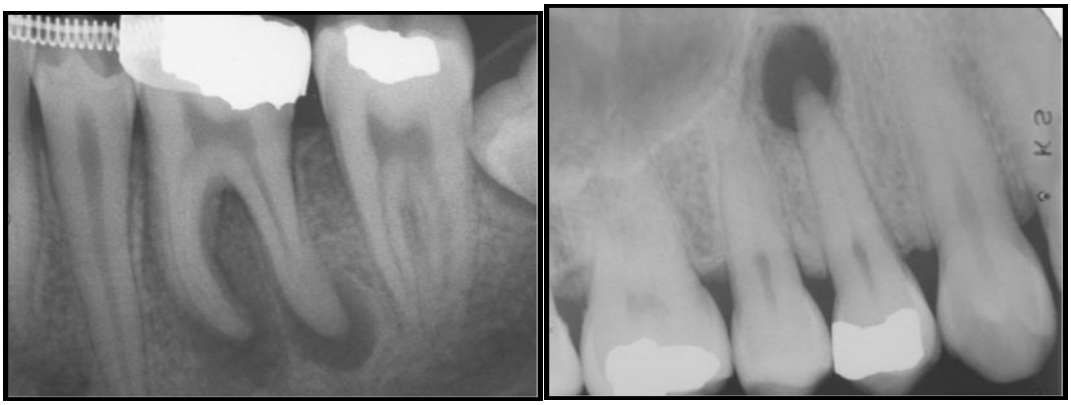
1-Variable radiolucenies ranging from very small to 2 cm in diameter.

2 -Affected teeth typically reveal loss of the apical lamina dura.

3 -The lesion may be circumscribed or ill-defined and may or may not demonstrate a surrounding radiopaque rim.

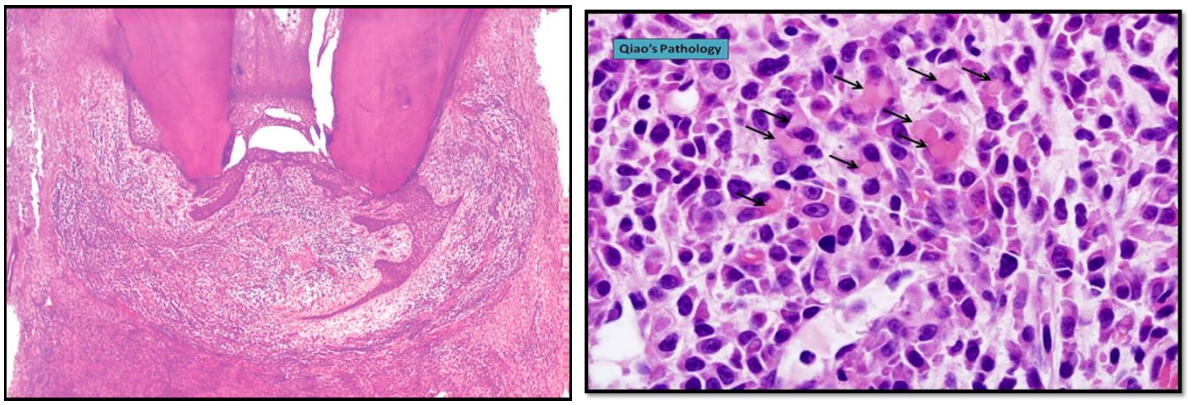
4 -Root resporption may be seen.

The radiographic features are suggested but not diagnostic



Histopathological Features

Periapical granulomas consist of an inflamed granulation tissue surrounded by fibrous connective tissue wall. The central part of the lesion contains macrophages with **foamy cytoplasm** caused by the phagocytosis of cholesterol. Cholesterol crystals may be present surrounded by multinucleated giant cells. A diffuse infiltrate of lymphocytes and plasma cells. When numerous plasma cells are present, scattered eosinophilic globules of gamma globulin **(Russell bodies)** may be seen. A frequent finding is the presence of irregular islands of epithelium, a result of prolonged, mild stimulation of the rest malassez, which are remnants of the Hertwig root sheath.



Treatment and prognosis: Treatment depend on the reduction and control of the offending micro-organisms or their toxic products in the root canal or apical tissues. A successful treatment depends on the complexity of the canal system and size of the periapical granuloma (more than 2 canals is difficult to be treated by conservative endodontic therapy.Non restorable teeth may be extracted, followed by curettage of all apical tissues, with non-steroidal anti-inflammatory drugs in symptomatic cases. Antibiotic are not recommended unless systemic signs and symptoms are present.The teeth after conventional endodontic should be evaluated at 1-3-6 months and 1-2 years.If initial conventional therapy is unsuccessful, periapical surgery

is indicated which include through curettage of all periradicular soft tissue, amputation of the apical portion of the root and scaling of the lumen of the canal, all tissues should be submitted for histopathological examination to exclude more serious conditions, like neoplastic process.

Sequelae- :

1- Periapical granuloma may continue to enlarge with continued bone resorption
2- Acute exacerbation to an acute periapical periodontitis
3- A suppuration to form an acute periapical abscess
4- Formation of a radicular cyst
5- Low grade irritation may cause osteosclerosis (bone apposition) or cementum apposition (hypercementosis).

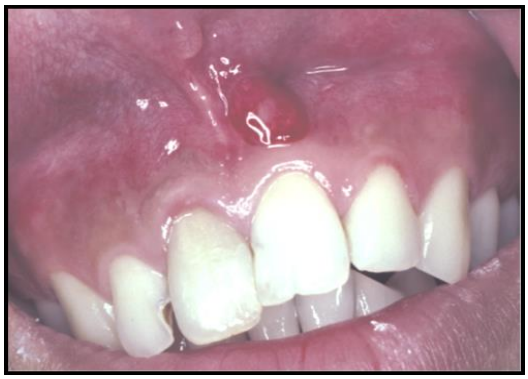
3- Acute Periapical Abscess

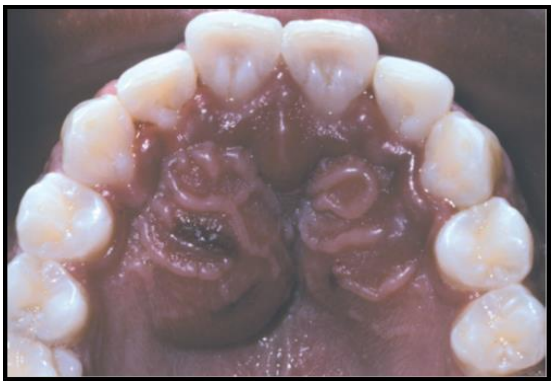
The accumulation of acute inflammatory cells at the apex of a nonvital tooth is termed a periapical abscess.

Causes:

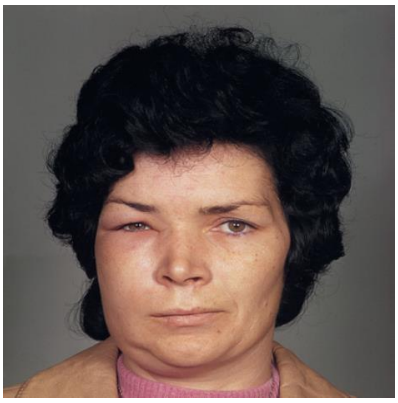
1-It is a progression of an acute pulpitis in which exudates extend into the adjacent soft and hard tissue. Because it often contains one or more strains of virulent bacterial organisms, the exudates usually contain potent exotoxins and lytic enzymes capable of rapidly breaking down tissue barriers.

2-Another cause is the acute exacerbation of a chronic periapical granuloma.





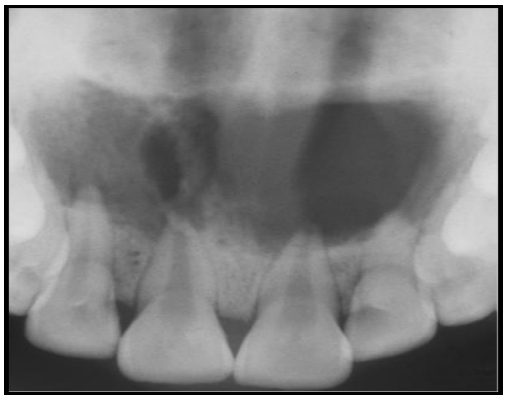
Clinical features Patients have severe pain in the area of the non-vital tooth because of pressure and the effects of inflammatory chemical mediators on nerve tissue. The exudates and neutrophilic infiltrate of an abscess cause pressure on the surrounding tissue, often resulting in slight extrusion of the tooth from its socket. Pus associated with a lesion, if not focally drained from the tooth ((e.g. by endodontic treatment)), seeks the path of least resistance and spread into contagious structures. The affected area of the jaw may be tender

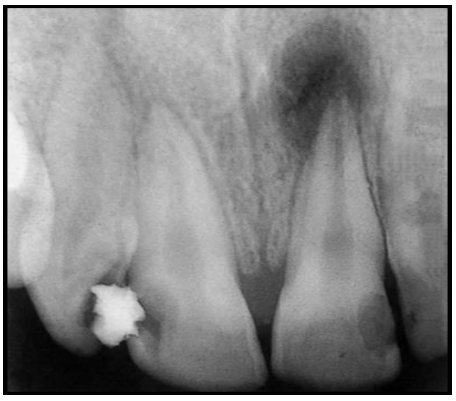


to palpation, and the patient may be hypersensitive to tooth percussion. The tooth is not responding to electric pulp tester, or thermal stimuli, headache, malaise, fever and chills may be present.

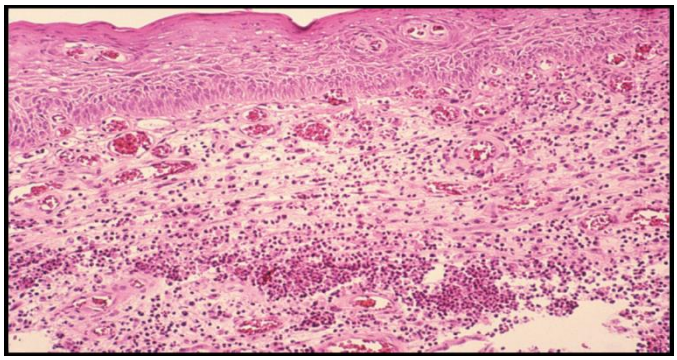
Radiographic features- :

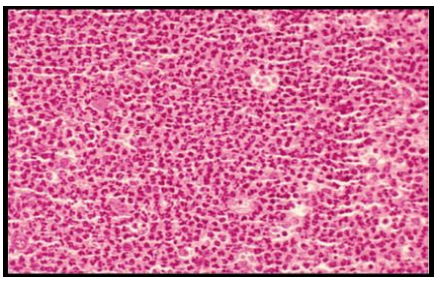
Abscess may demonstrate a thickening of apical periodontal ligament, an ill-defined radiolucency, or both. However, often no appreciable alterations can be detected because insufficient time has occurred for significant bone destruction. If the condition is an exacerbation of a chronic periapical periodontitis or periapical granuloma. It could demonstrate the outline of the original chronic lesion with or without the associated bone loss.

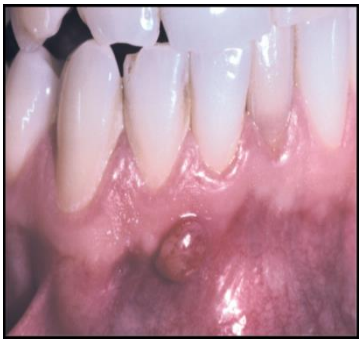




Histopathology-Microscopically A periapical abscess appears as a zone of liquefaction, composed of pertinacious exudates, necrotic tissue and viable and dead neutrophils, (pus). Adjacent tissues containing dilated vessels and a neutrophilic infiltrate surrounds the area of liquifactive necrosis.







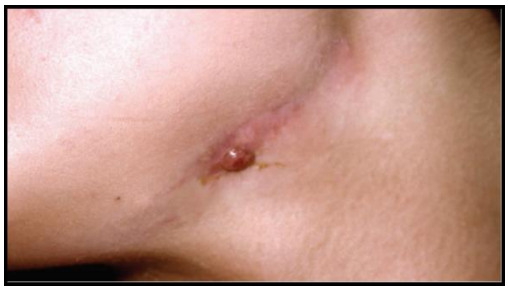
Sequelae:

1-With progression, the abscess spreads along the path of least resistance and discharge into the oral cavity through a sinus tract following local penetration of overlying periosteium and mucosa. This is usually not painful.

2- On other occasions the pus may accumulate beneath the mucosa and the patient may complain of a swelling at the intraoral opening of a sinus tract, which is a mass of subacutely inflamed granulation tissue known as parulis ((Gum boil))

3- May extend through the medullary spaces away from the apical area, resulting in osteomyelitis

4 -It may perforate the cortex and spread diffusely through the overlying soft tissue as cellulitis.



5 -Dental abscesses may discharge through the skin and drain via a cutaneous sinus. →

6 Periapical infection occasionally spread the blood stream and result in systemic symptoms such as fever, lymphadenopathy and malaise.

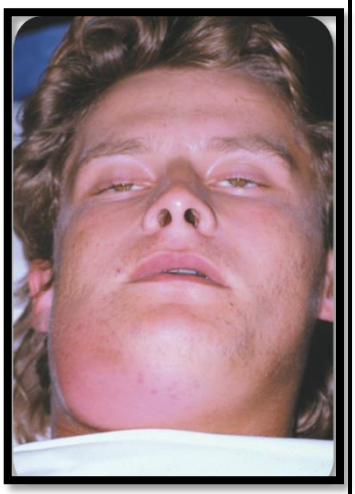
7 It may spread diffusely through facial planes of the soft tissues. This acute and edematous spread of an acute inflammatory process is termed cellulitis.

Cellulitis

Is a misnomer, because the process is not an inflammation of the cells but an acute condition in which purulent forms of bacteria, involve the facial and perioral mucosa. The most common cause is extension from a periapical abscess. However other causes may also result in cellulitis like fractures.

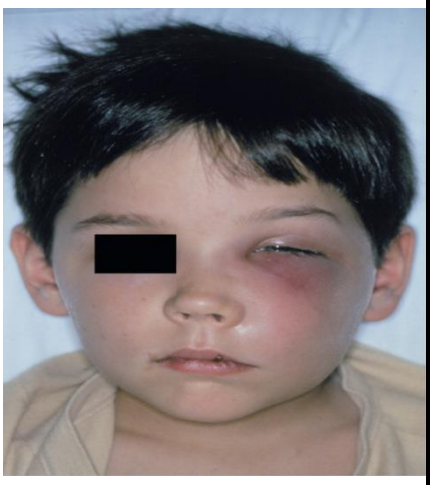
Sequelae:

1-**Oroantral fistula**: Occasionally the exudates track onto the palate, producing a large swelling, when a periapical abscess erodes into the maxillary sinus, destroying the intervening bone and lining, and the offending tooth is extracted, a communication between the floor of the maxillary sinus and the oral cavity may result. This tract may remain permanently patent, particularly if it becomes lines by epithelium of the maxillary sinus and the oral cavity. This abnormal open communication is called oroantral fistula.



2-Ludwig's angina: When the muscle layers overlying the body of the mandible are involved, patients experience a puffy swelling on the side of the face. Extension of the pus lingually into the tissue spaces of the posterior floor of the mouth may result in swelling of the structures around the epiglottis which is a life threatening, as it restricts the airway and may cause suffocation. So a Cellulitis of this area ((submental , submandibular and sublingual spaces)) is called Ludwig's angina.

3- Thrombophlebitis: Another serious complication is the extension of the exudates into the maxillary cavernous sinus area, resulting in thrombophlebitis. From this location fatal forms of brain abscess or acute meningitis are possible unless rapid intervention is undertaken.



Treatment and prognosis:Treatment of periapical abscess consist of drainage and elimination of the focus of infection.Localized abscess should be drained by incision and drainage. If the abscess is localized with no systemic features ((fever, lymphadenopathy and malaise)), the patient is healthy, antibiotics are not recommended. However, if the patient is compromised (e.g. diabetic) or, systemic symptoms are present antibiotics are recommended. NSAID is needed if not contraindicated. The tooth should be endodontically treated or extracted. Sinus and fistula tracts if not treated spontaneously after extraction, should be removed surgically

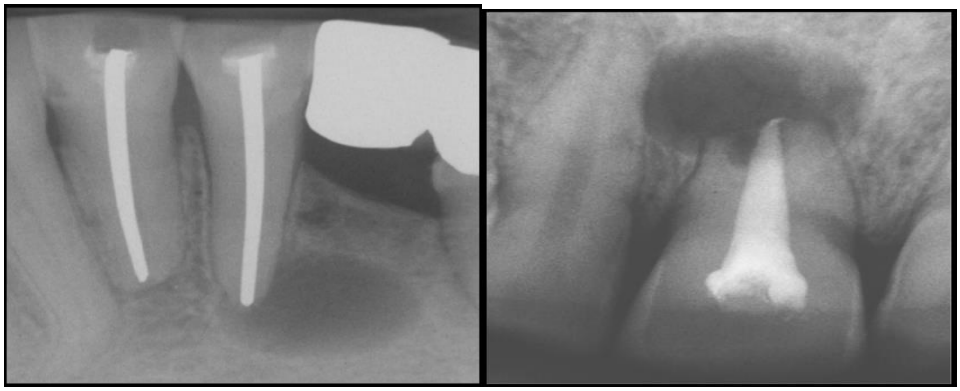
Radicular cyst

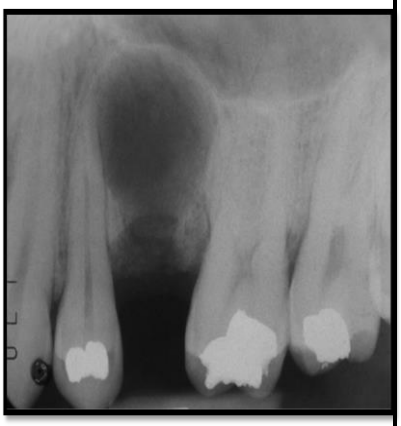
1-**Apical radicular cyst** Apical radicular cyst are the most common cystic lesions in the jaws and are always associated with apex of non-vital teeth, they account for about 75% of all radicular cyst. When small they are frequently symptomless and are usually discovered during routine radiographical examination as they enlarge, they produce expansion of alveolar bone and ultimately may discharge through sinus. However, the majority of radicular cyst does not grow to large dimension. The expansion of the alveolar bone is due to deposition of successful layers of new bone by overlying periosteium. As the cyst enlarge and cause bone resorption centrally. Increments of new sub periosteoal bone are lead down to maintain the integrity of the cortex. Producing a bony hard expansion. However, the rates of expansion tens to out strip the rate of subperiosteol deposition. Leading to progressive thinning of the cortex which can be default on palpitation producing the clinical signs of oil

can be bottoming and egg shell is crackling. Eventually the cyst may perforate the cortex and present as a bluish fluctuant sub mucosal swelling.

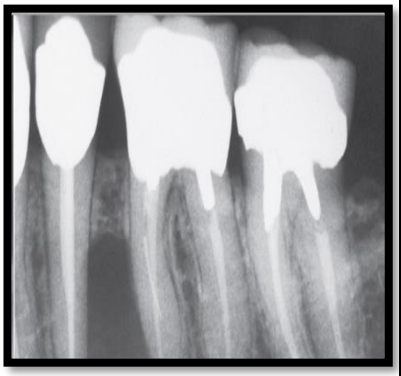
Clinical Features: Pain is seldom a feature unless there is an acute exacerbation which may readily progress to abscess formation. The cyst can rise at any age after the tooth eruption but are rare in deciduous dentition. They are most common between the ages of 20-60. They can occur in relation to ant tooth in the arch although 60% are found in the maxilla where there is a particular high incidence in anterior teeth. In addition to dental caries pulp death from trauma and irritant restorative material is more likely in anterior teeth than at other sites. Pulp death in maxillary lateral incisors may also be associated with an invaginated odontoma in the mandible the majority of cyst occur posterior to the canine tooth.

Radiographically: The apical radicular cyst presents as a round or avoid radiolucency at the root apex. The lesion is often well circumscribed and may be surrounded by peripheral radio-opaque margins continues with lamina dura of the involved tooth. However, whether or not cyst formation has occurred in an apical radiolucency cannot be detected from radiographic appearance alone.





2-The residual cyst Is a radicular cyst that has remained in the jaw and failed to resolve following extraction of the involved tooth. About 20% of radicular cysts are of this type. However, it should be noted that most periapical inflammation will resolve after removal of the causative agents. The reasons why some lesion persists as residual cyst are unknown. Are more frequent in older persons and present with expansion of the jaw.



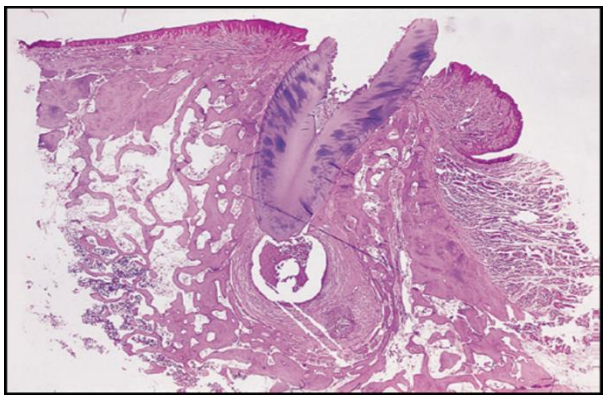
3-The lateral cyst Is very uncommon and arises as a result of extension of inflammation from the pulp to into the lateral periodontal along the lateral root canal .

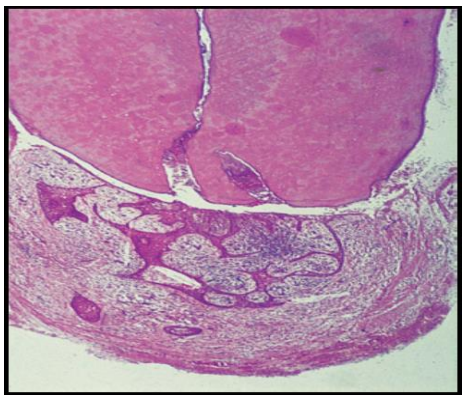
Pathogenesis Radicular cyst arises from proliferation of rest of malassez within chronic periapical granulomas but not all granulomas progress to cyst. The factors which determine why cystic transformation occurs in some and the mechanism involved in the formation of cyst are controversial. Persistence of chronic inflammatory stimuli are derived from the necrotic pulp appears essential since as mentioned above. Most periapical inflammation will resolve spontaneously once the causative agent has removed. It is assumed that the environment within chronically inflamed granuloma. Which is likely to be rich in cytokines including growth factors? Stimulates the rate of malassez to proliferate strands and sheets of squamous epithelium derived from proliferation of the rest are common finding in the periapical granulomas. The mechanism of formation of an epithelial lined cyst cavity within granuloma is unclear. Two main mechanism have been proposed

1- Degeneration and death of central cells within a proliferating mass of epithelium. Epithelium is a vesicular and transport of metabolites and gaseous exchange occur by diffusion. It argued that when the mass proliferating epithelium within granuloma reaches a critical size. The central cells further away from the surrounding vascular bed. Degenerate and die, the micro cyst so formed then continues to expand

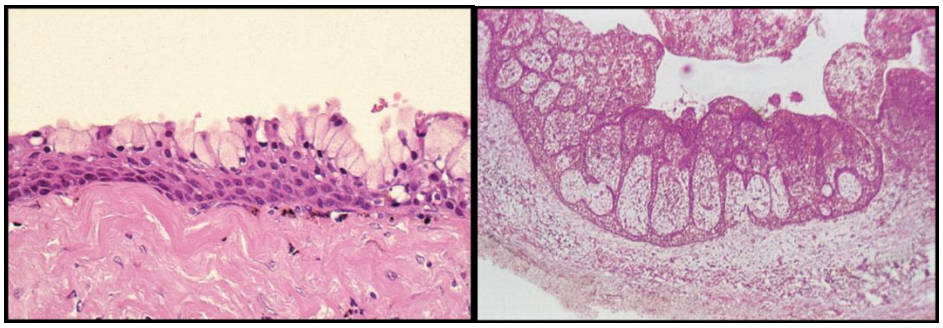
2- Degeneration and liquifactive necrosis of granulation tissue. It is suggested that areas of granulation tissue within the granuloma may undergo necrosis due to enclavement by proliferating strands of epithelium or to release toxic products from a dead pulp or from infecting organism. Epithelial proliferation to surround such an area of necrosis results in the formation of cyst.

Histopathology: Radicular cyst are lined wholly or impart by know keratinized stratified squamous epithelium supported by a chronically inflamed fibrous tissue capsule. In a newly formed cyst the epithelial lining is irregular and may vary considerably in thickness. Hyperplasia is a prominent feature in long anastomosing cords of epithelium forming complex arcades extending into the surrounding capsule. The latter is richly vascular and diffusely infiltrated by inflammatory cells often predominant.

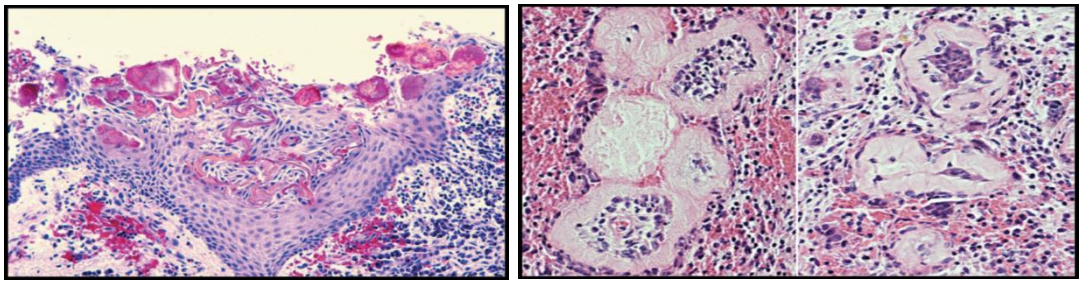




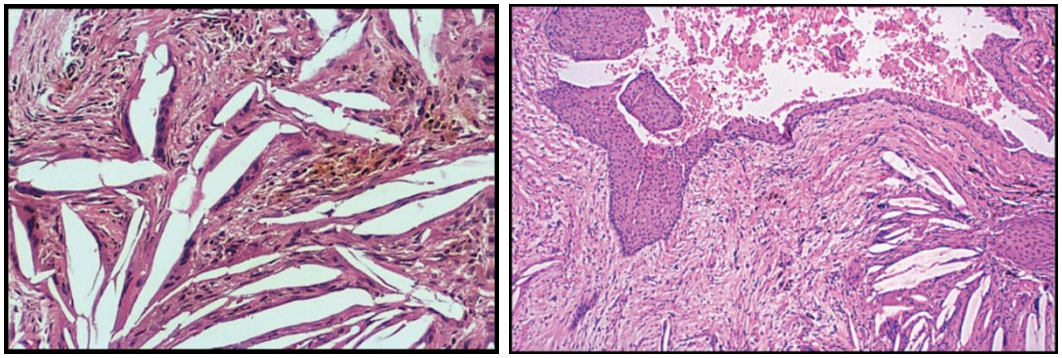
In established cyst the epithelial lining is more regular in appearance and fairly even thickness breaks in the linings epithelial discontinuities are common. Metaplasia of epithelial lining may give rise to a mucus cell. Found in about 40% of radicular cyst lining and more rarely ciliated cells and area of respiratory type epithelium.



In most cases the lining contains hyaline eosinophilic bodies **Rushton bodies** of varying size and shape. They appear to have no clinical or diagnostic significant and they origin is unknown. But they may represent some type of epithelial product. Within time the connective tissue capsule tends to become more fibrous and less vascular and there is reduction in the density of inflammatory cell infiltration, myofibroblast in capsule may help to constrain the tendency of the cyst to expand.



Deposits of cholesterol crystals are common within the capsules of many radicular cysts. In histological sections cholesterol clefts may be few in number of forms large mural nodules in which case they are often associated with epithelial discontinuity and project into cyst lumen. They are the probable of cholesterol crystals found in the cyst fluid; mural cholesterol clefts are associated with foreign body giant cells. As a periapical granulomas the cholesterol probably derived from the breakdown of red blood cells as a result of hemorrhage in the cyst capsule and deposits of hemosiderin are commonly associated with the clefts.



Cyst Contents: The cyst contents vary from a watery straw color fluid through to semi solid brownish material of paste like consistency. Cholesterol crystals impart a shimmering appearance the composition of cyst fluid is a complex of variable it is hypertonic compared with serum and contents

1-Breakdown products of degenerating epithelial cell and inflammatory cell and connective tissue components

2 -Serum proteins all groups of serum proteins are present in cyst fluid Compared with serum the fluid contain higher level of immunoglobulin which probably reflect local production of plasma cells in the capsule

3 -Water and electrolytes

4 Cholesterol crystal.

Cyst expansion:

Cysts expansion is dependent on osteoclastic resorption of surrounding bone. Osteoclasts are derived from haematopoietic precursors and are transported via the blood.

- Osteoclasts are recruited to and activated at sites of resorption by mediators. The cytokines interleukin-1 and interleukin-6 (IL-1, IL-6), tumor necrosis factor and prostaglandin E2 are key mediators in cyst expansion.

- Mediators are generated locally by a variety of cells e.g.: macrophage, lymphocytes, epithelial cells, fibroblast.

- Activated osteoclast attached to the bone surface and release acids resulted in de mineralization. The organic matrix is then degraded by matrix metalloproteinase MMP's, collagenases, and lysosomal proteases.

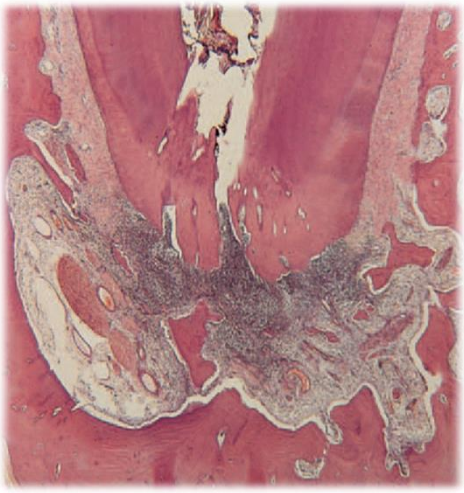
- MMP's synthesized by other cells in the cyst wall e.g.: fibroblasts, epithelial and inflammatory cells, may contribute to matrix degradation.

- Bone resorption is followed by cyst expansion which may involve hydrostatic pressure.

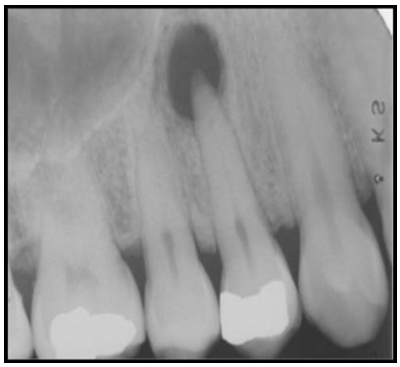
- Cyst contents are hypertonic. The wall acts as a semi permeable membrane and retains the osmotically active molecules in the lumen creating an osmotic gradient. Water moves into the lumen along the gradient increasing the hydrostatic pressure in the cyst leading to enlargement.

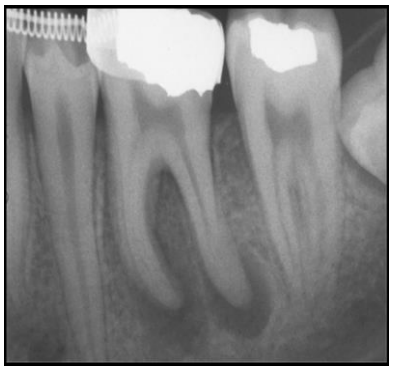
Treatment of radicular cyst: The treatment of periapical radicular cyst depend on the condition of the tooth as whole, if the tooth is restorable, the root canals can be filled, if the root canals cannot be filled and the apical area is in a location accessible for surgery, an apicoectomy with complete surgical enuculation may be performed to remove the cystic lesion, followed by histopathological examination; otherwise, the tooth is extracted and the periapical cyst is curreted through the tooth socket.

Lab.3 **Periapical pathology**

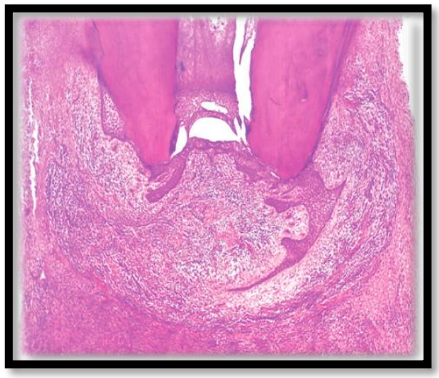


Acute periapical periodontitis

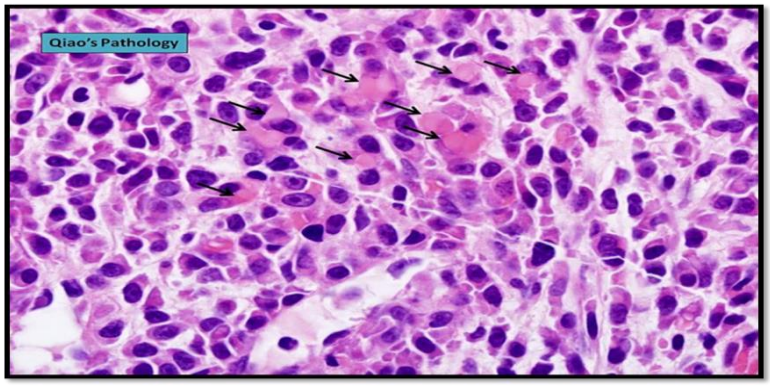




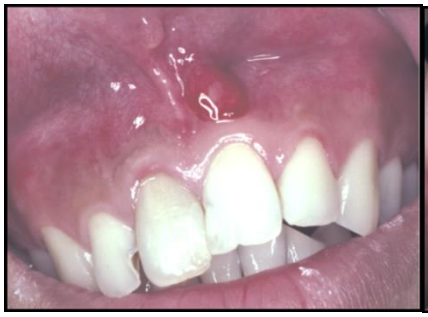
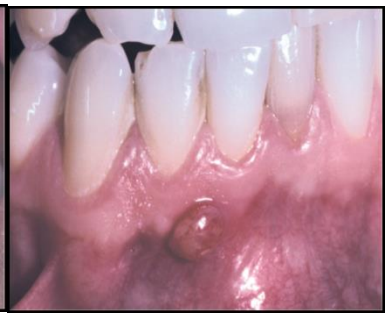
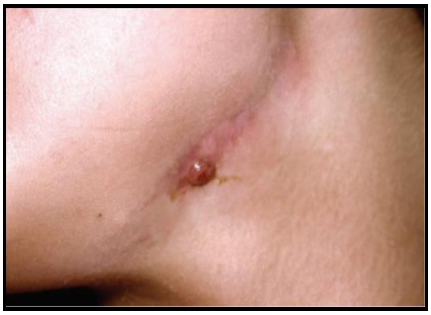
Periapical granuloma



Periapical granuloma

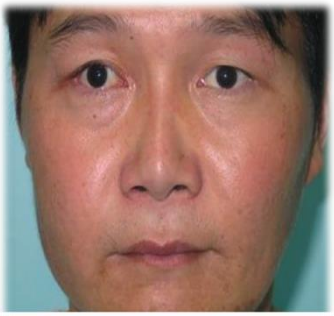


Russel bodies

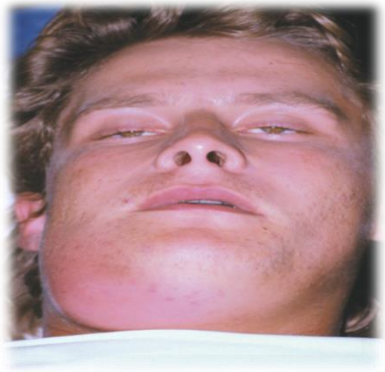
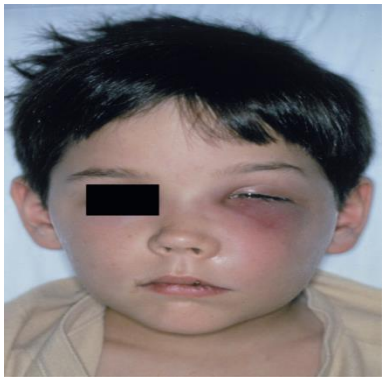




Gum boil

cutanious sinus

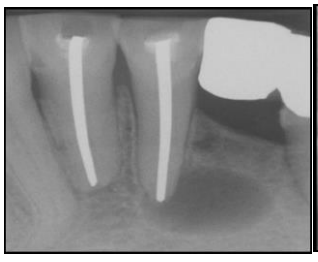
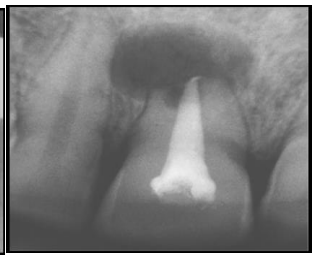
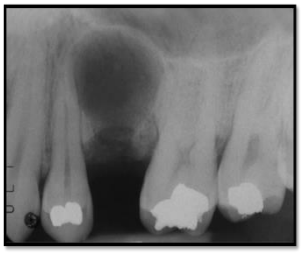
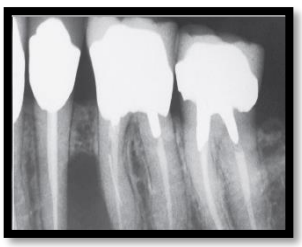



Cellulitis

Ludwig's angina.

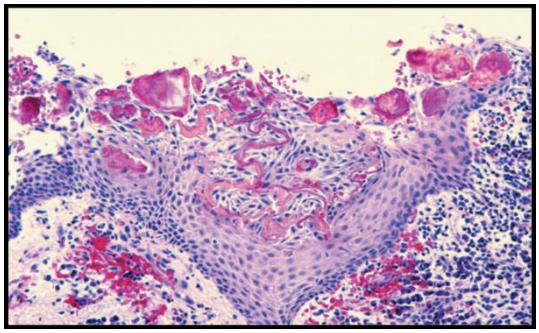
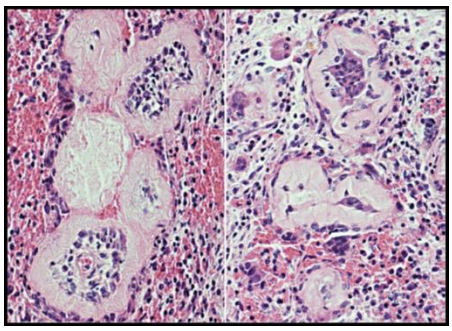
Thrombophlebitis

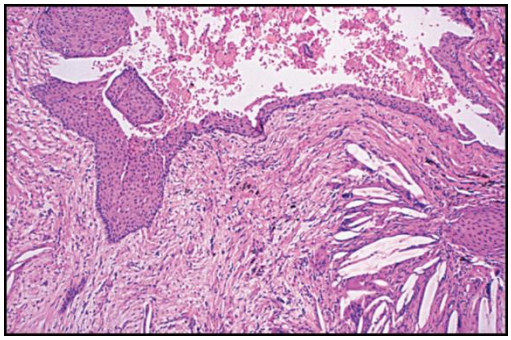
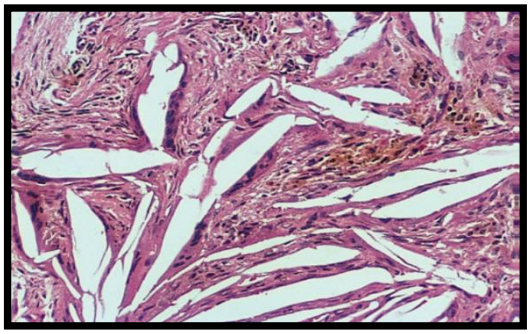
Apical radicular cyst

Residual cyst

Lateral cyst

Radicular cyst (Rushton bodies)

Radicular cyst (cholesterol crystals)

Oral Pathology

Lec. 5

DEVELOPMENTAL DEFECTS OF THE ORAL AND MAXILLOFACIAL REGION

Developmental disturbances of the oral region are of these broad categories:

1. Developmental disturbances affecting teeth
2. Developmental disturbances limited to soft tissue.
3. Developmental disturbances affecting bone.

The Disorders of development of teeth

The development of teeth is regulated by genes, but the genetic program is very sensitive to disturbances in the environment such as infection, or toxic chemicals. The causes of developmental disorders of teeth are multifactorial, involving the interaction of genetic and environmental factors.

These disorders may be prenatal or postnatal in origin and may inherit or acquired. Disorders of development of teeth may be due to abnormalities in the differentiation of the dental lamina and the tooth germs, causing anomalies number, size, form of teeth and abnormalities of morph differentiation or abnormalities in the formation of the dental hard tissue resulting in disturbances in tooth structure.

Developmental Alterations in the Number of Teeth

Hypodontia, when one or several teeth are missing.

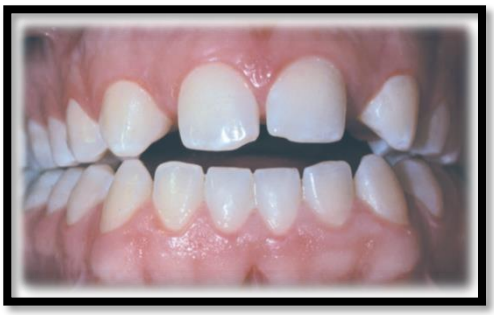
Hyperdontia, is the development of an increased number of teeth, and the additional teeth are termed supernumerary.

Anodontia: Absence of teeth, when all teeth are missing.

Pseudoanodontia: when teeth are absent clinically because of impaction or delayed eruption.

False anodontia: when teeth have been exfoliated or extracted.

Oligodontia (a subdivision of hypodontia) indicates the lack of development of six or more teeth excluding third molars.



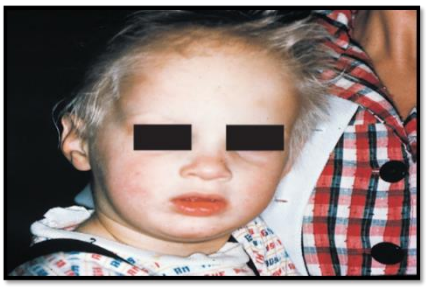
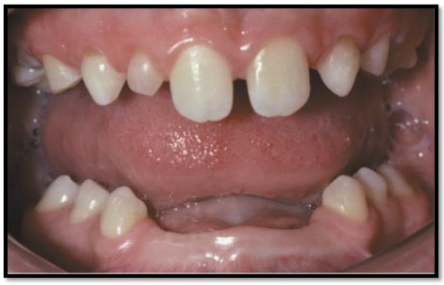
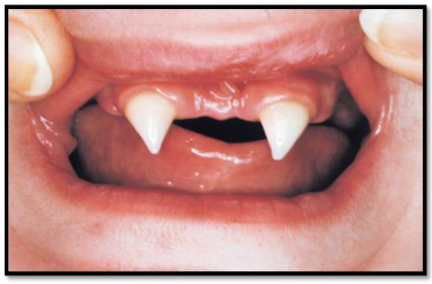
Hypoanodontia: Is relatively common. Congenitally missing teeth are usually third molars, followed by second premolars and maxillary lateral incisors.

Several regulatory genes are involved in tooth formation and development which may be mutated in hypodontia. Thus, hypodontia may be associated with other craniofacial anomalies and syndromes.

Hypodontia is more common in the permanent dentition, occurring in 2-10% in different population (excluding absent third molar) compared to the primary dentition where the prevalence is less than 1%. It is more common in females in racial differences

Hypodontia may be symmetrical when particular teeth or groups of teeth are involved or haphazard when the patient is discoverable. When the deciduous teeth to be congenitally absent, which is very unusual is likely that is such cases the permanent teeth will be also fail to form.

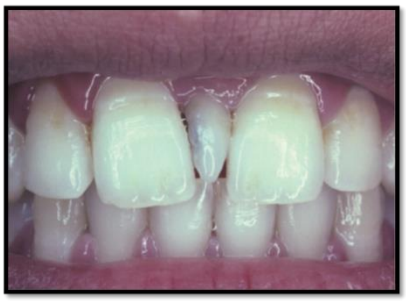
Complete anodontia is rare but is often associated with a syndrome known as *hereditary ectodermal dysplasia,* which usually is transmitted as an X-linked recessive disorder. Partial anodontia is more typical of this syndrome, however. The few teeth that are present are usually conical. Hair, cutaneous appendages, and nails are also poorly developed in this syndrome.

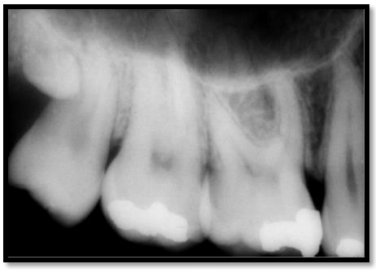
Hyperdontia (Supernumerary Teeth)

Extra, or supernumerary, teeth in the dentition most probably result from continued proliferation of the permanent or primary dental lamina to form a third tooth germ. The resulting teeth may have a normal morphology or may be rudimentary and miniature. Most are isolated events, although some may be familial and others may be syndrome associated (Gardner's syndrome and cleidocranial dysplasia). Supernumerary teeth are found more often in the permanent dentition than in the primary dentition and are much more commonly

seen in the maxilla than in the mandible. Mostly in the females than males. The anterior midline of the maxilla is the most common site, in which case the supernumerary tooth is known as a ***mesiodens.***

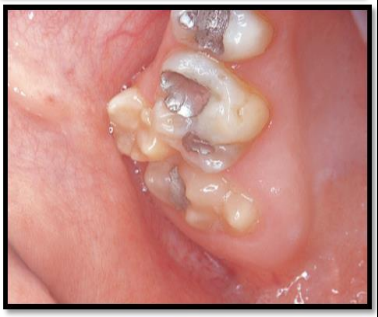


The maxillary molar area is the second most common site (distomolar or distodensor) or situated lingually or buccally to a molar tooth is termed (paramolar).



Supernumerary teeth are divided into:

- Supplemental (normal size and shape.)
- Rudimentary (abnormal shape and smaller size).

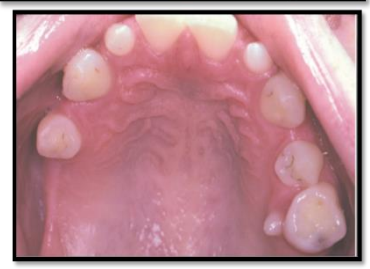


Another classification:

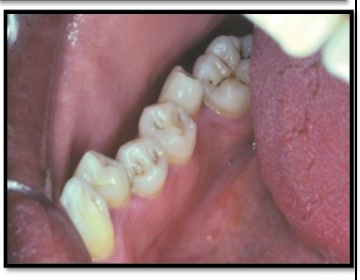
Conical (small, peg-shaped)

Tuberculate (barrel-shaped anterior with more than one cusp)

Molariform (small premolar-like or molar-like)



The significance of supernumerary teeth is that they occupy space. When they are impacted, they may block the eruption of other teeth, or they may cause delayed eruption or maleruption of adjacent teeth. If supernumerary teeth erupt, they may cause malalignment of the dentition and may be cosmetically objectionable.



Supernumerary teeth appearing after loss of the permanent teeth are known as *postpermanent dentition*. This is generally regarded as a rare event. Most teeth appearing after extraction of the permanent teeth are believed to arise from eventual eruption of previously impacted teeth.

Management

The patient with hypodontia depends on the severity of the case . No treatment may be required for a single missing tooth . Prosthetic replacement often is needed when multiple teeth are absent. In some cases of hypodontia, orthodontic therapy may improve the restorative treatment.

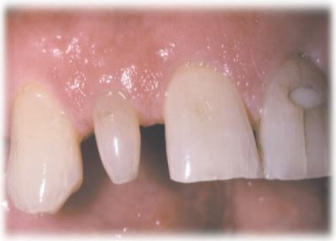
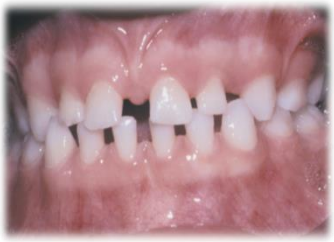
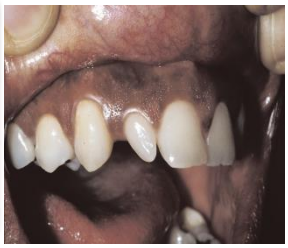
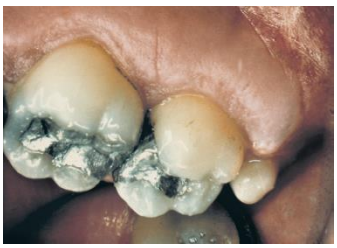
The standard care in hyperdontia is removal of the accessory tooth during the time of the early mixed dentition to allow full eruption for permanent teeth .Permanent teeth that fail to erupt are treated best by surgical exposure with orthodontic eruption.

Developmental Alterations in the Size of Teeth

Microdontia

In generalized microdontia, all teeth in the dentition appear smaller than normal. Teeth may actually be measurably smaller than normal, as in pituitary dwarfism, or they may be relatively small in comparison with a large mandible and maxilla.

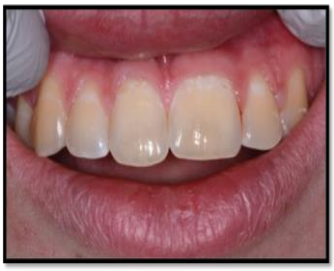
In focal, or localized microdontia, a single tooth is smaller than normal. The shape of these microdonts is often altered with the reduced size. This phenomenon is most commonly seen with **maxillary lateral incisors** in which the tooth crown appears cone or peg shaped, prompting the designation ***peg lateral***. An autosomal-dominant inheritance pattern has been associated with this condition. Peg laterals are of no significance other than cosmetic appearance. The second most commonly seen microdont is the maxillary third molar, followed by supernumerary teeth.

Macrodontia

Generalized macrodontia is characterized by the appearance of enlarged teeth throughout the dentition. This may be absolute, as seen in pituitary gigantism, or it may be relative owing to a disproportionately small maxilla and mandible. The latter results in crowding of teeth and possibly an abnormal eruption pattern caused by insufficient arch space.

Focal, or localized, macrodontia is characterized by an abnormally large tooth or group of teeth. This relatively uncommon condition usually is seen with mandibular third molars. In the rare condition known as *hemifacial*

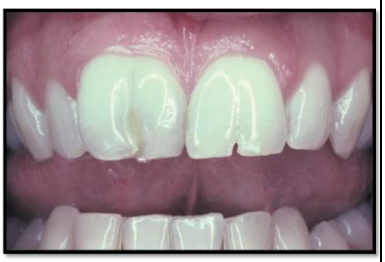


hypertrophy, teeth on the affected side are abnormally large compared with the unaffected side.

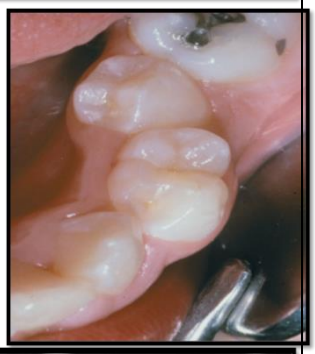
Developmental Alteration s in the Shape of Teeth

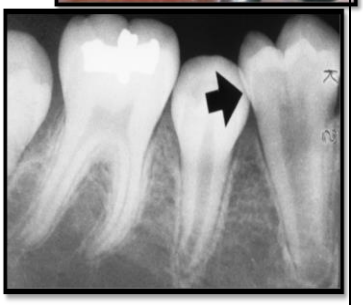
Disturbances in tooth form may involve the crown, the roots or both. The most frequent variations of the crowns of the teeth affect maxillary permanent lateral incisors which may be peg-shaped. Premolars and molars with an increased or decreased number of cusps are also frequently seen.

Double teeth: - a descriptive term used to describe a developmental anomaly where two teeth appear joined together. This is variable and may involve the crown, roots, or both. The teeth are united by dentine or pulp. It occurs mostly in primary than permanent dentition especially anterior teeth. The etiology of double teeth remains unclear. A genetic basis has been suggested also double teeth should be differentiated from concrescence which is an acquired condition.

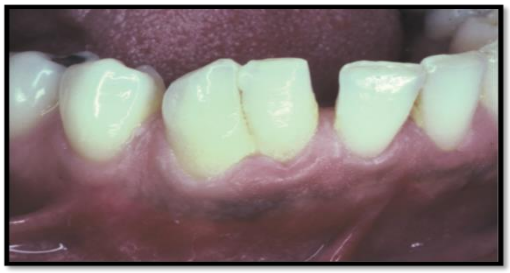
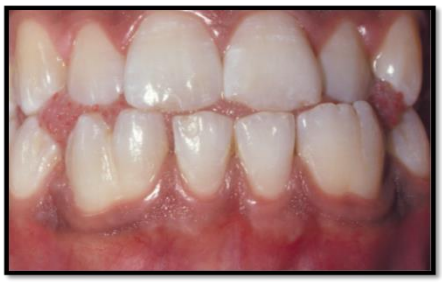
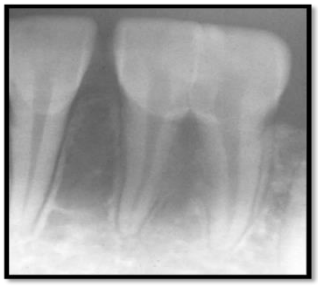


1-Gemination Is defined as an attempt of a single tooth bud to divide, with the resultant formation of a tooth with a bifid crown and, usually, a common root and root canal. The typical result is partial cleavage, with the appearance of two crowns that share the same root canal. Complete cleavage, or twinning, occasionally occurs, resulting in two teeth from one tooth germ. Although trauma has been suggested as a possible cause, the cause of gemination is unknown. These teeth may be cosmetically unacceptable and may cause crowding.



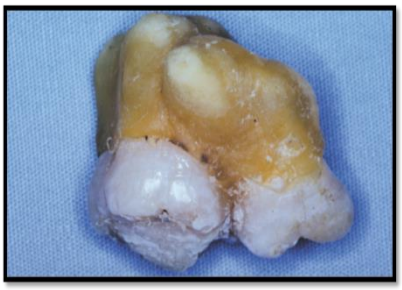
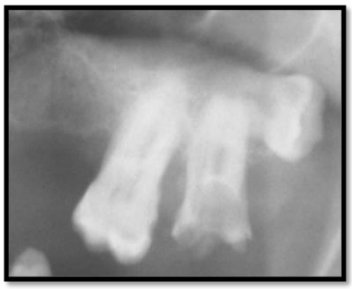
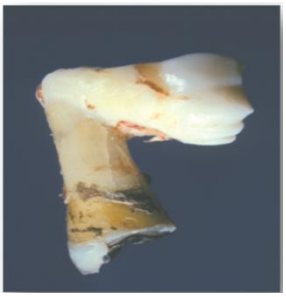
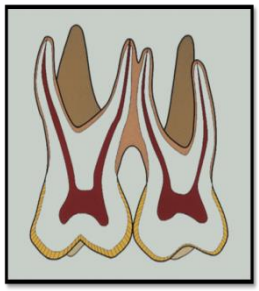


2-Fusion Is the joining of two developing tooth germs, resulting in a single large tooth structure. The fusion process may involve the entire length of the teeth, or it may involve the roots only, in which case cementum and dentin are shared. Root canals may also be separate or shared. It may be impossible to differentiate fusion of normal and supernumerary teeth from gemination. The cause of this condition is unknown, although trauma has been suggested.

Concrescence:

Concrescence is an acquired union form in which adjacent, already formed teeth are joined by cementum only. This may take place before or after eruption of teeth and is believed to be related to trauma or overcrowding. Mostly seen in permanent than primary dentition. Concrescence is most commonly seen in association with the maxillary second and third molars. This condition is of no significance, unless one of the teeth involved requires extraction. Surgical sectioning may be required to save the other tooth.

ACCESSORY CUSPS

The cuspal morphology of teeth exhibits minor variations among different populations of these. Three distinctive patterns deserve further discussion:

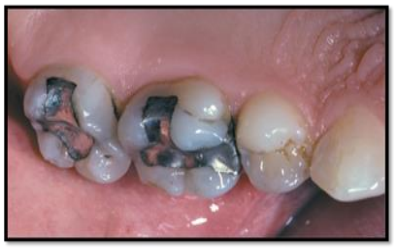
(1) Cusp of Carabelli.

(2) Talon cusp.

(3) Dens Evaginatus

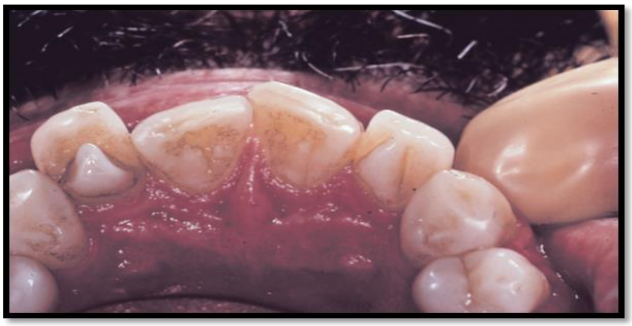
When an accessory cusp is present, the other permanent teeth often exhibit a slightly increased tooth size.

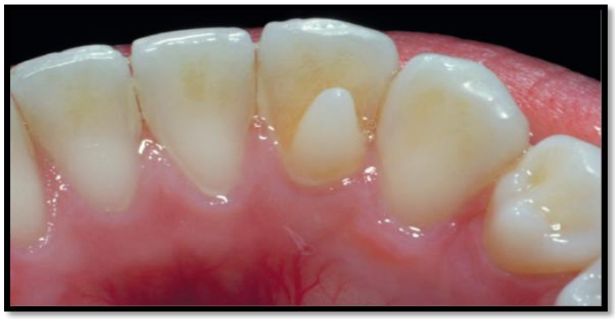
1-The cusp of Carabelli is an accessory cusp located on the palatal surface of the mesio lingual cusp of a maxillary molar. The cusp may be seen in the permanent or deciduous dentitions and varies from a definite cusp to a small indented pit or fissure. When present. The cusp is most pronounced on the first molar.



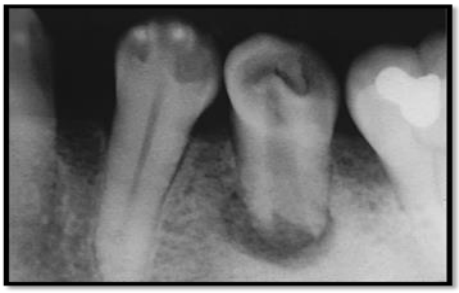
An analogous accessory cusp is seen occasionally on the mesiobuccal cusp of a mandibular permanent or deciduous molar and is termed a protostylid.

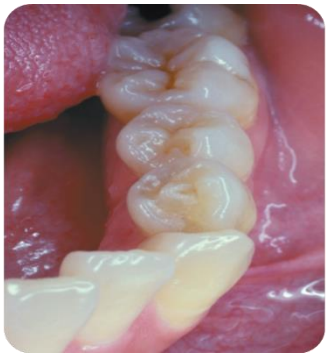
2-Talon Cusp A talon cusp (dens evaginatus of anterior tooth) is a well-delineated additional cusp that is located on the surface of an anterior tooth and extends at least half the distance from the cementoenamel junction to the incisal edge. Three fourths of all reported talon cusps are located in the permanent dentition.





3-Dens Evaginatus: - Is a relatively common developmental condition affecting predominantly premolar teeth (Leung's premolars). It has been reported almost exclusively in Asians, Inuits, and Native Americans. The defect, which is often bilateral, is an anomalous tubercle, or cusp, located at the center of the occlusal surface. Because of occlusal abrasion, the tubercle wears relatively quickly causing early exposure of an accessory pulp horn that extends into the tubercle. This may result in periapical pathology in young, caries-free teeth, often before completion of root development and apical closure, making root canal fillings more difficult. Judicious grinding of opposing tooth or accessory tubercle to stimulate secondary dentin formation may prevent periapical sequelae associated with this defect. Sealants, pulp capping, and partial pulpotomy have been suggested as measures to allow complete root development.

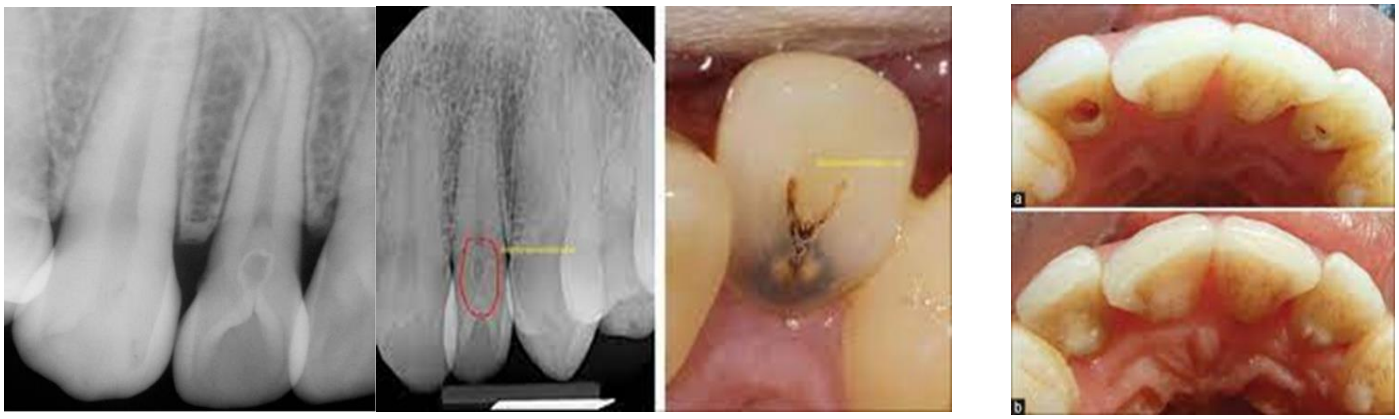




Dens Invaginatus: Also known as dens in dente or tooth within a tooth arises as a result of invagination of a portion of enamel organ into the dental papilla at an early stage in odontogenesis before the formation of calcified tissue, dens invaginatus is an uncommon tooth anomaly that represents an exaggeration or accentuation of the lingual pit. This defect ranges in severity from superficial, in which only the crown is affected, to deep, in which both the crown and the root are involved.

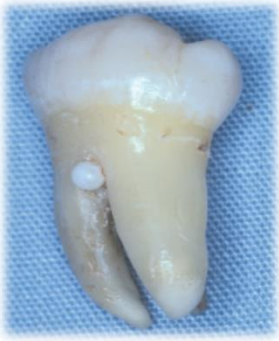
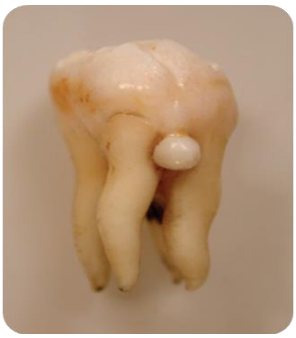
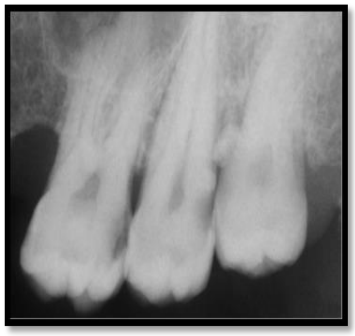
The permanent maxillary lateral incisors are most commonly involved, although any anterior tooth may be affected. Bilateral involvement is commonly seen. The cause of this developmental condition is unknown. Genetic factors are believed to be involved in only a small percentage of cases.

Because the defect cannot be kept free of plaque and bacteria, dens invaginatus predisposes the tooth to early decay and subsequent pulpitis. Prophylactic filling of the pit is recommended to avoid this complication. Because the defect may often be identified on radiographic examination before tooth eruption, the patient can be prepared in advance of the procedure. In cases in which pulpitis has led to non-vitality, endodontic procedures may salvage the affected tooth.

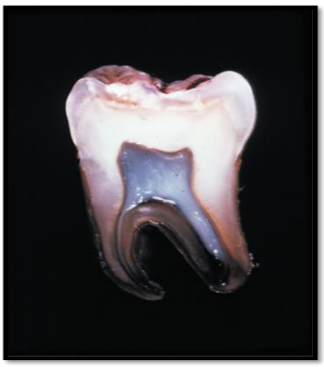


Enamel Pearls (enamelonoma): Droplets of ectopic enamel, or so-called enamel pearls, may occasionally be found on the roots of teeth. They occur most commonly in the bifurcation or trifurcation of teeth but may appear on single-rooted premolar teeth as well. Maxillary molars are more commonly affected than mandibular molars. These deposits are occasionally supported by dentin and rarely may have a pulp horn extending into them. This developmental disturbance of enamel formation may be detected on radiographic examination. It generally is

of little significance except when located in an area of periodontal disease. In such cases, it may contribute to the extension of a periodontal pocket, because a periodontal ligament attachment would not be expected and hygiene would be more difficult.

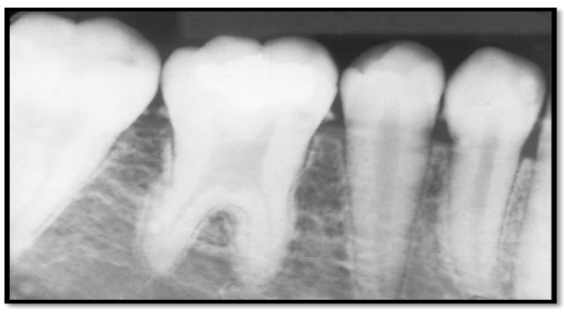
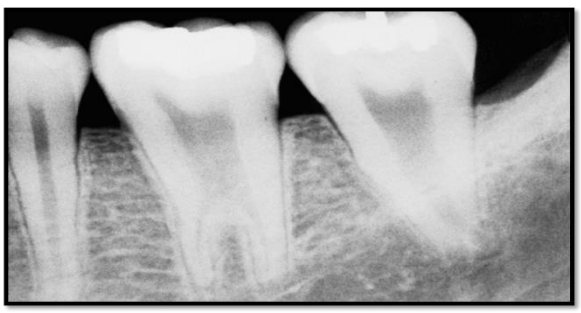




Taurodontism



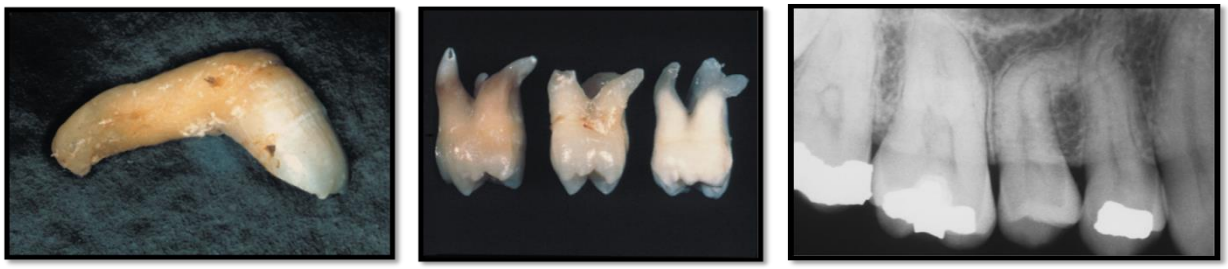
Taurodontism is a variation in tooth form in which teeth have elongated crowns or apically displaced furcations, resulting in pulp chambers that have increased apical-occlusal height. Because this abnormality resembles teeth in bulls and other ungulates, the term *taurodontism* was coined. Various degrees of severity may be seen, but subclassifications that have been developed to describe them appear to be of academic interest only.

Taurodontism may be seen as an isolated incident, in families, and in association with syndromes such as Down syndrome and Klinefelter's syndrome. Although taurodontism is generally an uncommon finding, it has been reported to have a relatively high prevalence in Eskimos, and incidence has been reported to be as high as 11% in a Middle Eastern population. Other than a possible relationship to other genetically determined abnormalities, taurodontism is of little clinical significance unless the tooth becomes nonvital, in which case it becomes a challenging endodontic problem. No treatment is required.

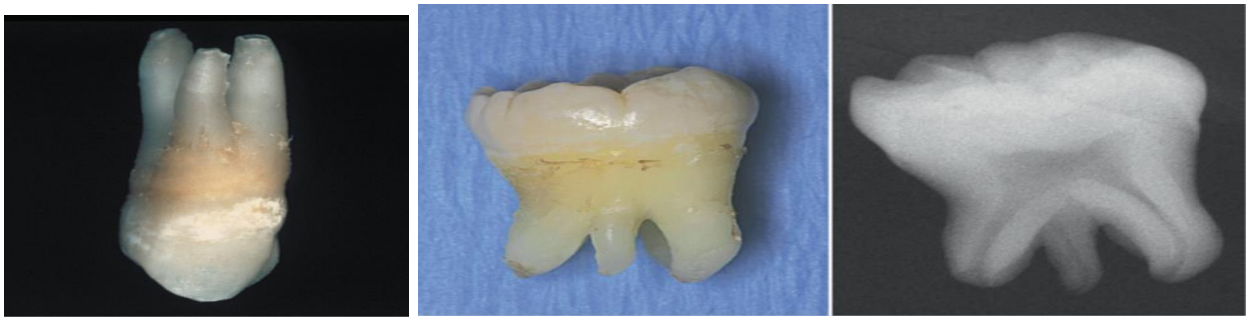
Dilaceration

A term used to describe a deformity in which the crown is displaced from its normal alignment with the root, so that the tooth is severely bent along its long axis. The cause of this condition has been related to trauma during root development. Movement of the crown or of the crown and part of the root from the remaining developing root may result in sharp angulation after the tooth completes development. Hereditary factors are believed to be involved in a small number of cases. Eruption generally continues without problems. However, extraction may be difficult. Obviously, if root canal fillings are required in these teeth, the procedure is challenging.



Supernumerary Roots

Accessory roots are most commonly seen in mandibular canines, premolars, and molars (especially third molars). They are rarely found in upper anterior teeth and mandibular incisors. Radiographic recognition of an extraordinary number of roots becomes important when extractions or root canal fillings are necessary.



Localized Disturbances in Eruption

I. **Delayed eruption**: Refers to the first appearance of deciduous teeth relative to the normal age range. This occurrence is relatively uncommon and is usually idiopathic or associated with certain systemic conditions such as rickets, cleidocranial dysplasia, or cretinism. Local factors such as gingival fibromatosis, in which dense fibrous connective

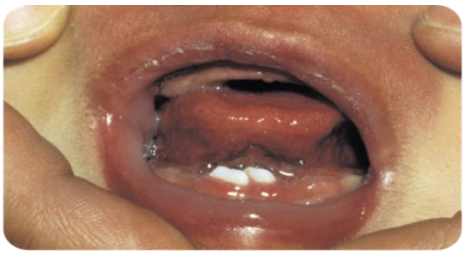
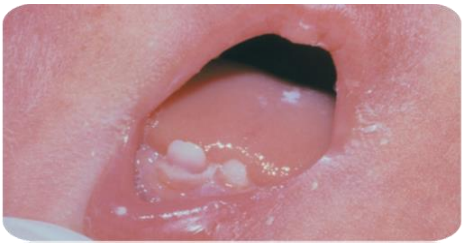
tissue impedes tooth eruption, can result in delayed eruption of the deciduous dentition . Treatment of the systemic condition or the causative local factors may alleviate the eruption problem.

II. Premature Eruption: Premature eruption usually involves only one or two teeth, most commonly the deciduous mandibular central incisors.

Natal teeth: Teeth appearing at the time of birth.

Neonatal teeth: those appearing within 6 months following birth.

Most of these teeth represent prematurely erupted deciduous teeth, usually mandibular central incisors. A small percentage represent supernumerary teeth .Although the cause of this phenomenon is unknown, a familial pattern is sometimes observed. Prematurely erupted primary teeth should be preserved (If not cause injury to the infant or the mother).

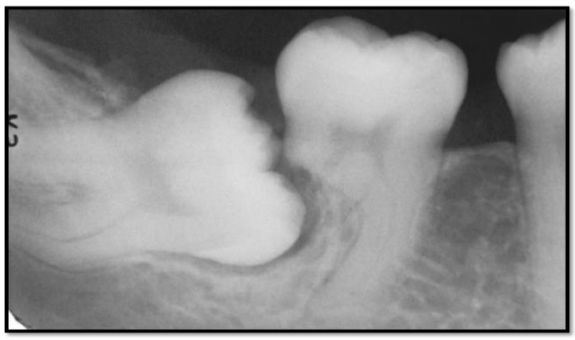



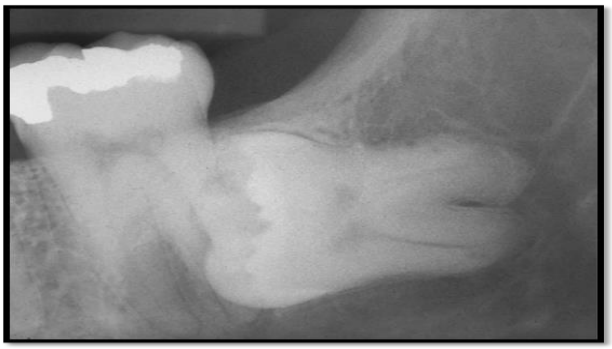

Premature eruption of permanent teeth is usually a consequence of premature loss of the preceding deciduous teeth . This becomes readily apparent when a single deciduous tooth has been prematurely lost . In the event that the entire permanent dentition is obviously erupting prematurely, the possibility of an endocrine dysfunction such as hyperthyroidism should be considered.

Primary Impaction and Ankylosis

Impaction: Impaction of teeth is a common event that most often affects the mandibular third molars and maxillary canines. Less commonly, premolars, mandibular canines, and second molars are involved. It is rare to see impactions of incisors and first molars. Impaction occurs because of obstruction from crowding or from some other physical barrier. Occasionally, it may be due to an abnormal eruption path, presumably caused by unusual orientation of the tooth germ. ***Ankylosis***, the fusion of a tooth to surrounding bone, is another cause of impaction. This usually occurs in association with erupted primary molars. It may result in impaction of a

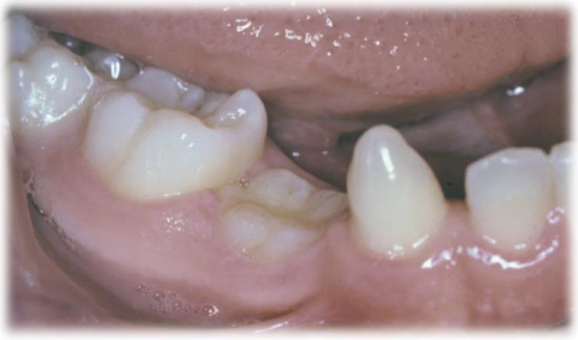
subjacent permanent tooth. The reason for ankylosis is unknown, but it is believed to be related to periapical inflammation and subsequent bone repair. With focal loss of the periodontal ligament, bone and cementum become inextricably mixed, causing fusion of the tooth to alveolar bone.





Ankylosis:

Eruption continues after the emergence of the teeth to compensate for masticatory wear and the growth of the jaws. The cessation of eruption after emergence is termed ankylosis and occurs from an anatomic fusion of tooth cementum or dentin with the alveolar bone. Although the areas of union may be too subtle to be detected clinically and radiographically, histopathologic examination will demonstrate fusion between the affected toot h and the adjacent bone in almost all cases. Although any tooth may be affected, the most commonly involved teeth in order of frequency are the mandibular primary first molar, the mandibular primary second molar, the maxillary primary first molar, and the maxillary primary second molar. The reason for ankylosis is unknown, but it is believed to be related to periapical inflammation and subsequent bone repair. With focal loss of the periodontal ligament, bone and cementum become inextricably mixed, causing fusion of the tooth to alveolar bone. Other terms for this process within the literature include infra occlusion, secondary retention submergence, Re impaction and re inclusion.



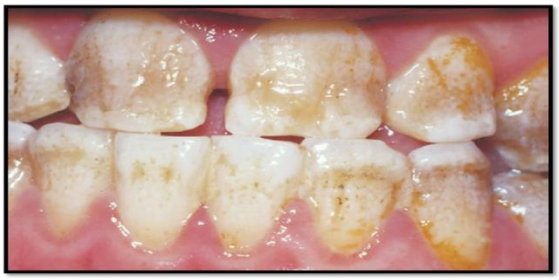
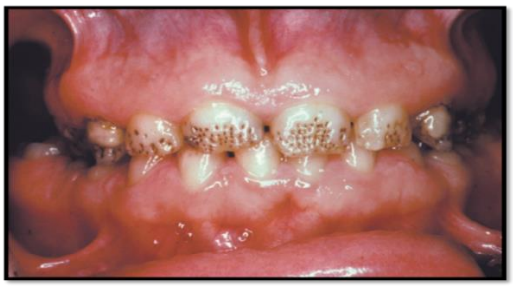
Developmental Alterations in the Structure of Teeth

Amelogenesis Imperfecta

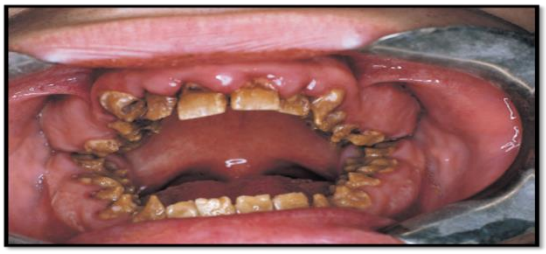
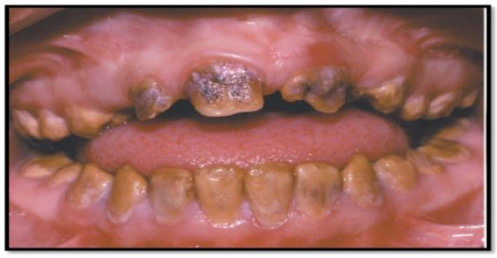
It is a clinically and genetically heterogeneous group of disorders of enamel formation that affect both dentitions. Most cases of amelogenesis imperfecta fall into one of two clinical types: ***hypoplastic*** or ***hypocalcified***. A third type, known as ***hypomaturation***, has been added to the list. Numerous subtypes of the three major groups are also recognized; these are based on different inheritance patterns, clinical appearances, and radiographic features.

Several genes that are involved in enamel formation (amelogenin, enamelin, kallikrein 4, MMP20, others) are mutated in various forms of this condition.

In the ***hypoplastic*** type of amelogenesis imperfecta, teeth erupt with insufficient amounts of enamel, ranging from pits and grooves in one patient to complete absence (aplasia) in another. Because of reduced enamel thickness in some cases, abnormal contour and absent interproximal contact points may be evident.

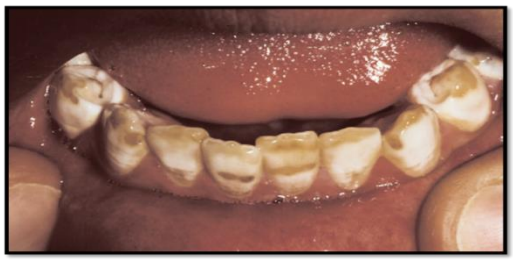
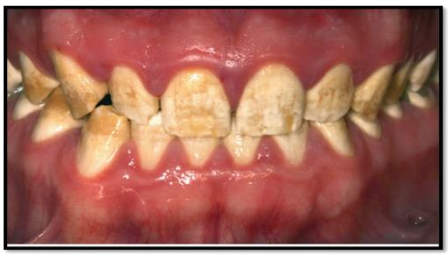



In the ***hypocalcified*** type, the quantity of enamel is normal, but it is soft and friable, so that it fractures and wears readily. The color of the teeth varies from tooth to tooth and from patient to patient—from white opaque to yellow to brown. Teeth also tend to darken with age as a result of exogenous staining.

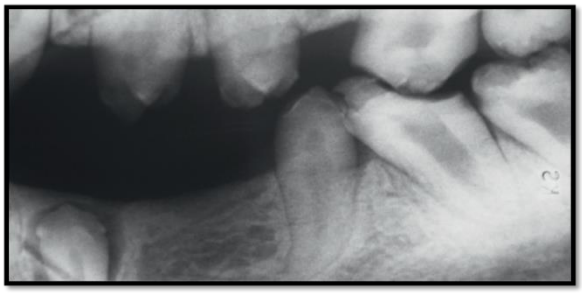
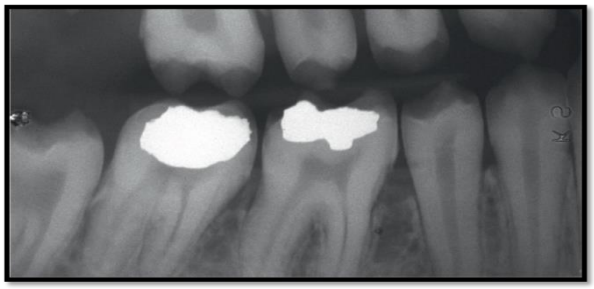



The hypomaturation type, which exhibits a less severe alteration in mineralization, the enamel is of normal thickness but not of normal hardness and translucency, enamel can be pierced

with the point of a dental explorer with firm pressure and can be chipped away from the underlying normal dentin.

Radiographically, enamel appears reduced in bulk, often showing a thin layer over occlusal and interproximal surfaces. Dentin and pulp chambers appear normal. Although the enamel is soft and irregular, teeth are not caries prone.Treatment focuses on esthetics and protection of tooth tissue. Restorative dental procedures at an early age not only preserve teeth but have a significant effect on the patient's self-esteem.

DEFECTS OF DENTIN

Dentinogenesis Imperfecta

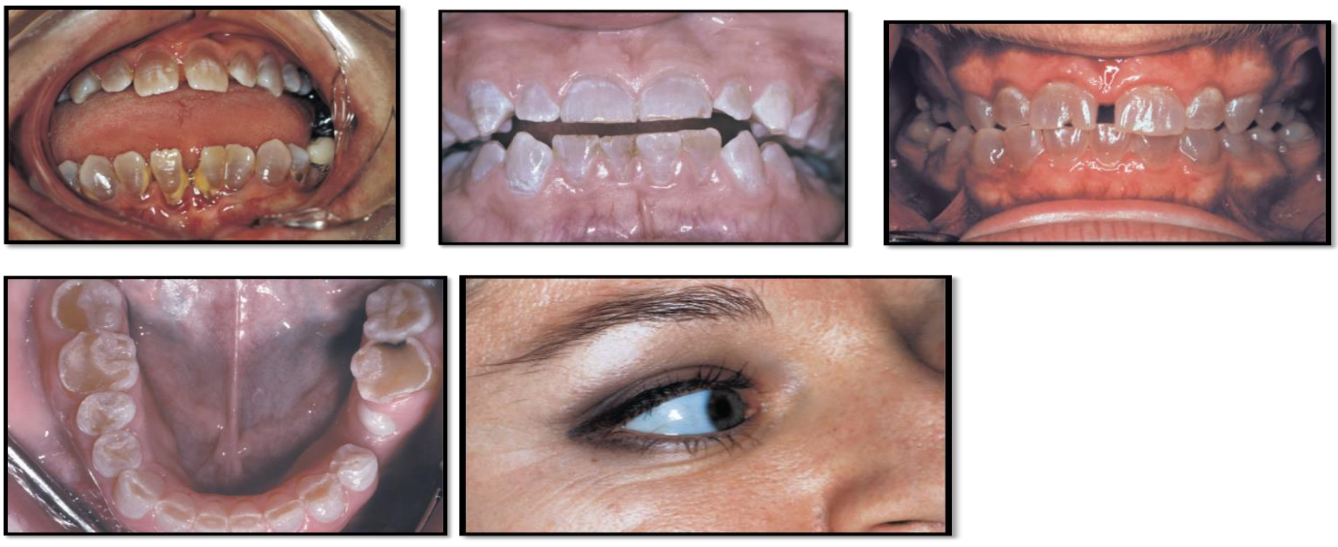
It is an autosomal-dominant trait with variable expressivity. Mutations in the dentin sialo phosphoprotein gene have been described. It typically affects the dentin of both primary and permanent dentitions. Because of the clinical discoloration of teeth, this condition has also been known as (hereditary) ***opalescent dentin.*** Dentinogenesis imperfecta has been divided into three types.

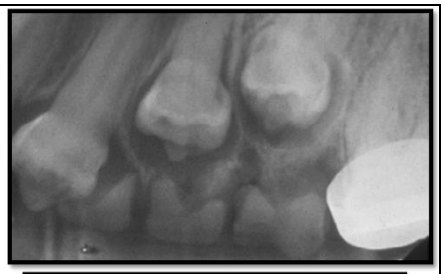
1-Type I or syndrome-associated, in which the dentin abnormality occurs in patients with concurrent osteogenesis imperfecta, primary teeth are more severely affected than permanent teeth.

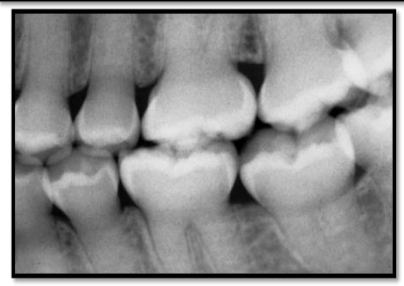
2- Type II, patients have only dentin abnormalities and no bone disease.

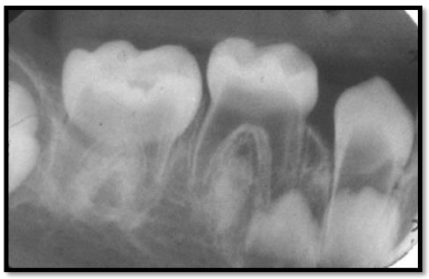
3-Type III or the Brandywine type, only dental defects occur. This type is similar to type II, but has some clinical and radiographic variations. Features of type III that are not seen in type I and II include multiple pulp exposures, periapical radiolucencies, and a variable radiographic appearance. Dentinogenesis imperfecta type I (syndromal dentinogenesis imperfecta) is caused by mutations in the genes that encode collagen type I. Dentinogenesis imperfecta types II and III, on the other hand, have been shown to be related to mutations in a gene known as dentin sialophosphoprotein that encodes non-collagen proteins of dentin. Other genes that encode dentin proteins, such as osteopontin, do not appear to be mutated in dentinogenesis imperfecta.

Clinically All three types share numerous features. In both dentitions, the teeth exhibit an unusual translucent, opalescent appearance, with color variation from yellow-brown to gray. The entire crown appears discolored because of the abnormal underlying dentin. Although the enamel is structurally and chemically normal, it fractures easily, resulting in rapid wear. The enamel fracturing is believed to be due to the poor support provided by abnormal dentin, and possibly in part to the absence of the microscopic scalloping normally seen between dentin and enamel, which is believed to help mechanically lock the two hard tissues together. Overall tooth morphology is unusual for its excessive constriction at the cement-enamel junction, giving the crowns a tulip or bell shape. Roots are shortened and blunted. The teeth do not exhibit any greater susceptibility to caries, and they may in fact show some resistance because of the rapid wear and absence of interdental contacts.









Radiographically

Types I and II exhibit identical changes. Opacification of dental pulps occurs as the result of continued deposition of abnormal dentin. The short roots and the bell-shaped crowns are also obvious on radiographic examination.

In type III, the dentin appears thin and the pulp chambers and root canals extremely large, giving the appearance of thin dentin shells—hence the previous designation of ***shell teeth*.**

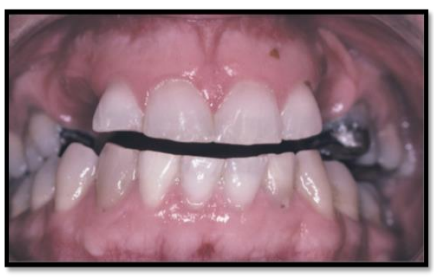
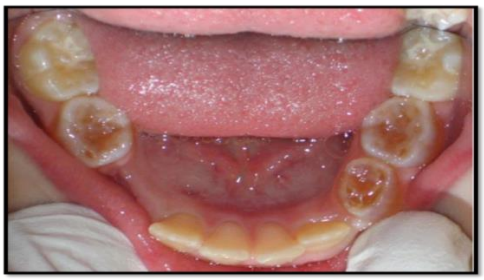
Treatment: Directed toward protecting tooth tissue from wear and toward, thereby improving the esthetic appearance of the teeth. Generally, fitting with full crowns at an early age is the treatment of choice. Despite the qualitatively poor dentin, support for the crowns is adequate. These teeth should not be used as abutments because the roots are prone to fracture under stress.

Dentin Dysplasia

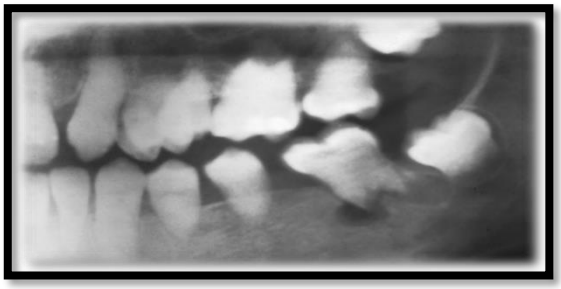
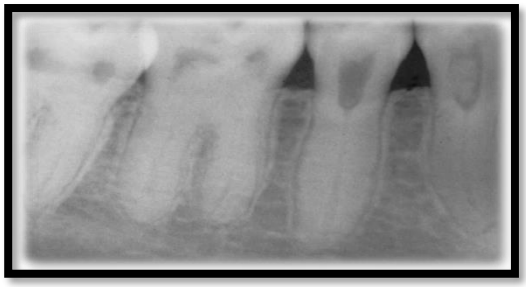
Dentin dysplasia, subdivided into types I and II, is another autosomal-dominant condition that affects dentin. The incidence of this rare disorder is approximately 10 times less than that of dentinogenesis imperfecta. As in dentinogenesis imperfecta II and III, genetic mutations occur in the dentin sialophosphoprotein gene in dentin dysplasia type II. Genetic lesions have yet to be elucidated in dentin dysplasia type I.

In dentin dysplasia type II, the color of the primary dentition is opalescent and the permanent dentition is normal; in type I, both dentitions are of normal color. The coronal pulps in type II are usually large (thistle tube appearance) and are filled with globules of abnormal dentin. Also, periapical lesions are not a regular feature of type II, as they are of type I.

Clinically: The crowns in dentin dysplasia type I appear to be normal in color and shape. Premature tooth loss may occur because of short roots or periapical inflammatory lesions. Teeth show greater resistance to caries when compared with normal teeth.

Radiographically: In dentin dysplasia type I, roots appear extremely short and pulps are almost completely obliterated. Residual fragments of pulp tissue appear typically as horizontal lucencies (chevrons). Periapical lucencies are typically seen; they represent chronic abscesses, granulomas, or cysts. In dentin dysplasia type II, deciduous teeth are similar in radiographic appearance to those in type I, but permanent teeth exhibit enlarged pulp chambers that have been described as thistle tube in appearance.

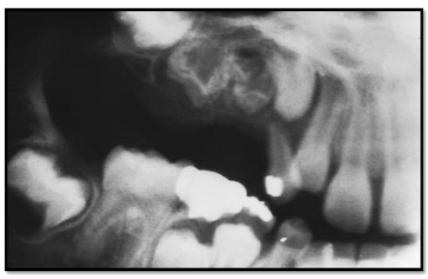
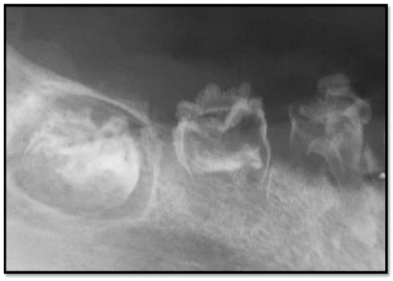
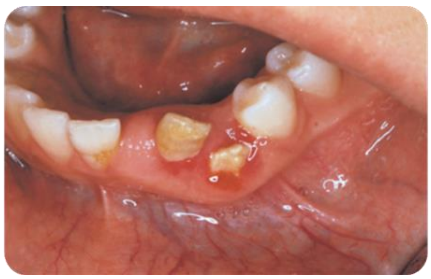



Treatment: Directed toward retention of teeth for as long as possible. However, because of the short roots and periapical lesions, the prognosis for prolonged retention is poor. This dental condition has not been associated with any systemic connective tissue problems.

DEFECTS OF ENAMEL AND DENTIN

Regional Odontodysplasia Regional odontodysplasia is a dental abnormality that involves the hard tissues derived from both epithelial (enamel) and mesenchymal (dentin and cementum) components of the tooth-forming apparatus. The teeth in a region or quadrant of the maxilla or mandible are affected to the extent that they exhibit short roots, open apical foramina, and enlarged pulp chambers. The thinness and poor mineralization quality of the enamel and dentin layers have given rise to the term ***ghost teeth***. One or both dentitions may be affected. The permanent teeth are more affected than the primary teeth, and the maxillary anterior teeth are more affected than other teeth. Eruption of the affected teeth is delayed or does not occur.

The cause of this rare dental abnormality is unknown, although numerous causative factors have been suggested, including trauma, nutritional deficiency, infection, metabolic abnormality, systemic disease, local vascular compromise, and genetic influences. Because of the poor quality of the affected teeth, their removal is usually indicated. The resulting edentulous zone can then be restored with a prosthesis or implant.

ENVIRONMENTAL EFFECTS ON TOOTH STRUCTURE DEVELOPMENT

DEFECTS OF ENAMEL

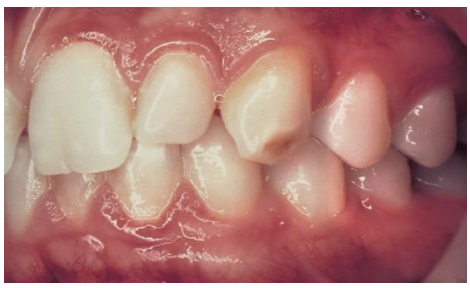
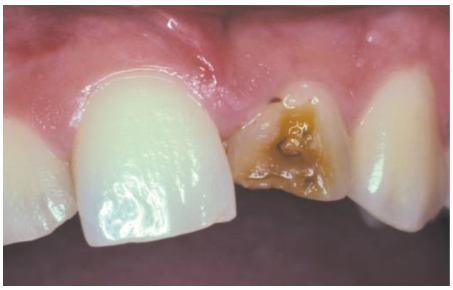
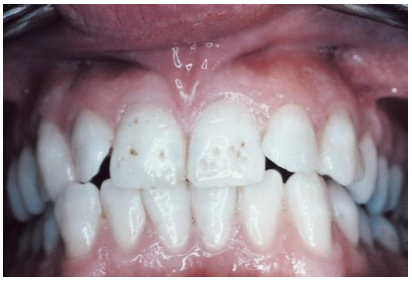
Environmental Defects of Enamel

During enamel formation, ameloblasts are susceptible to various external factors that may be reflected in erupted teeth. Metabolic injury, if severe enough and long enough, can cause defects in the quantity and shape of enamel or in the quality and color of enamel. Quantitatively defective enamel, when of normal hardness, is known as ***enamel hypoplasia***. Qualitatively defective enamel, in which normal amounts of enamel are produced but are hypomineralized, is known as ***enamel hypocalcification*****.** In this defect, the enamel is softer than normal. The extent of the enamel defect is dependent on three conditions:

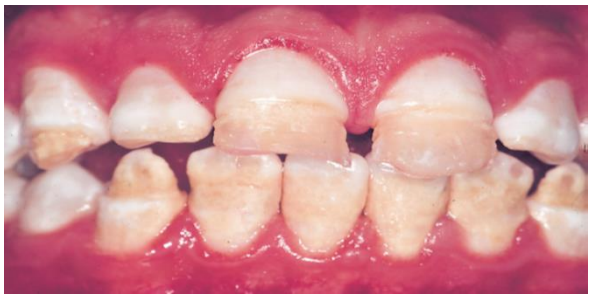
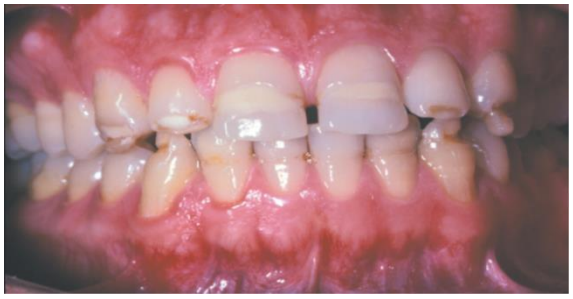
1- The intensity of the causative factor.
2- The duration of the factor's presence.
3- The time at which the factor occurs during crown development.

Factors that lead to ameloblast damage are highly varied, although the clinical signs of defective enamel are the same. Causative factors may occur locally(focal hypoplasia) , affecting only a single tooth, or they may act systemically(generalized hypoplasia) , affecting all teeth in which enamel is being formed. Local trauma or abscess formation can adversely affect the ameloblasts overlying a developing crown, resulting in enamel hypocalcification or hypoplasia. Affected teeth may have areas of coronal discoloration, or they may have actual

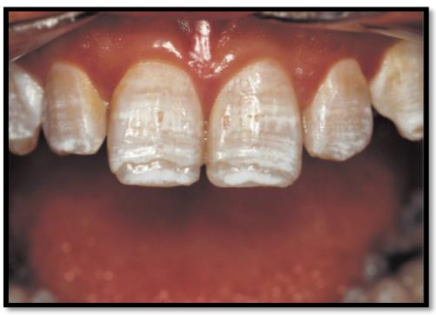
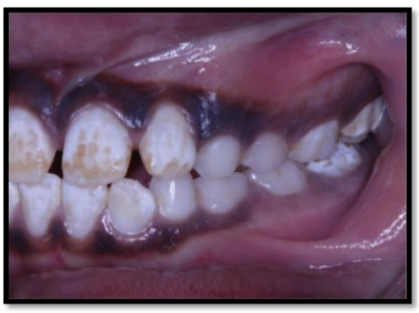
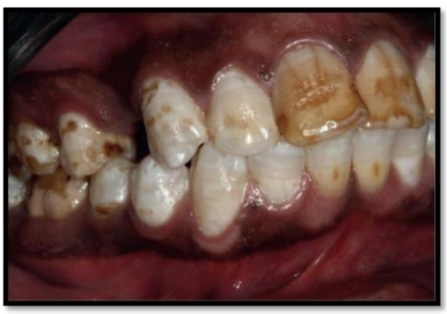
pits and irregularities. This is most commonly seen in permanent teeth in which the overlying deciduous tooth becomes abscessed or is physically forced into the enamel organ of the permanent tooth. The resulting hypoplastic or hypocalcified permanent tooth is sometimes known as ***Turner's tooth*** (Turners hypoplasia).

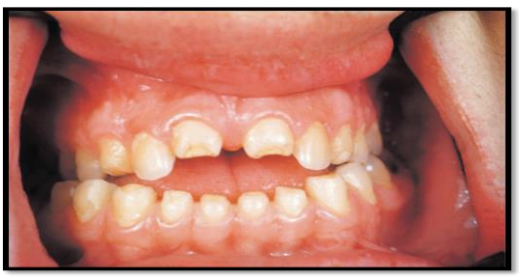
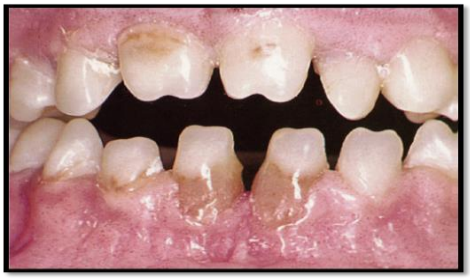
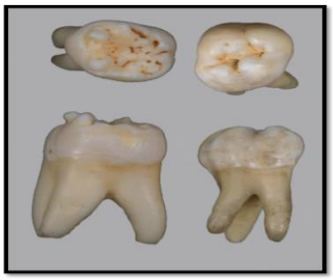
Short-term systemic environmental factors inhibit functioning ameloblasts at a specific period during tooth development and are manifested clinically as a horizontal line of small pits or grooves on the enamel surface that correspond to the time of development and the duration of the insult. If the duration of the environmental insult is brief, the line of hypoplasia is narrow, whereas a prolonged insult produces a wider zone of hypoplasia and may affect more teeth.

Dental fluorosis. The ingestion of excess amounts of fluoride also can result in significant enamel defects known as dental fluorosis. Although the fluoride produced an unusual permanent dental stain, a resistance to caries also was noted. it was discovered that fluoride in the water at 1.0 ppm reduced caries by 50% to 70%. In addition, this level of fluoride in the water supply was associated with a low and mostly mild prevalence of mottled enamel.

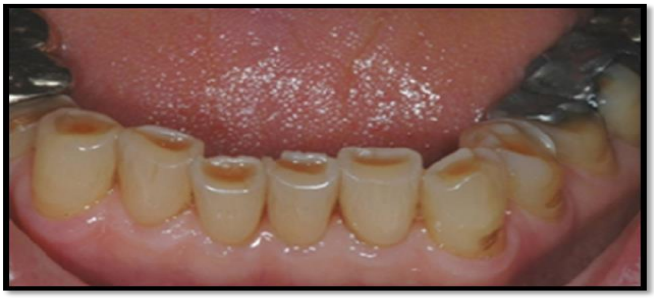
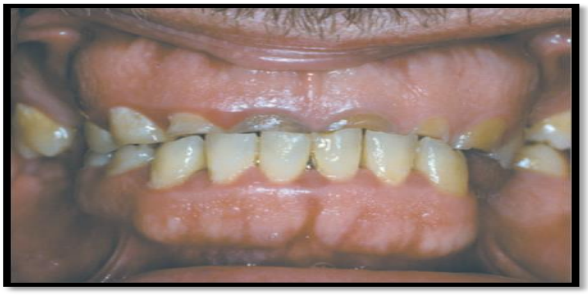
Syphilitic hypoplasia. Congenital syphilis results in a pattern of enamel hypoplasia that is well known but currently so rare that lengthy discussion is not warranted. Anterior teeth altered by syphilis are termed **Hutchinson's incisors** and exhibit crowns that are shaped like straight-edge screw drivers. With the greatest circumference present in the middle one third of the crown and a constricted incisal edge. The middle portion of the incisal edge often demonstrates a central hypoplastic notch. Altered posterior teeth are termed **mulberry molars** and demonstrate constricted occlusal tables with a disorganized surface anatomy that resembles the bumpy surface of a mulberry.

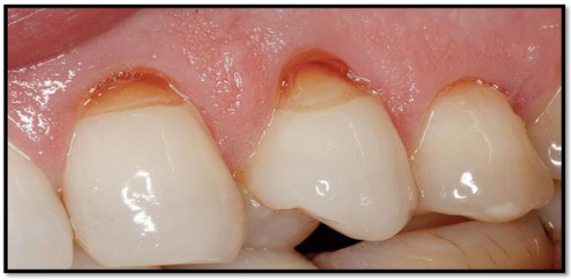
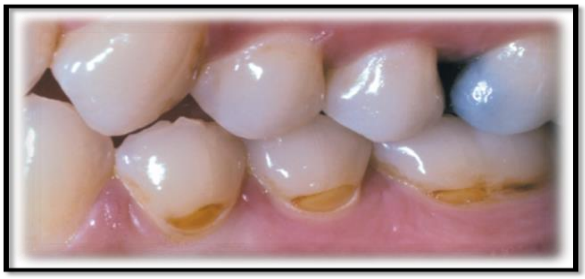
Post developmental Loss of Tooth

Attrition, Abrasion, Erosion and Abfraction

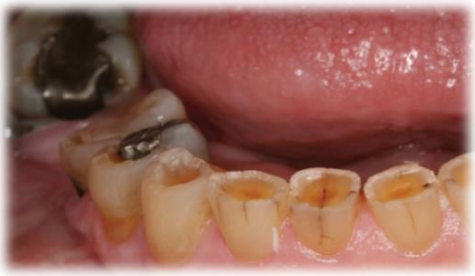
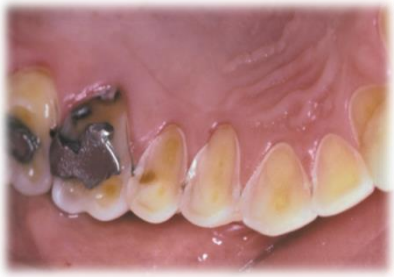
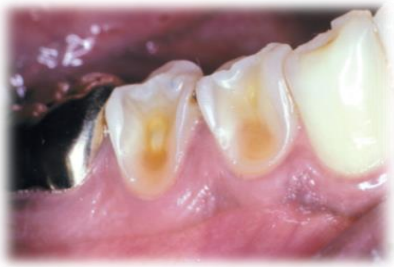
Attrition: Is the physiologic wearing of teeth as a result of mastication. It is an age-related process that varies from one individual to another. Factors such as diet, dentition, jaw musculature, and chewing habits can significantly influence the pattern and extent of attrition.

Abrasion: Is the pathologic wearing of teeth caused by an abnormal habit or abnormal use of abrasive substances orally. Pipe smoki smoking, tobacco chewing, aggressive tooth brushing, and use of abrasive dentifrices are among the more common causes. The location and pattern of abrasion are directly dependent on the cause, with so-called toothbrush abrasion along the cementoenamel junction an easily recognized pattern.

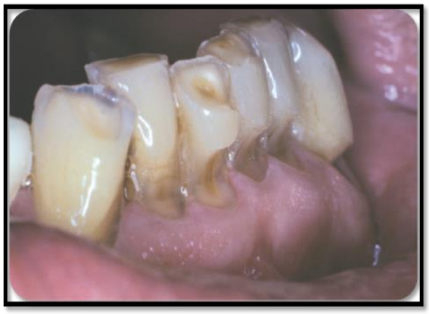
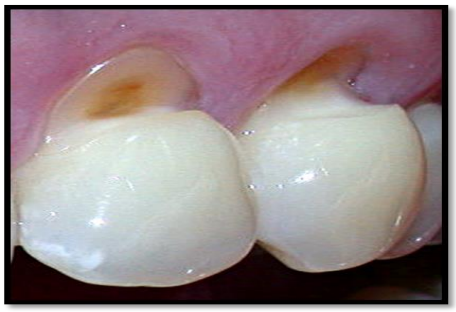
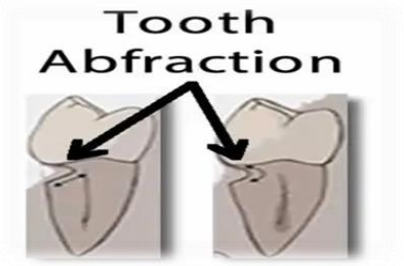



Erosion: Is the loss of tooth structure through a non-bacterial chemical process. Most commonly, acids are involved in the dissolution process from an external or an internal source. Externally, acid may be found in the work environment (e.g., battery manufacturing) or in the diet (e.g., citrus fruits, acid-containing soft drinks). The internal source of acid is most probably regurgitation of gastric contents. This may be seen in any disorder of which chronic vomiting is a part. Self-induced vomiting, as a component of bulimia or, less commonly, anorexia nervosa, has become an increasingly important cause of dental erosion and other oral abnormalities. The pattern of erosion associated with vomiting is usually generalized tooth loss on the lingual surfaces of maxillary teeth. However, all surfaces may be affected, especially in individuals who compensate for fluid loss by excessive intake of fruit juices. In many cases of tooth erosion, no cause is found.

Abfraction: loss of tooth from occulusal stress that create repeated tooth flexure with failure of enamel and dentin at a location away from the point of locking, it appears as wedge-shaped defects limited to the cervical area of the teeth and may closely resemble cervical abrasion or erosion. Clues to the diagnosis include defects that are deep, narrow, and V-shaped (which do not allow the tooth brush to contact the base of the defect) and often affect a single tooth with adjacent unaffected teeth. In addition, Occasional lesions are subgingival, a site typically protected from abrasion and erosion. The lesions are seen almost

exclusively on the facial surface and exhibit a much greater prevalence in those with bruxism. A higher frequency is noted in the mandibular dentition, presumably because the lingual orientation makes them more susceptible to the concentration of tensile stresses at the cervical regions.

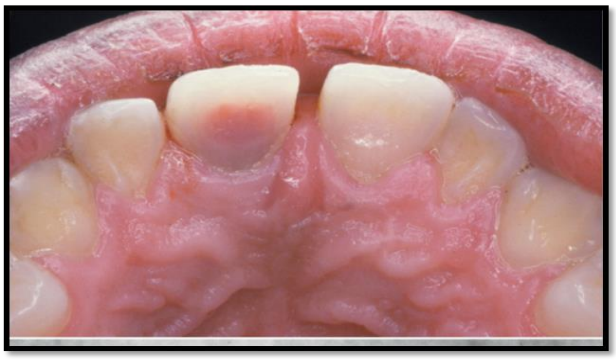
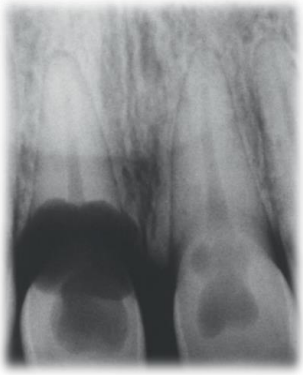
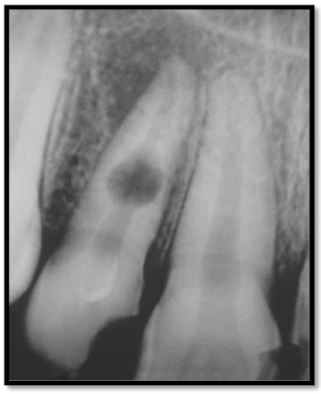




Internal and External Resorption

- **Internal Resorption**

Resorption of the dentin of the pulpal walls may be seen as part of an inflammatory response to pulpal injury, or it may be seen in cases in which no apparent trigger can be identified. The resorption occurs as a result of activation of osteoclasts or dentinoclasts on internal surfaces of the root or crown. Resorption lacunae containing these cells and chronic inflammatory cells are seen. Reversal lines may also be found in adjacent hard tissue, indicating attempts at repair. In time, the root or crown is perforated by the process, making the tooth useless.

Any tooth may be involved, and usually only a single tooth is affected, although cases in which more than one tooth is involved have been described. In advanced cases, teeth may appear pink because of the proximity of pulp tissue to the tooth surface. Until root fracture or communication with a periodontal pocket occurs, patients generally have no symptoms.

The treatment of choice is root canal therapy before perforation. Once communication between pulp and periodontal ligament occurs, the prognosis for saving the tooth is very poor. Occasionally, the process may spontaneously stop for no apparent reason.

- **External Resorption**

Resorption of teeth from external surfaces may have one of several causes. This change may be the result of an adjacent pathologic process, such as

(1) Chronic inflammatory lesions

(2) Cysts

(3) Benign tumors

(4) Malignant neoplasms.

The pathogenesis of external resorption from these causes has been related to the release of chemical mediators, increased vascularity, and pressure.External resorption of teeth may also be seen in association with

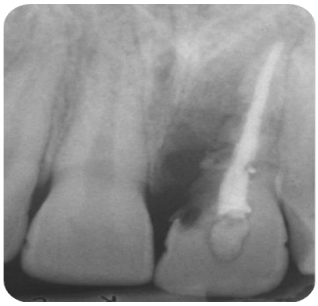
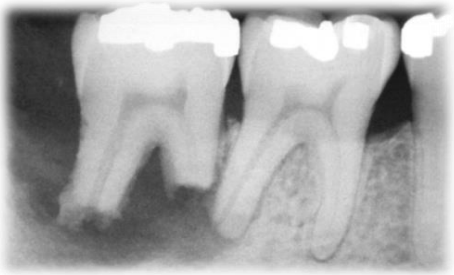
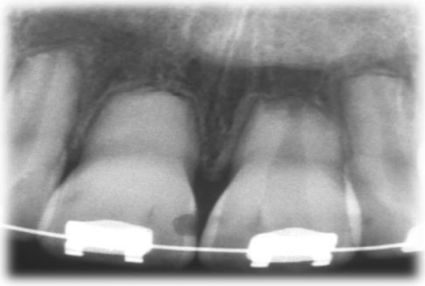
(1) Trauma

(2) Reimplantation or transplantation of teeth

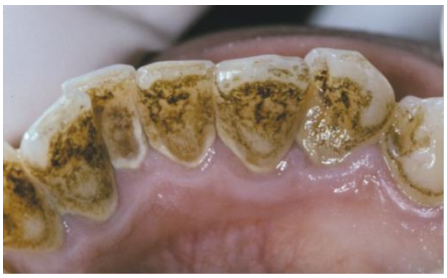
(3) Impaction.

Trauma that causes injury to or necrosis of the periodontal ligament may initiate resorption of tooth roots. This trauma may result from a single event, from malocclusion, or from excessive orthodontic forces. Because reimplanted and transplanted teeth are nonvital and have no surrounding viable periodontal ligament, they eventually are resorbed and replaced by bone. This is basically a natural physiologic process in which the calcified collagen matrix of the tooth serves as a frame-work for the deposition of new, viable bone. Impacted teeth, when they impinge or exert pressure on adjacent teeth, may cause root resorption of the otherwise normally erupted tooth. Impacted teeth themselves occasionally may undergo resorption. The cause of this phenomenon is unknown, although it is believed to be related to partial loss of the protective effect of the periodontal ligament or reduced enamel epithelium.

Finally, external resorption of erupted teeth may be idiopathic. This may occur in one or more teeth. Any tooth may be involved, although molars are least likely to be affected . External resorption eventually causes loss of the affected teeth.

Environmental Discoloration of Teeth



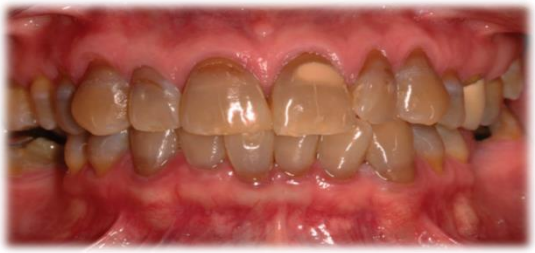
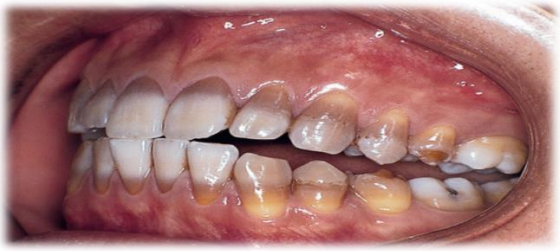
Exogenous Stains

Stains on the surfaces of teeth that can be removed with abrasives are known as exogenous or extrinsic stains. The color change may be caused by pigments in dietary substances (e.g., coffee, “betel” areca nut, tobacco) or by the colored by-products of chromogenic bacteria in dental plaque. Chromogenic bacteria are believed to be responsible for brown, black, green, and orange stains observed predominantly in children. Brown and black stains typically are seen in the cervical zone of teeth, either as a thin line along the gingival margin or as a wide band. This type of stain is also often found on teeth adjacent to salivary duct orifices. Green stain is tenacious and usually is found as a band on the labial surfaces of the maxillary anterior teeth. Blood pigments are thought to contribute to the green color. Orange or yellow-orange stains appear on the gingival third of teeth in a small percentage of children. These generally are easily removed.

Endogenous Stains Discoloration of teeth resulting from deposits of systemically circulating substances during tooth development is defined as endogenous or intrinsic staining.

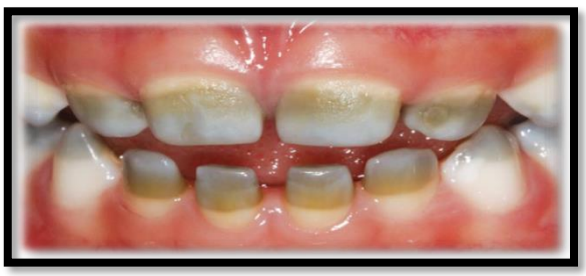
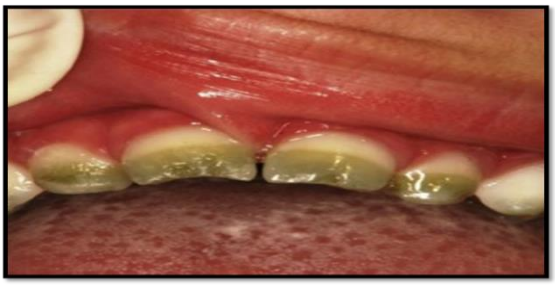
Systemic ingestion of tetracycline during tooth development is a well-known cause of endogenous staining of teeth. Tetracycline binds calcium and therefore is deposited in developing teeth and bones. The bright yellow color of the drug is reflected in subsequently

erupted teeth. The fluorescent property of tetracycline can be demonstrated with an ultraviolet light in clinically erupted teeth. Over time, the tetracycline oxidizes, resulting in a change from yellow to gray or brown with loss of its fluorescent quality. Because tetracycline can cross the placenta, it may stain primary teeth if taken during pregnancy. If it is administered between birth and age 6 or 7 years, permanent teeth may be affected. Only a small minority of children given tetracycline for various bacterial diseases, however, exhibit clinical evidence of discoloration. Staining is directly proportional to the age at which the drug is administered and the dose and duration of drug usage. The significance of tetracycline staining lies in its cosmetically objectionable appearance. Because other, equally effective antibiotics are available, tetracycline should not be prescribed for children younger than 7 years except in unusual circumstances.

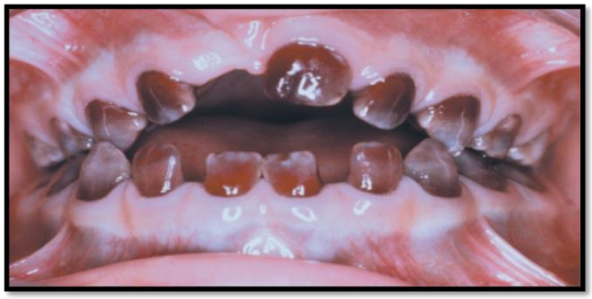



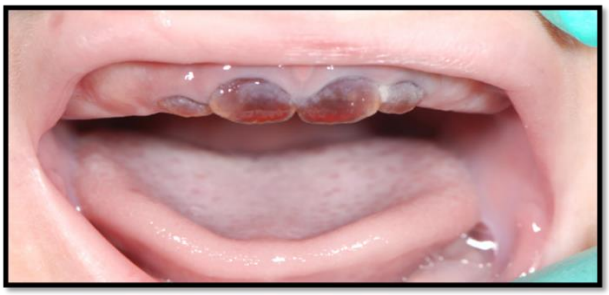
It should be noted that minocycline, a semisynthetic derivative of tetracycline, can stain the roots of adult teeth. It also may stain skin and mucosa in a diffuse or patchy pattern.

Rh incompatibility (erythroblastosis fetalis) has been cited as a cause of endogenous staining in primary teeth. Because of red blood cell hemolysis resulting from maternal antibody destruction of fetal red blood cells, blood breakdown products (bilirubin) are deposited in developing primary teeth. The teeth appear green to brown. Treatment is not required because only primary teeth are affected.

Congenital porphyria, one of several inborn errors of porphyrin metabolism, is also a potential cause of endogenous pigmentation. This autosomal-recessive trait is associated with photosensitivity, vesiculobullous skin eruptions, red urine, and splenomegaly. Teeth may appear red to brown because of deposition of porphyrin in the developing teeth. Affected teeth fluoresce red with ultraviolet light.





Liver disease, biliary atresia, and neonatal hepatitis may produce discoloration of the primary dentition. In biliary atresia, the teeth may assume a green discoloration; a yellowish-brown color is noted in cases of neonatal hepatitis. This is a result of the deposition or incorporation of bilirubin in developing enamel and dentin.

Oral Pathology

Lec.6

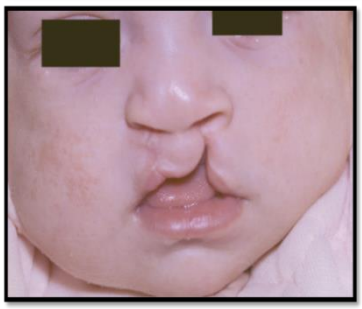
Developmental Defects of the Soft tissue

OROFACIAL CLEFTS:

The formation of the face and oral cavity is complex in nature and involves the development of multiple tissue processes that must merge and fuse in a highly orchestrated fashion. Disturbances in the growth of these tissue processes or their fusion may result in the formation of **orofacial clefts.**

1-***CLEFTS OF THE LIP AND PALATE:*** Clefts can form in the lip or palate alone or in both. The aetiology is unknown but there is a genetic component in approximately 40% of cases. The risk of having such defects is greatly increased if one, and particularly if both, of the parents are affected.

Classification: Generally, clefts of the lip and palate are classified into 4 major types:



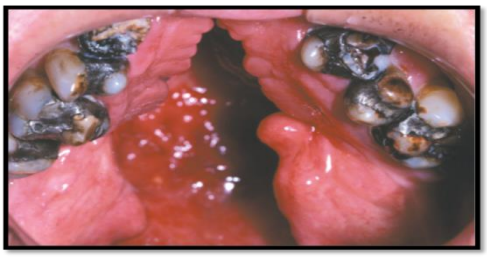
1- Cleft lip.
2- Cleft palate.
3- Unilateral cleft lip and palate.
4- Bilateral cleft lip and palate.

Nine environmental factors that have been postulated to plan accessory role in the development of cleft lip and palate include

1. Nutritional factors.
2. Physiologic, emotional, or traumatic stress.
3. Relative ischemia to the area.
4. Mechanical obstruction by an enlarged tongue.
5. Substances such as alcohol, drugs, or toxins.
6. Infections.
7. Maternal alcohol consumption.
8. Maternal cigarette smoking.
9. Anticoagulants therapy.

Cleft lip (CL): Developing defects usually of the upper lip characterized by a wedge-shape defect resulting from the failure of two parts of the lips to fuse into single structure. defective fusion of the medial nasal process with the maxillary process.

Cleft palate (CP): failure of the palatal shelves to fuse.



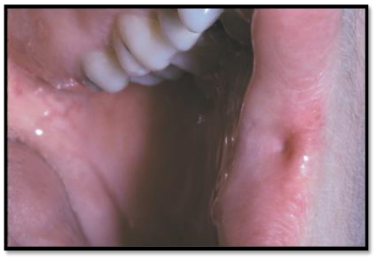
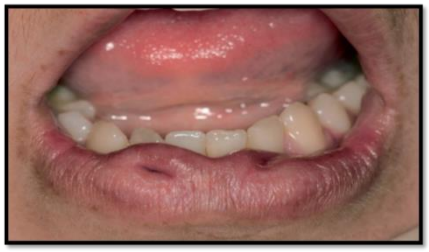
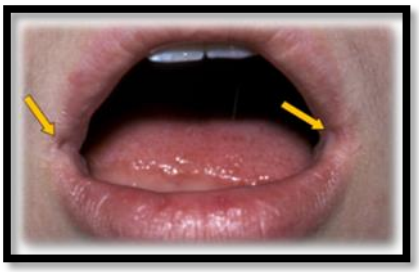

Treatment should involve a multidisciplinary approach, including a pediatrician, oral and maxillofacial surgeon, otolaryngologist, plastic surgeon, pediatric dentist, orthodontist, prosthodontist, speech pathologist, and geneticist. Surgical repair often involves multiple primary and secondary procedures throughout childhood.

B- Oblique facial cleft: -It represents failure of fusion of the lateral nasal process with the maxillary process. It extends from the upper lip to the eye and always associated with cleft palate.


C- Lateral facial cleft: - It results from lack of fusion of the maxillary and mandibular processes. Occurs as isolated defects or may be associated with other disorders as mandibular dysostosis. It is either unilateral or bilateral extending from the commissures toward the ear resulting in macrosomia.

Congenital lip pits: Congenital lip pits are developmental defects that may involve the paramedical portion of the vermillion of the lower and upper lip ***(paramedical lip pit)*** or the labial commissure area ***(commercial lip pit).*** Both types of lip pits appear to be inherited as autosomal dominant trait. The paramedical lower lip pit may occur as an isolated finding or

may be associated with cleft lip or cleft palate ***(van der woude syndrome)***. The paramedical lip pits are occasionally excised for cosmetic reasons; commissural lip pits required no treatment.

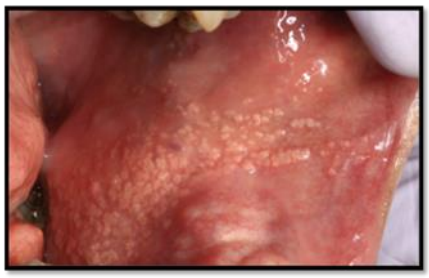
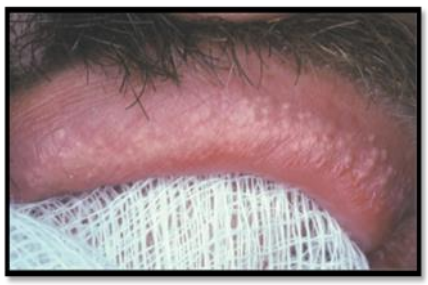




Double lip:

A double lip is an anomaly characterized by a horizontal fold of redundant mucosal tissue that is usually located on the inner aspect of the upper lip, although the lower lip can also be occasionally involved. This redundant tissue can be congenital or acquired. The double lip is usually visible when the lip is tense but not when the lip is at rest.

Fordyce's Granules:

Fordyce's granules represent ectopic sebaceous glands or sebaceous ***choristomas*** *(normal tissue in an abnormal location)*. This condition is regarded as developmental and can be considered a variation of normal. Fordyce's granules are multiple and often are seen in aggregates or in confluent arrangements. Sites of predilection include the buccal mucosa and the vermilion of the upper lip. Lesions generally are symmetrically distributed and tend to become obvious after puberty, with maximal expression occurring between 20 and 30 years of age. Lesions are asymptomatic and often are discovered incidentally by the patient or by the practitioner during a routine oral examination. A large proportion of the population—more than 80% of individual is affected by this particular condition.

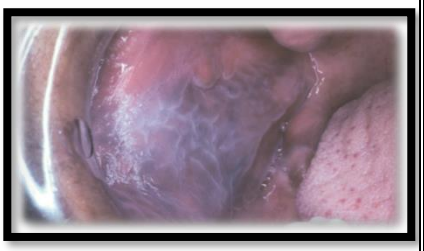
Microscopically, lobules of sebaceous glands are aggregated around or adjacent to excretory ducts. The heterotopic glands are well formed and appear functional

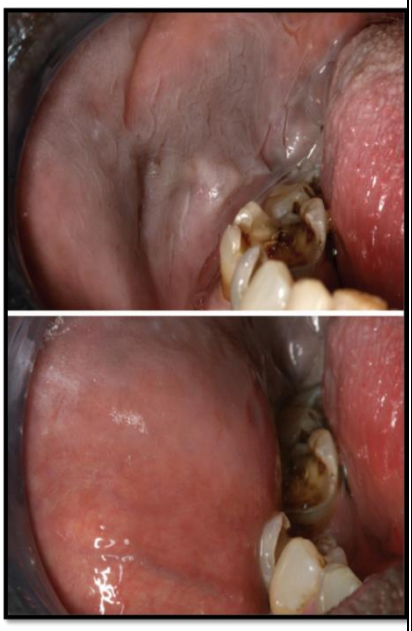
No treatment is indicated for this particular condition because the glands are normal in character and do not cause any untoward effects.

Leukoedema:

Leukoedema is a generalized mild opacification of the buccal mucosa that is regarded as a variation of normal. It can be identified in the majority of the population.

Clinical Features: Leukoedema is usually discovered as an incidental finding. It is asymptomatic and symmetrically distributed in the buccal mucosa and to a lesser extent over the labial mucosa. It appears as a gray-white, diffuse, filmy, or milky surface alteration. In exaggerated cases, a whitish cast with surface textural changes, including wrinkling or corrugation, may be seen. With stretching of the buccal mucosa, the opaque changes dissipate. It is more apparent in nonwhites, especially African Americans.



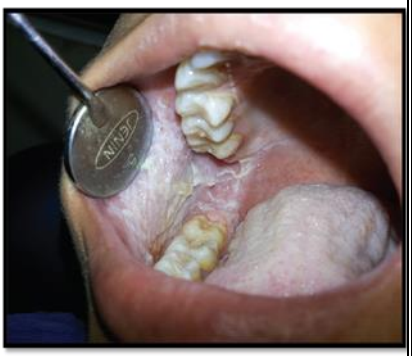


Histopathology: In leukoedema, the epithelium is parakeratotic and acanthotic, with marked intracellular edema of spinous cells. The enlarged epithelial cells have small, pyknotic (condensed) nuclei in optically clear cytoplasm.

Treatment and Prognosis: Treatment is not necessary because the changes are innocuous and no malignant potential exists. If the diagnosis is in doubt, a biopsy can be performed.

White sponge nevus:

Relatively uncommon, autosomal dominant hereditary disorder that manifests as a white lesion of the oral mucosa. The condition exhibits a variable penetrance; some patients exhibit lesion at birth, whereas in others, lesions may not appear until early childhood or even adolescence.



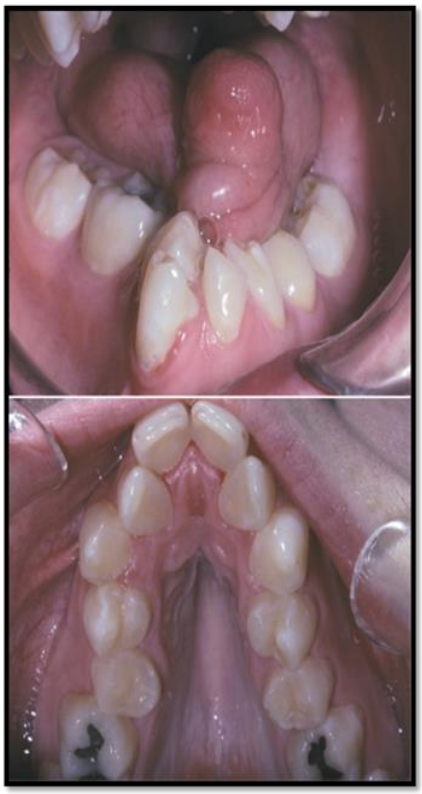
Clinical features: Lesions are asymptomatic, whitish and often folded (corrugated). They may exhibit a translucent opalescence similar to that seen in leukoedema. Lesions may be widespread and involve various sites including the buccal mucosa, gingiva, tongue, palate and floor of the mouth.

Histopathology: a mild to moderate hyperpara keratosis, acanthosis, and intracellular edema of the spinous cells are shrunken (pyknotic). The

associated connective tissue is usually free of inflammation. The diagnosis is generally reached by combining its histopathologic features, clinical appearance, and the patient's family history.

Treatment: the condition requires no treatment, because it is entirely benign.

TONGUE DISORDER



MICROGLOSSIA (HYPOGLOSSIA):

Microglossia is an uncommon developmental condition of unknown cause that is characterized by an abnormally small tongue. In rare instances, virtually the entire tongue may be missing (aglossia). However, most reported cases have been associated with one of a group of overlapping conditions known as oromandibular-limb hypogenesis syndromes.

MACROGLOSSIA

Macroglossia is an uncommon condition characterized by enlargement of the tongue. The enlargement may be caused by a wide variety of conditions including both congenital malformations and acquired diseases. The most frequent causes are vascular malformations and muscular hypertrophy.

Causes of Macroglossia

☒ ***congenital and hereditary***

- Down syndrome
- Neurofibromatosis
- Multiple endocrine neoplasia type 2B

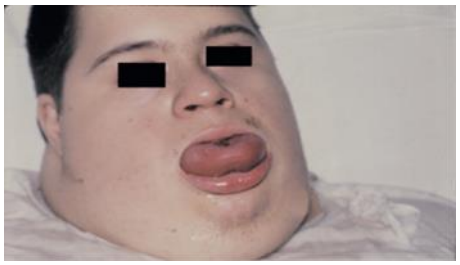
Vascular malformations

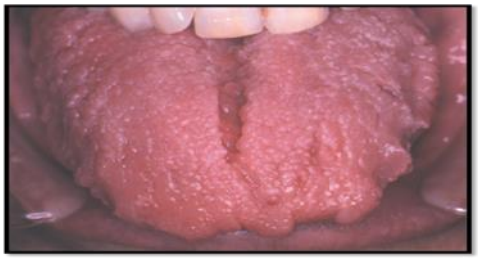
- Lymphangioma
- Hemangioma

☒ ***Acquire***

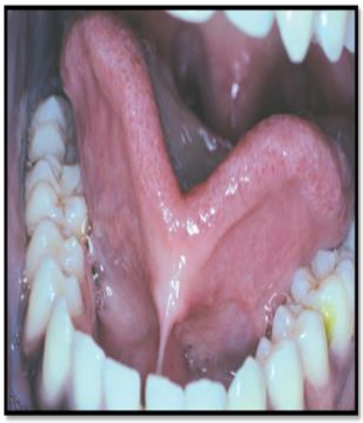
- Cretinism
- Amyloidosis
- Carcinoma and other tumor
- Acromegaly

Clinical Features: Macroglossia most commonly occurs in children and can range from mild to severe in degree. Macroglossia may be manifested first by noisy breathing, Drooling and difficulty in eating. The tongue enlargement may result in a lisping speech the pressure of the tongue against the mandible and teeth can produce a crenated lateral border to the tongue, open bite and mandibular prognathism.





ANKYLOGLOSSIA (TONGUE-TIE):

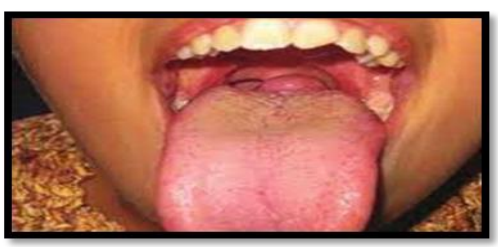


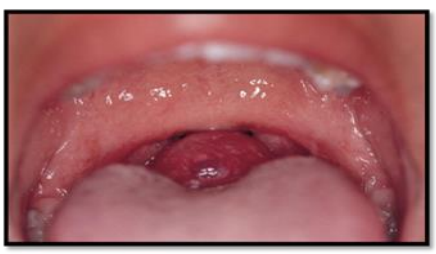
Ankyloglossia is a developmental anomaly of the tongue characterized by an abnormally short and anteriorly positioned lingual frenum that results in severely restricted tongue movements and impaired speech.

Treatment and Prognosis: Treatment is often unnecessary. If there are functional or periodontal difficulties, a frenectomy may allow greater freedom of tongue movement.

Lingual thyroid nodule: is a rare anomaly characterized by the development of a submucosal mass of thyroid tissue on the mid posterior dorsum of the tongue. Embryologically, the thyroid gland anlage arises at the site of the foramen caecum and migrates inferiorly along the thyroglossal tract to its ultimate destination in the anterior neck. If all or part of the thyroid anlage fails to migrate, remnant of thyroid tissue can develop along its path of migration; a lingual thyroid nodule represents a thyroid remnant in the region of the thyroid glands origin.

Clinical features: It presents as a 2 to 3 cm smooth sessile mass located on the mid posterior dorsum of the tongue, in the foramen caecum. The chief symptoms are dysphagia, dysphonia, dyspnea, and a feeling of tightness in the area.

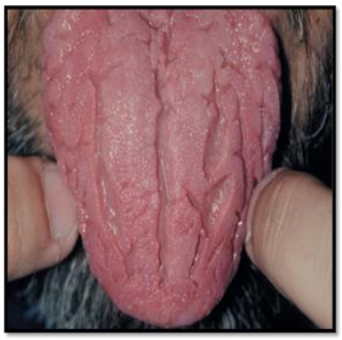




Histopathology: most cases are composed of normal mature thyroid tissue although embryonic or fetal thyroid tissue may be seen.

Treatment: before excision of a lingual thyroid nodule is planned, it should be determined if the patient possesses a functioning thyroid gland in the anterior neck with sufficient secretion to support the daily requirement when the supplementary source in the tongue is removed. If a normal thyroid gland is present, then the lingual nodules can be excised.

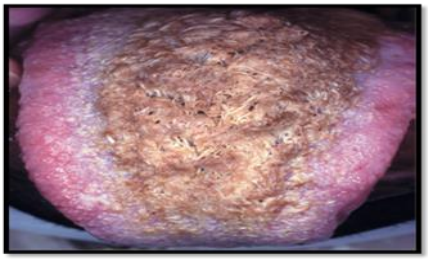
FISSURED TONGUE (SCROTAL TONGUE)

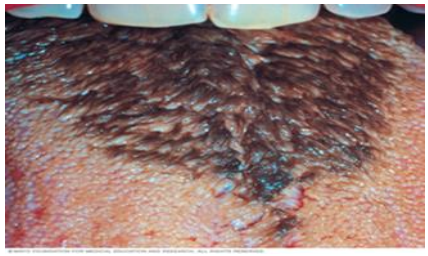


Fissured tongue is relatively common numerous grooves or fissures are present on the dorsal tongue surface. The cause is uncertain, but heredity appears to play a significant role. Aging or local environmental factors also may contribute to its development.

HAIRY TONGUE (BLACK HAIRY TONGUE)

Hairy tongue is characterized by marked accumulation of keratin on the filiform papillae of the dorsal tongue, resulting in a hair like appearance; The condition apparently represents an increase in keratin production or a decrease in normal keratin desquamation. Although the cause is uncertain, many affected people are heavy smokers.



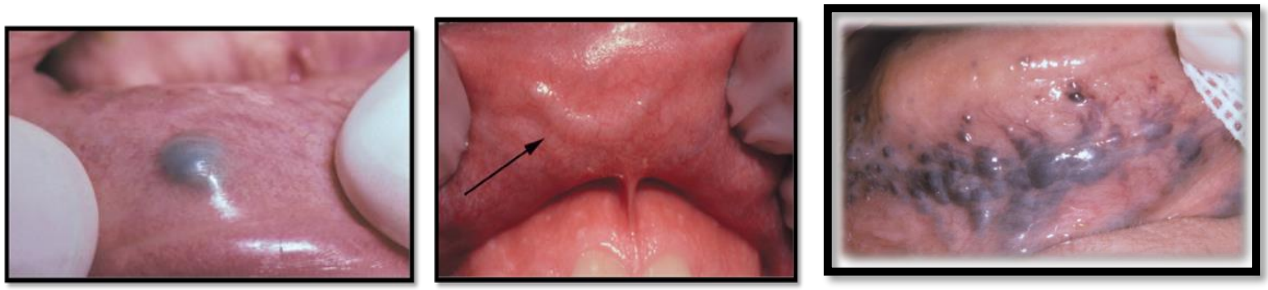


❖ Other possible associated factors include the following:

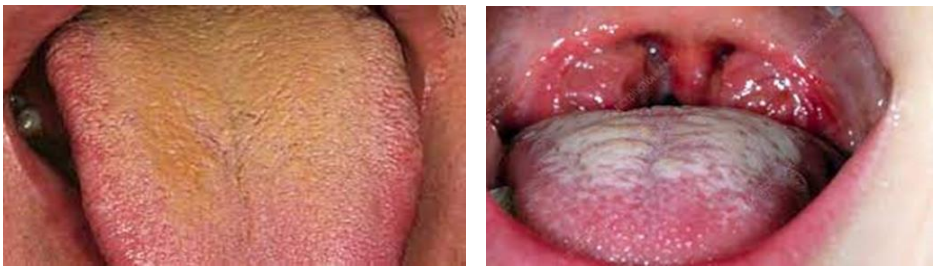
- Antibiotic therapy
- Poor oral hygiene
- General debilitation
- Radiation therapy
- Use of oxidizing mouthwashes or antacids
- Overgrowth of fungal or bacterial organisms

VARICOSITIES (VARICES): Varicosities or varices are abnormally dilated and tortuous veins. Age appears to be an important etiologic factor because varices are rare in children but common in older adults. This suggests that their development may be an age-related degeneration in which there is a loss of connective tissue tone supporting the vessels.

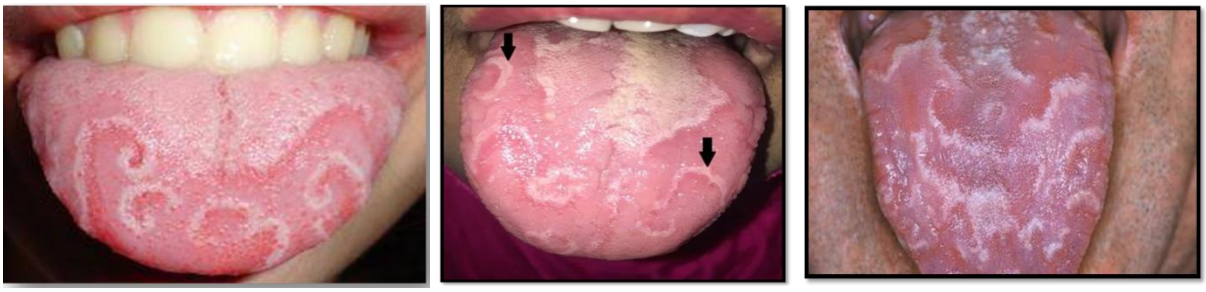
Oral varices have not been associated with systemic hypertension or other cardiopulmonary diseases. Sublingual varicosities are typically asymptomatic, and no treatment is indicated. Solitary varicosities of the lips and buccal mucosa may need to be surgically removed to confirm the diagnosis or for an esthetic purpose.



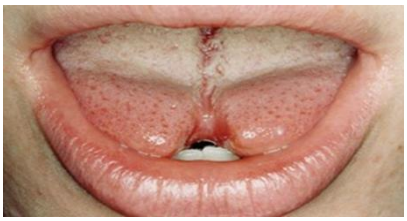
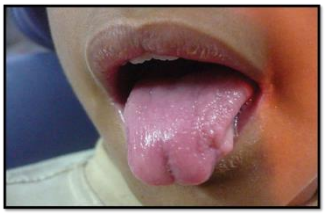
FURRED TONGUE: Tongue become coated with desquamated cells and debris in those who smoke heavily, in many systemic upsets, especially of gastrointestinal tract, and infections in which mouth becomes dry and little food is taken .A furred tongue is often seen in childhood fevers ,especially scarlet fever.



Geographical tongue (erythema migrans linguae: It is the recurrent appearance and disappearance of red areas on the tongue. The cause is unknown but sometimes there is a clear family history of its presence in several generations. In many patients geographical tongue seems to be a developmental anomaly but there also appears to be an association with psoriasis. Clinically: an irregular, smooth, red area appears, usually with a sharply defined edge. It extends for a few days, and then heals, only to appear again in another area. Sometimes the lesion is annular with a slightly raised pale margin, and several of these areas may coalesce to form a scalloped pattern. Most patients have no symptoms but some adults complain of soreness.



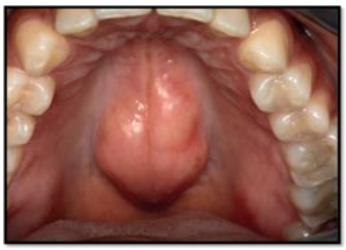
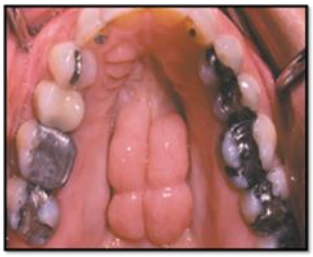
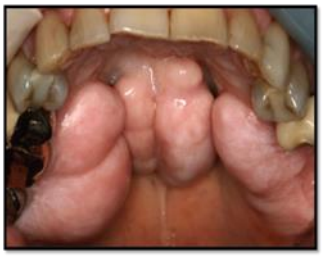
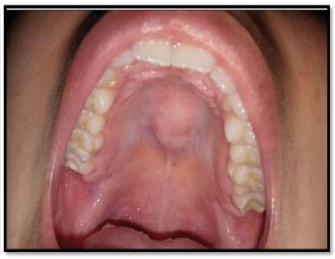
Cleft tongue: Disunion of tongue usually occurs due to failure of fusion of two lateral part of the tongue (mainly anteriorly) and this will lead to bifid tongue or cleft the tongue.

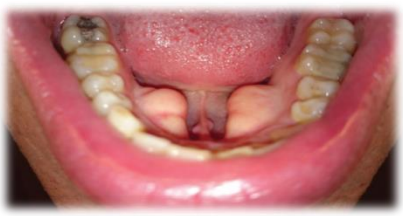
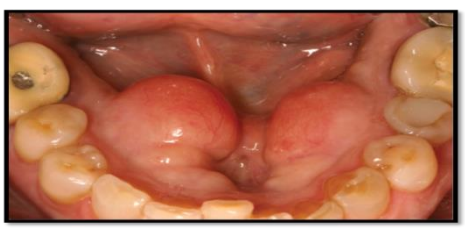

Developmental defects of the Bone

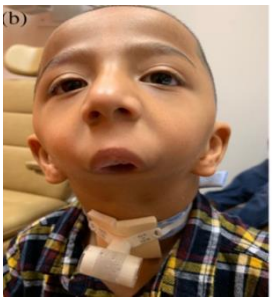
1-**Exostoses**: are localized bony protuberances that arise from the cortical plate; these benign growths frequently affect the jaws, the best-known oral exostoses: The torus palatinus and the torus mandibularis.

TORUS PALATINUS: The torus palatlnus is a common exostosis that occurs in the midline of the vault of the hard palate. The pathogenesis of these tori has long been debated with arguments centering on genetic *versus* environmental factors such as masticatory stress. Some authorities have suggested that the torus palatinus is inherited as an autosomal dominant trait. However, others believe that the development of this lesion is multifactorial, including both genetic and environmental influences. Most palatal tori can be diagnosed clinically based on their characteristic appearance; therefore, biopsy rarely is necessary. In edentulous patients, the torus may need to be removed surgically to accommodate a denture base. Surgical removal may also be indicated for palatal tori that become repeatedly ulcerated or that interfere with oral function.

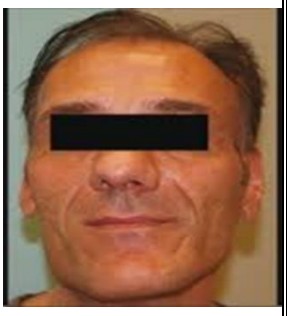





TORUS MANDIBULARIS: The torus mandibularis is a common exostosis that develops along the lingual aspect of the mandible. As with torus palatinus, the cause of mandibular tori is probably multifactorial, including both genetic and environmental influences. Most mandibular tori are easily diagnosed clinically and no treatment is necessary. However, surgical removal may be required to accommodate a lower full or partial denture.



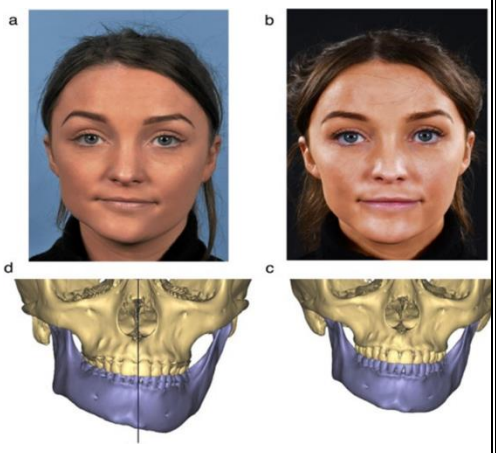
2- Agnathia:-(nathia= jaw, Ag = Agenesis). Developmental congenital absence of one of jaws; it is a rare condition and mostly occurs as part of mandible is absent.



3-*Macrognathia- :* Abnormally large jaw, sometimes called prognathism . Occurs either due to local cause, e.g. fibrous dysplasia of bone, reactive or neoplastic bone tumor ,odontogenic cysts and tumors or associated with systemic diseases as Acromegaly an Pagets disease of bone.

4-Micrognathia: - very small jaw. Developmental disturbance affecting one of jaws and lead to abnormally small jaw .Gives rise to numerous dental problems. Micrognathia may be associated with other developmental defect like in Pierre Rboins syndrome which is characterized by cleft palate, micrognathia and glossoptosis (posterior displacement of tongue, lack of support of tongue musculature and airway obstruction).

5-Coronoid hyperplasia- :Rare developmental anomaly which results in limitation of mandibular movement. May be unilateral which result from osteoma and osteosarcoma or bilateral which may result from endocrine influence during puberty.

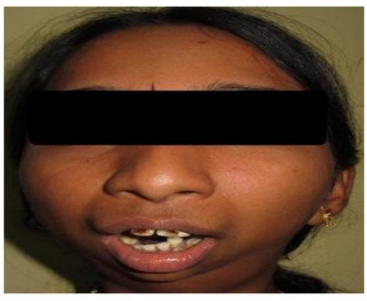


6-Condylar hyperplasia: -Excessive growth of one condyle is of unknown cause but local circulatory problems, endocrine disturbances and trauma have been suggested as possible etiological factors.

7-Condylar hypoplasia:

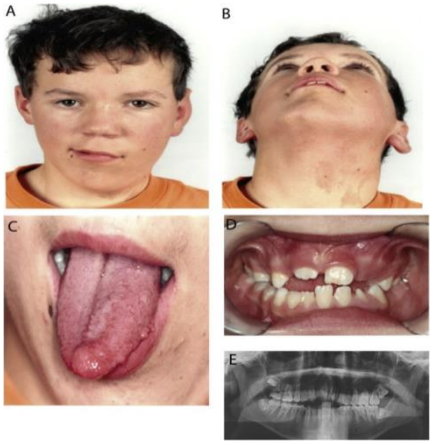
Congenital: - associated with mandibulofacial dysostosis and hemifacial macrosomia.

Acquired: - result from disturbance of growth center of developing condyle secondary to trauma, radiation or rheumatoid arthritis.



8-Bifid condyle-: Double-headed mandibular condyle of uncertain cause.Anteroposterior bifid condyle may be traumatic in origin during childhood . Mediolateral bifid condyle may result from abnormal muscle attachment.

9 -Hemifacial hypertrophy: Significant unilateral enlargement of face as a result of an increased neurovascular supply to affected side of face. Unilateral enlargement of the facial tissues, bones and teeth is usually present resulting in asymmetry of face with malocclusion and deviation of affected side to unaffected side of face.

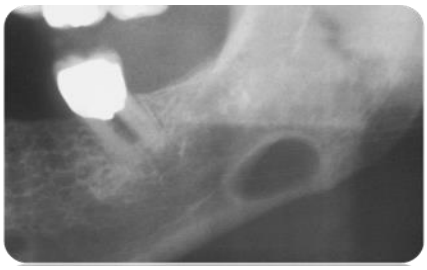


10-Hemifacial atrophy- : Uncommon poorly understood degenerative condition, characterized by:

1-Atrophic changes affecting one side of the face.

2- -Mouth and nose are deviated toward the defective side.

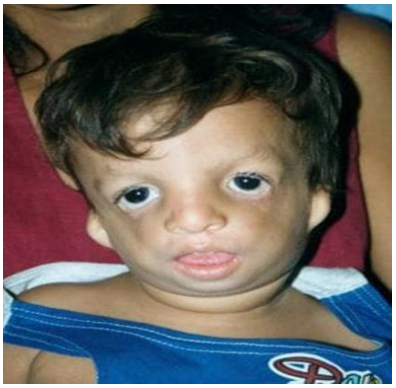
3- Covering skin often exhibit dark pigmentation.



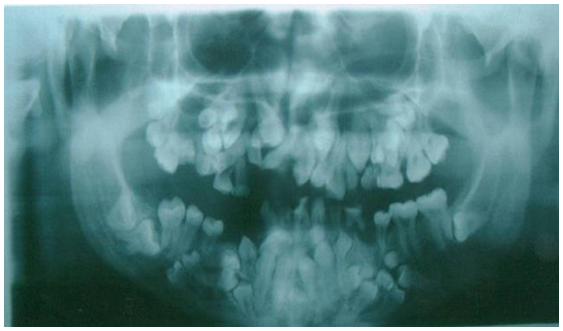
***11- STAFNE DEFECT*:** Stafne described a series of asymptomatic radiolucent lesions located near the angle of the mandible. The classic Stafne defect presents as an asymptomatic radiolucency below the mandibular canal in the posterior mandible, between the molar teeth and the angle of the mandible the lesion is typically well circumscribed and has a sclerotic border. Sometimes the defect may interrupt the continuity of the inferior border of the mandible, with a palpable notch observed clinically in this area. Most Stafine defects are unilateral although bilateral cases may be seen. Although the defect is believed to be developmental in nature, it does not appear to be present from birth. Most cases have been reported in middle-aged and older adults.

12- Mandibular Dysostosis (Treacher-Collins syndrome): Autosomal dominant disorder characterized by- :

1- Hypoplastic zygoma ,resulting in narrow face with depressed check and downward slanting of palpubral fissures.
2- Underdeveloped mandible with retruded chin and cleft palate may be seen.




13-Cleidocranial Dysplasia or Dysostosis: Rare familial disorder characterized by defective formation of clavicles, delayed closure of fontanelles and sometimes retrusion of the maxilla . There are Partial or complete absence of clavicles allows patient to bring the shoulders together in front of chest. One of few recognizable causes of delayed eruption of permanent dentition .Many permanent teeth may remain embedded in jaw and frequently become enveloped in dentigerous cysts. Supernumerary teeth may be seen radiographically.

Oral pathology

Lec. 7

Inflammatory diseases of the bone

Inflammatory diseases of bone can be divided into three broad but overlapping categories depending largely on the extent on involvement of the bone

1-Osteitis: - this term is used to describe a localized inflammation of bone with no progression through the marrow spaces. Particularly that associated with infected sockets following removal of teeth, (dry socket).

2-Osteomyelitis: - extensive inflammation of the interior of the bone involving, and typically spreading through the marrow spaces.

3-Periostitis: - inflammation of the periosteal spaces of the bone and may not be associated with osteomyelitis.

I- Alveolar osteitis (Dry socket ; fibrinolytic alveolitis)

The most frequent painful complication of extraction. After extraction of a tooth, a blood clot is formed at the site, with eventual organization of the clot by granulation tissue, gradual replacement by coarse fibrillar bone, and, finally, replacement by mature bone. Destruction of the initial clot prevents appropriate healing and causes clinical syndrome known as alveolar osteitis. Extensive investigations have shown that the clot is lost secondary to transformation of plasminogen to plasmin, with subsequent lysis of fibrin and formation of kinins (fibrinolytic alveolitis): these are potent pain mediators. Local trauma, estrogens, and bacterial pyrogens are known to stimulate fibrinolysins.

Causes:

- Traumatic extractions (unexperienced surgeons)
- Presurgical infections
-Oral contraceptive use
- Inadequate irrigation at surgery

-Use of tobacco products.

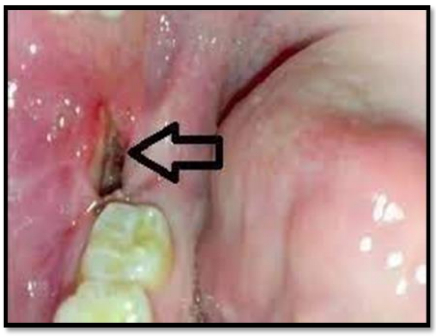
-Radiotherapy.

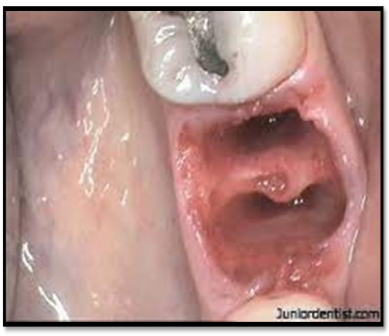
-Osteosclerotic disease: Paget's disease, cementoosseous dysplasia.

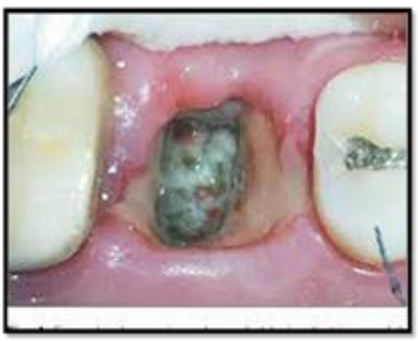
-Not follow the instruction.

Clinical Features: The frequency of alveolar osteitis is higher in the mandible and the posterior areas. After oral contraceptive use is taken into account. They do not appear to be a significant sex predilection. The prevalence is between 1% and 3% of all extractions, but it increases to 25% to *30%* for impacted mandibular third molars. The frequency appears to be decreased when impacted teeth are prophylactically removed rather than for therapeutic reasons after development of chronic inflammation of pericoronal tissues.

The overall prevalence is highest between 20 and 40 years of age (when the majority of teeth are extracted. although the likelihood of developing alveolar osteitis appears greatest for extractions in the *40*- to 45-year-old age group. The affected extraction site is filled initially with a dirty gray clot that is lost and leaves a bare bony socket (dry socket). The detection of the bare socket may be hindered by partial retention of the clot or by overlying inflamed tissue that covers the site. The diagnosis is confirmed by probing of the socket, which reveals exposed and extremely sensitive bone. Typically, severe pain, foul odor, and (less frequently) swelling and lymphadenopathy develop 3 to 4 days after extraction of the tooth. The signs and symptoms may last from 10 to 40 days.







Treatment and Prognosis: On evaluation of the patient complaining of post extraction pain, a radiograph should be taken of the affected area to rule out the possibility of a retained root tip or a foreign body. All sutures should be removed. The socket is irrigated with warm saline, followed by thorough clinical inspection of the socket for any unexpected pathosis. Curettage of the socket is not recommended, because this typically increases the associated pain. Potent oral analgesics should be prescribed, and the patient should be given a plastic syringe with instructions to keep the socket clean via home irrigation with a chlorhexidine or saline solution. This irrigation should continue until debris no longer collects within the healing socket (usually 3 to 4 weeks).

II- Osteomyelitis

Is an acute or chronic inflammatory process in the medullary spaces or cortical surfaces of bone that extends away from the initial site of involvement. Osteomyelitis of the jaw was a common complication of dental sepsis before the advent of antibiotics, now it is a rare disease. Various clinical subtypes were recognized, leading to confusion in typing and classification, due to variation in the clinical and pathological features of osteomyelitis being acute, chronic, suppurative or sclerotic, this reflecting the balance between the nature and severity of the irritant, the host defense, local and systemic predisposing factors.

Predisposing factors:

1- Chronic systemic diseases, immunocompromised status, and disorders associated with decreased vascularity of bone.
2- Tobacco use, alcohol abuse and intravenous drug abuse.
3- Diabetus mellitus.
4- exanthematous fever and malaria
5- sickle cell anemia
6- malnutrition
7- malignancy
8- collagen vascular disease
9- AIDS

10- Radiation.

11- osteopetrosis, dysosteosclerosis, pagets disease, end-stage cemento-osseous dysplasia, may result in hypovascularized bone that is predisposed to necrosis and inflammation.

Types of Osteomyelitis

- **Suppurative osteomyelitis** (bacterial osteomyelitis)

Are caused by bacterial infections and result in an expanding lytic destruction of the involved bone, with suppuration and sequestra formation.

- **Diffuse sclerosing osteomyelitis**

An ill-defined group of idiopathic inflammatory disorders of bone that do not respond consistently to antibacterial medications and typically demonstrate ultimate sclerosis of bone without suppuration or sequestra formation.

- **Focal sclerosing osteomyelitis.**

A. Suppurative osteomyelitis:

Acute suppurative osteomyelitis the condition results when an acute inflammatory process spreads through the medullary spaces of the bone and insufficient time has passed for the body to react to the presence of the inflammatory infiltrate.

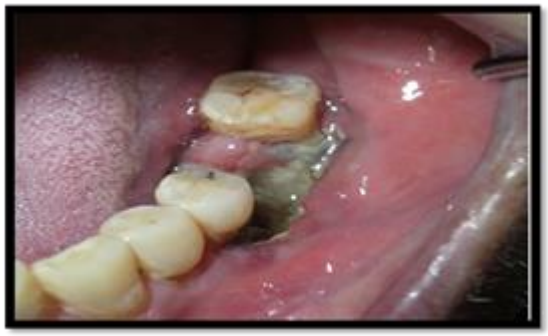
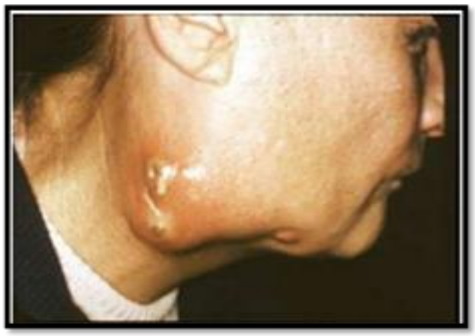
Chronic suppurative osteomyelitis: the condition result when the defensive response leads to the production of granulation tissue, which subsequently forms dense scar tissue in an attempt to wall of the infected area. The encircled dead space acts as a reservoir for bacteria, and antibiotics are difficult to reach the site. This pattern begins to evolve about one month after the spread of the initial acute infection and results in a smoldering process that is difficult to manage unless the problem is treated aggressively.

Clinical Features:

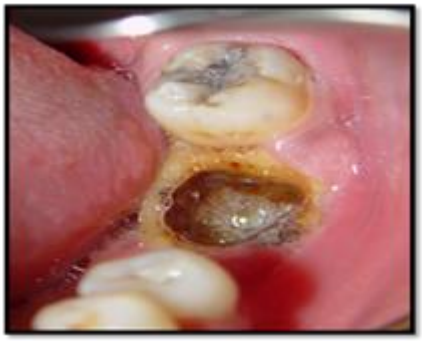
Acute osteomyelitis.

Patients with acute osteomyelitis have signs and symptoms of an acute inflammatory process that has typically been less than 1 month in duration, Fever, leukocytosis, lymphadenopathy,

significant sensitivity and soft tissue swelling of the affected area may be present. On occasion; Paresthesia of the lower lip occur, drainage or exfoliation of fragments of necrotic bone may be discovered. A fragment of necrotic bone that has separated from the adjacent vital bone is termed a sequestrum.

Sequestra often exhibit spontaneous exfoliation, on occasion; Fragments of necrotic bone may become surrounded by vital bone and the mass of encased nonvital bone is called an involucrum.



Chronic osteomyelitis.

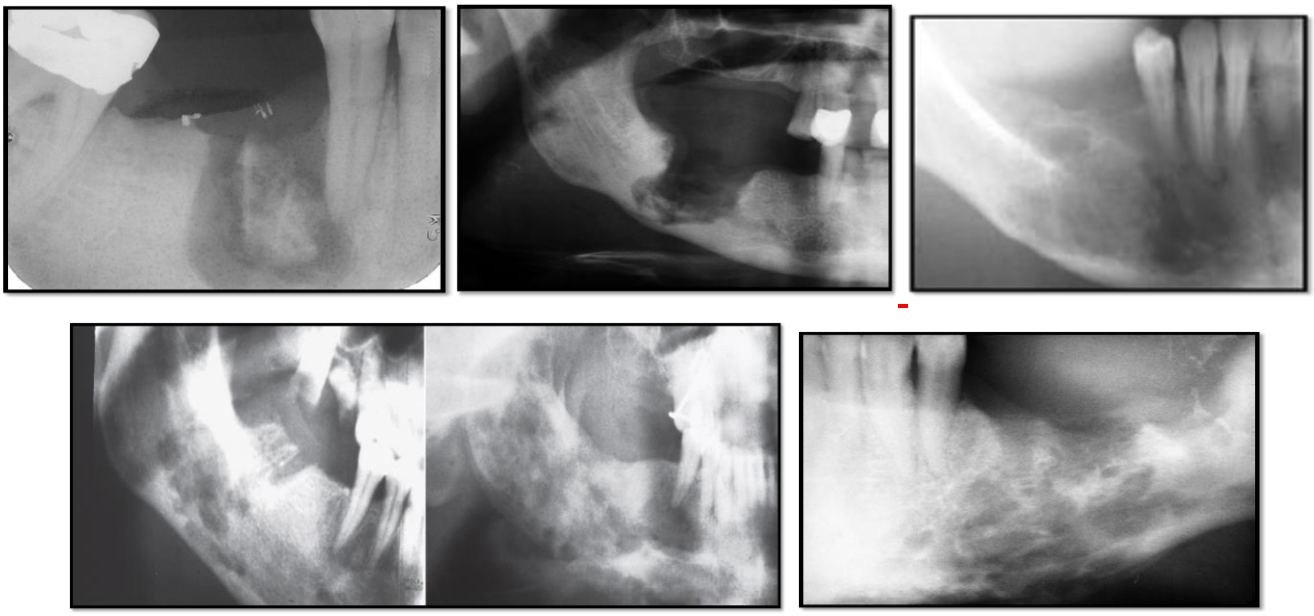
If acute osteomyelitis is not resolved expeditiously, the enhancement of chronic osteomyelitis occurs, or the process may arise primarily without a previous acute episode. There may be swelling, pain, sinus formation, purulent discharge, sequestrum formation, tooth loss, or pathologic fracture, Patients may experience acute exacerbation or periods of decreased pain associated with chronic smoldering progression.

Radiographically

Acute osteomyelitis: The radiographs may be unremarkable or may demonstrate an ill-defined radiolucency.

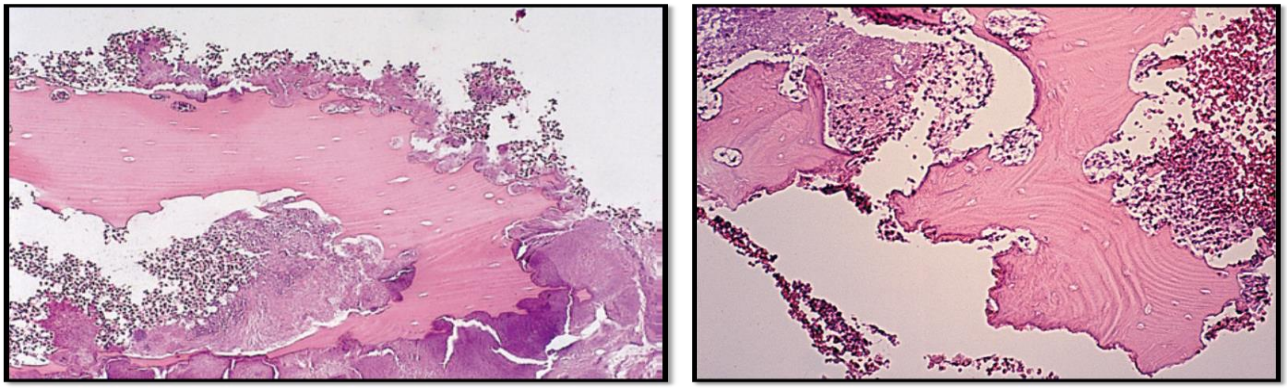
Chronic osteomyelitis: Radiographs reveal a patchy, ragged and ill-defined radiolucency that often contains central radiopaque sequestra, occasionally; the surrounding bone may exhibit an increased radiodensity, and the cortical surface can demonstrate significant osteogenic periosteal

hyperplasia. Sequestration that has involved an entire quadrant of the jaw has been reported in long-standing cases of chronic osteomyelitis.

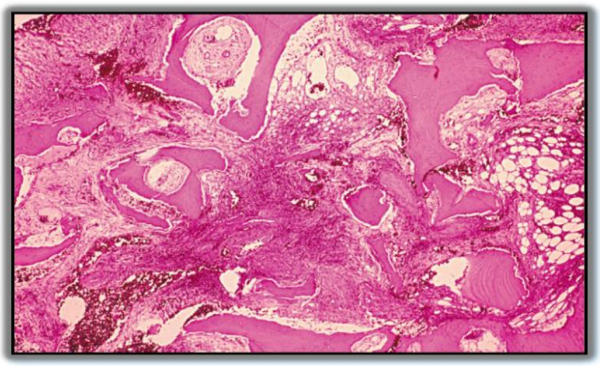


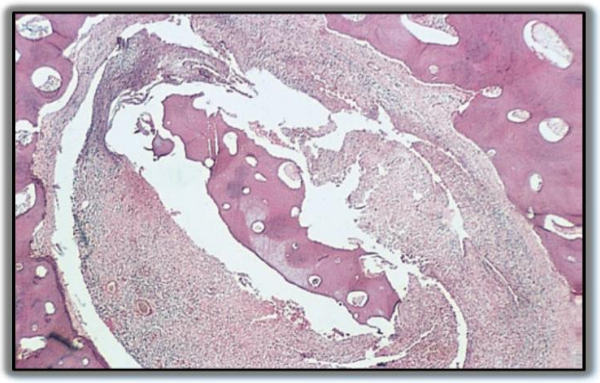
Histopathologic Features

Acute osteomyelitis.: Generation of biopsy material from patients with acute osteomyelitis is not common because of the predominantly liquid content and lack of a soft-tissue component. When submitted, the material consists predominantly of necrotic bone. The bone shows a loss of the osteocytes from their lacunae. Peripheral resorption and bacterial colonization. The periphery of the bone and the haversian canals contain necrotic debris and an acute inflammatory infiltrate consisting of polymorphonuclear leukocytes. The submitted material will be diagnosed as a sequestrum unless a good clinicopathologic correlation points to the appropriate diagnosis of acute osteomyelitis.



***Chronic osteomyelitis*.**: Biopsy material from patients with chronic osteomyelitis demonstrates a significant soft issue component that consists of chronically or sub acutely in flamed fibrous connective tissue filling the lntertrabecular areas of the bone. Scattered sequestra and pockets of abscess formation are common.





Treatment and Prognosis

Acute osteomyelitis.: If obvious abscess formation is note, the treatment of acute osteomyelitis consists of antibiotics and drainage. Microbiologic study of the infectious material typically reveals a polymicrobial infection of organisms normally present in the oral cavity. The antibiotics most frequently selected include penicillin, clindamycin,cephalexin,cefotaxime, tobramycin, and gentamicin. In most patients, a sufficient and appropriate antibiotic regimen aborts the infection and averts the need for surgical intervention. Several investigators have suggested that antibiotic therapy can bring about sterilization of the sequestra; therefore, these non vital bone fragments should be allowed to remain in place as scaffolding for the future development of new bone.

Chronic osteomyelitis: Chronic osteomyelitis is difficult to manage medically, presumably because pockets of dead bone and organisms are protected from antibiotics by the surrounding wall of fibrous connective tissue. Surgical intervention is mandatory. The antibiotics are similar to those used in the acute form but must be given intravenously in high doses. The extent of the surgical intervention depends on the spread of the process; removal of all infected material down to good bleeding bone is mandatory in all cases. For small lesions, curettage, removal of necrotic bone, and saucerization are sufficient.

In patients with more extensive osteomyelitis decortications or saucerization often is combined with transplantation of cancellous bone chips. In cases of persisting osteomyelitis, resection of the diseased bone followed by immediate reconstruction with an autologous graft is required. Weakened jawbones must be immobilized. The goal of surgery is removal of all infected tissue. Persistence of chronic osteomyelitis is typically due to incomplete removal of diseased tissue. Upon successful elimination of all infected material, resolution is expected. Adjunctive procedures (e.g. hyperbaric oxygen) are rarely necessary if thorough surgical curettage and sequestrectomy have been accomplished. Hyperbaric oxygen is primarily recommended for the rare patient who does not respond to standard therapy or for disease arising in hypovascularized bone (e.g., osteoradionecrosis, osteopetrosis, Paget's disease. cemento-osseous dysplasia).

B. DIFFUSE SClEROSING OSTEOMYELITIS

Diffuse sclerosing osteomyelitis is an ill-defined, highly controversial, evolving area of dental medicine. This diagnosis encompasses a group of presentations that are characterized by pain, inflammation, and varying degrees of gnathic periosteal hyperplasia, sclerosis, and lucency. On occasion, diffuse sclerosing osteomyelitis can be confused with secondarily inflamed intraosseous pathoses (florid cementosseous dysplasia) or Paget's disease of bone. In spite of the clinical and radiographic similarities, these processes can be separated from diffuse sclerosing osteomyelitis because of various clinical, radiographic and histopatholog differences the remaining pathoses can be grouped under three major categories:

1-Diffuse sclerosing oseomyelitis

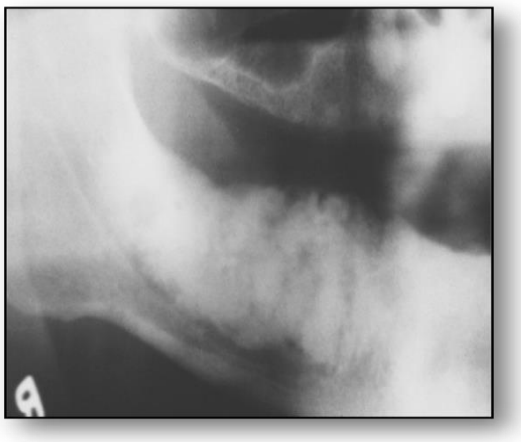
2-Primary chronic osteomylitis

3-Chronic tendoperiostitis

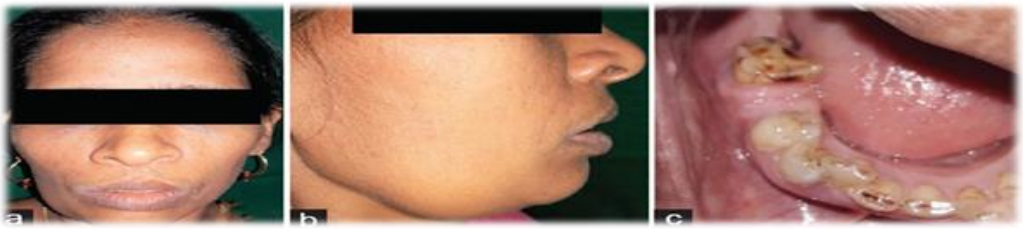
1-Diffuse sclerosing osteomyelitis: This term should be used only when an obvious infectious process directly is responsible for sclerosis of bone. In these cases, a chronic intraosseous bacterial infection creates a smoldering mass of chronically inflamed granulation tissue that incites sclerosis of the surrounding bone.

2-Primary chronic osteomyelitis: Often is confused with, but must be distinguished from, chronic suppurative osteomyelitis (Secondary chronic osteomyelitis). In contrast to suppurative osteomyelitis, an association with a bacterial infection is not obvious, and suppuration and sequestration characteristically are absent. A number of causes have been proposed, such as an altered immune response to an organism of low virulence, but no single theory has received widespread acceptance. In contrast to suppurative osteomyelitis, a primary infectious cause cannot be proven, because many studies have been unable to culture organisms and the condition does not respond to long-term antibiotic therapy.

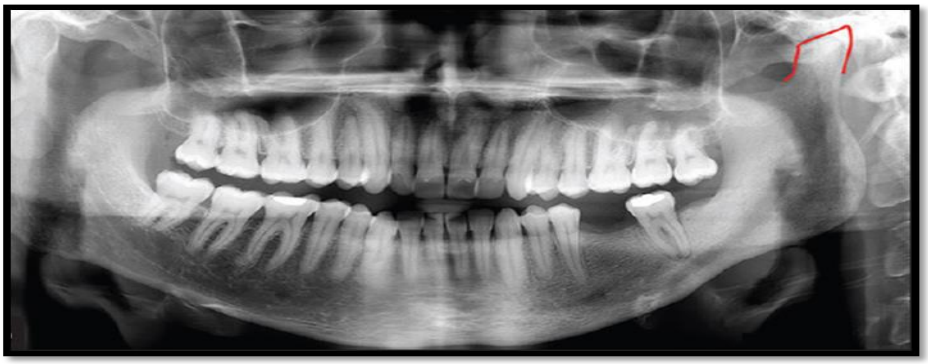
3.Chronic Tendoperiostitis: The clinical presentation is similar to that of primary chronic osteomyelitis; today many clinicians believe it represents a reactive alteration of bone that is initiated and exacerbated by chronic overuse of the masticatory muscles, predominantly the masseter and digastric. In a large series of patients, parafunctional muscle habits (e.g., bruxism, clenching, nail biting, co-contraction, and inability to relax jaw musculature) were known or became evident during follow-up. some investigators believe this disorder may represent a variation of primary chronic osteomyelitis, in which parafunctional muscle habits exacerbate the process but are not the initial cause.



Clinical Features: This condition may be seen in any age, in either sex, and in any race, but it tends to occur most often in middle-aged black women. The disease is typified by a protracted chronic course with acute exacerbations of pain, swelling, limited mouth opening and occasionally drainage. In addition to trismus in cases of chronic tendoperiostitis.



Radiographically: In cases of diffuse-sclerosing osteomyelitis, an increased radiodensity develops around sites of chronic infection (e.g., periodontitis, pericoronitis, and apical inflammatory disease). Typically, the altered area is restricted to a single site but may be multifocal or extend to fill an entire quadrant. In Primary Chronic Osteomyelitis, in the early stages of primary chronic osteomyelitis, radiographs tend to demonstrate a mixed pattern, with areas of radiolucent osteolysis intermingled with zones of sclerosis. Over time, the affected area becomes predominantly sclerotic. Overall, the predominant radiographic alteration of primary chronic osteomyelitis is medullary sclerosis. While in Chronic Tendoperiostitis, the sclerosis is limited to a single quadrant and centers on the anterior region of the mandibular angle and posterior portion of the mandibular Body.



Histopathology: Diffuse sclerosing osteomyelitis demonstrates sclerosis and remodeling of bone. The haversian canals are scattered widely and little marrow tissue can be found. Although the sclerosis occurs adjacent to areas of inflammation, the bone is not typically intermixed with a significant inflammatory soft tissue component. The same features seen on Primary Chronic Osteomyelitis and Chronic tendoperiostitis, where there are areas of sclerosis, numerous irregular trabeculae of pagetoid bone are present and demonstrate extensive evidence of remodeling with prominent reversal lines, osteoblastic rimming, and focal areas of osteoclastic activity.

Differential Diagnosis: Chronic sclerosing osteomyelitis shares many clinical, radiographic, and histological features with florid osseous dysplasia. The two should be separated, because the former is an inflammatory process and the latter a bony dysplastic process. Treatment and prognosis are therefore dissimilar. Florid osseous dysplasia appears to be an extensive form of

periapical cemental dysplasia and, unlike diffuse sclerosing osteomyelitis, may exhibit anterior periapical lesions and traumatic or simple bone cysts. Furthermore, florid osseous dysplasia is usually asymptomatic and appears as a fibroosseous lesion lacking an inflammatory cell infiltrate.

Treatment: The management of diffuse sclerosing osteomyelitis is problematic because of the relative avascular nature of the affected tissue and because of the large size of the lesion. Even with aggressive treatment, the course is protracted. If an etiologic factor such as periodontal disease or a carious tooth can be identified, it should be eliminated. Antibiotics are the mainstay of treatment and are especially helpful during painful exacerbations. Surgical removal of the diseased area is usually an inappropriate procedure because of the extent of the disease. However, decortication of the affected site has resulted in improvement in some cases. Low-dose corticosteroids have also been used with some success. Hyperbaric oxygen therapy may prove to be a valuable adjunct. Recently, treatment with pamidronate has shown promising results.

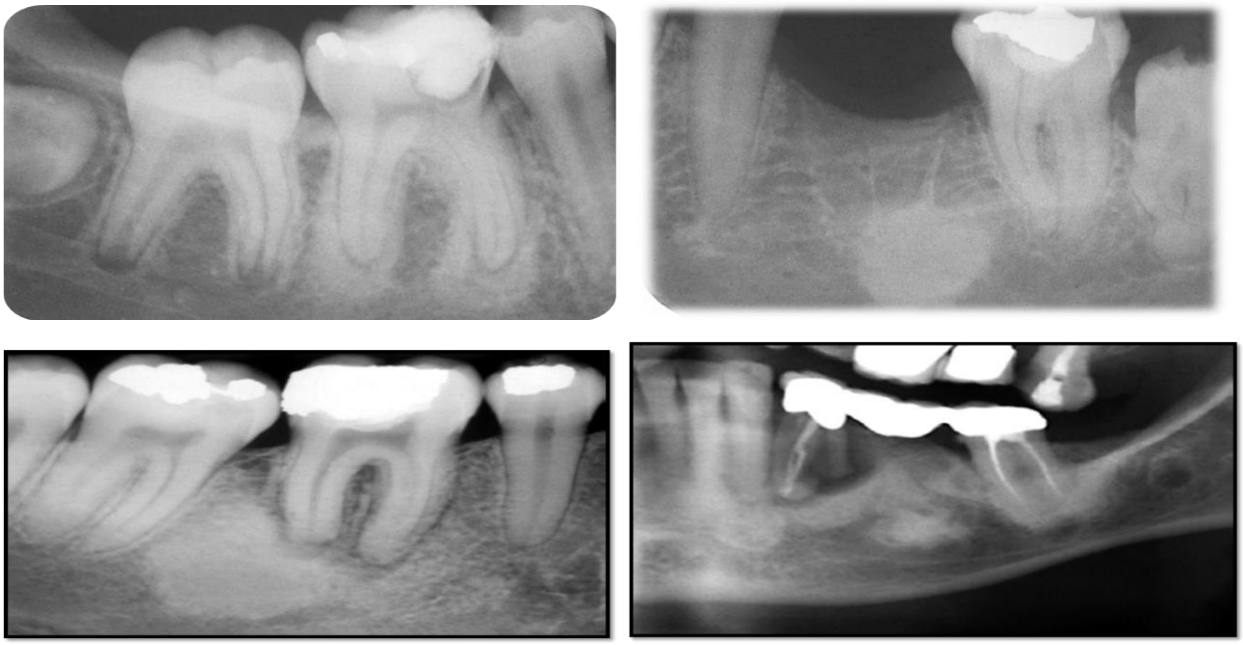
C. Focal Sclerosing Osteitis

Etiology

Focal sclerosing osteitis is a relatively common phenomenon that is believed to represent a focal bony reaction to a low-grade inflammatory stimulus. It is usually seen at the apex of a tooth with long-standing pulpitis. This lesion may occasionally be adjacent to a sound, unrestored tooth, suggesting that other etiologic factors such as malocclusion may be operative. Synonyms for focal sclerosing osteitis include focal sclerosing osteomyelitis, bony scar, condensing osteitis, and sclerotic bone. The term focal periapical osteopetrosis has also been used to describe idiopathic lesions associated with normal, caries-free teeth.

Clinical Features: Focal sclerosing osteitis may be found at any age but is typically discovered in young adults. Patients are usually asymptomatic, and most lesions are discovered on routine radiographic examination. A majority are found at the apices of mandibular first molars, with a minority associated with mandibular second molars and premolars. When teeth are extracted, these lesions remain behind indefinitely.

Radiographically: One of several patterns may be seen. The lesion may be uniformly opaque, it may have a peripheral lucency with an opaque center, it may have an opaque periphery with a lucent center, or it may be composed of confluent or lobulated opaque masses.



Histopathology: Microscopically, these lesions are masses of dense sclerotic bone; Connective tissue is scant, as are inflammatory cells.

Differential Diagnosis: Differential diagnosis should include periapical cemental dysplasia, osteoma, complex odontoma, cementoblastoma, osteoblastoma, and hypercementosis. In most cases, however, diagnosis can be made with confidence on the basis of historical and radiographic features.

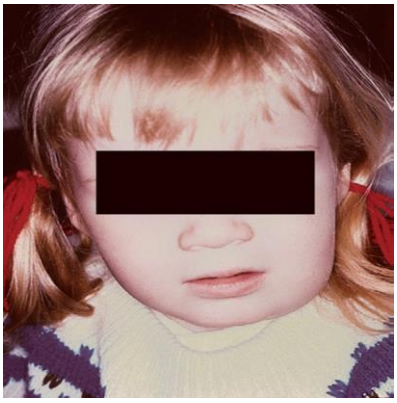
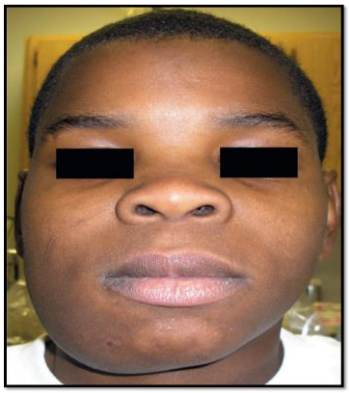
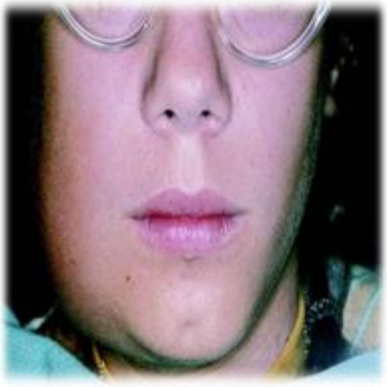
Treatment: Because it is believed to represent a physiologic bone reaction to a known stimulus, the lesion itself need not be removed. A biopsy might be contemplated to rule out more significant lesions that received serious consideration in the differential diagnosis. The inflamed pulp that stimulated the focal sclerosing osteomyelitis should be treated. The decision about whether the tooth should be restored, treated endodontically, or extracted should be made on a case-by-case basis according to findings.

III- Chronic Osteomyelitis with Proliferative Periostitis:(Garré's Osteomyelitis)

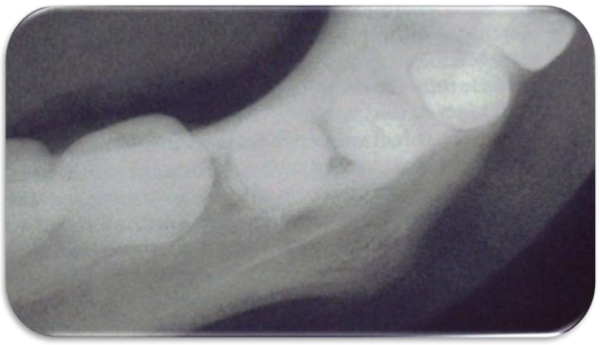
Etiology: Chronic osteomyelitis with proliferative periostitis, commonly known as Garré's osteomyelitis, is essentially a subtype of osteomyelitis that has a prominent periosteal inflammatory reaction as an additional component. It most often results from a periapical abscess of a mandibular molar tooth or an infection associated with tooth extraction or partially erupted molars. May due to Trauma, cysts, avitaminosis C, congenital syphilis, and neoplasms (such as, Ewing sarcoma, Langerhans cell histiocytosis, and osteogenic sarcoma).

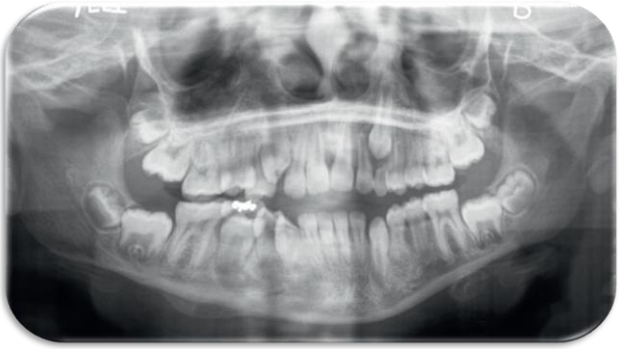
Clinical Features

This variety of osteomyelitis is uncommonly encountered. It has been described in the tibia, and in the head and neck area, it is seen in the mandible. It typically involves the posterior mandible and is usually unilateral. It is most common in children.Patients characteristically present with an asymptomatic bony, hard swelling with normal appearing overlying skin and mucosa. On occasion, slight tenderness may be noted. This presentation necessitates the differentiation of this process from benign mandibular neoplasms. Radiographs and a biopsy provide a definitive diagnosis.

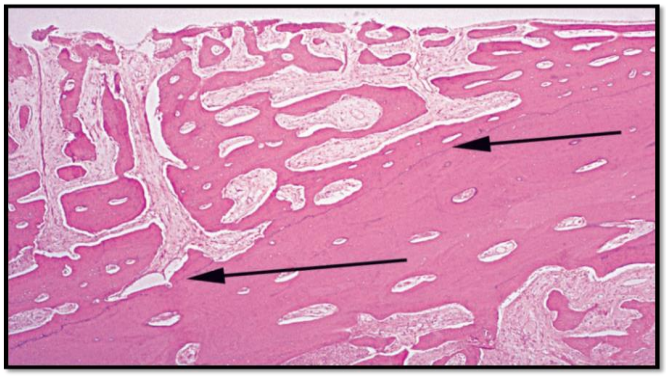




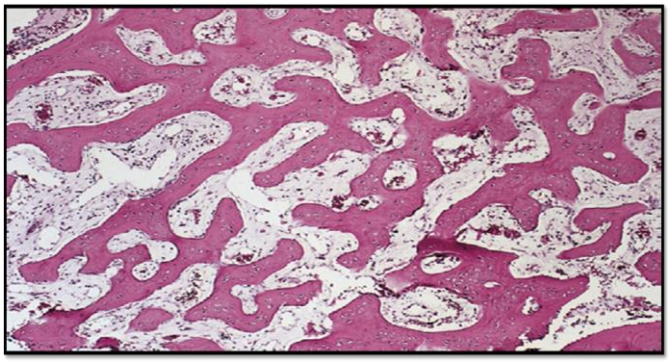
Radiographically: the lesion appears centrally as a mottled, predominantly lucent lesion in a pattern consistent with that of chronic osteomyelitis. The feature that provides the distinctive difference is the periosteal reaction. This, best viewed on an occlusal radiograph, appears as an expanded cortex, often with concentric or parallel opaque layers. Trabeculae perpendicular to the onion skin layers may also be apparent.



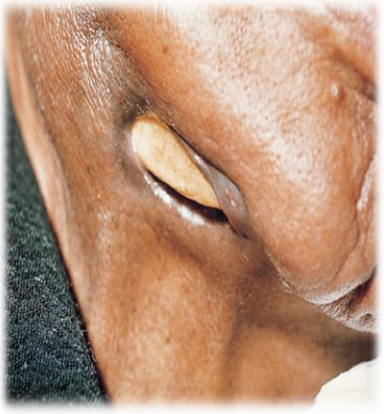


Histopathology: Reactive new bone typifies the subperiosteal cortical response. Perpendicular orientation of new trabeculae to redundant cortical bone is best seen under low magnification. Osteoblasts dominate in this area, and both osteoblasts and osteoclasts are seen centrally. Marrow spaces contain fibrous tissue with scattered lymphocytes and plasma cells. Inflammatory cells are often surprisingly scant, making microscopic differentiation from fibroosseous lesions a diagnostic challenge.



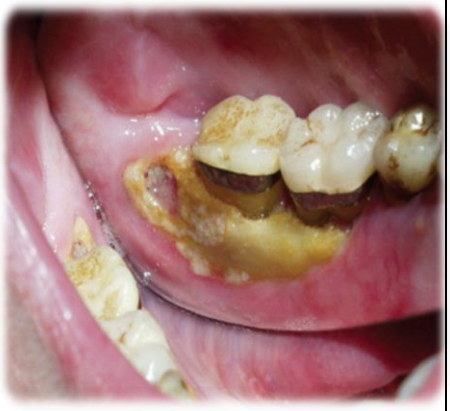


Treatment: Identification and removal of the offending agent are of primary importance in chronic osteomyelitis with proliferative periostitis. Removal of the involved tooth is usually required. Antibiotics are generally included early in this treatment. The mandible then undergoes gradual remodeling without additional surgical intervention.



IV- Osteoradionecrosis:

Osteoradionecrosis is one of the most serious complications of radiation to the head and neck but is seen less frequently today because of better treatment modalities and prevention. The current prevalence rate is less than 4%, whereas the frequency approached 15% less than 20 years ago. Although the risk is low, it increases dramatically if a local surgical procedure is performed within 21 days of therapy initiation or between 4 and 12 months after therapy. Radiation of bone results in permanent damage:' to the osteocytes and microvasculature system. The altered bone becomes hypoxic, hypovascular, and hypocellular. Osteoradionecrosis is the result of nonhealing, dead bone; infection is not necessarily present.



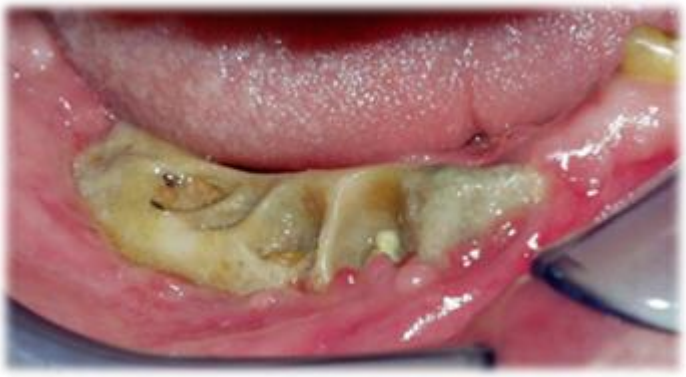
V- Bisphosphonate-Associated Osteonecrosis

A jaw necrosis may be seen as a complication of bisphosphonate therapy (e.g., pamidronate, and zoledronic acid) especially when administered long term and in high doses intravenously). This condition is now known to be induced by a variety of drugs that inhibit either osteoclast activity or angiogenesis. Bisphosphonates are currently used as part of the treatment regimen for patients with multiple myeloma, metastatic cancers to bone (e.g., breast or prostate cancer), Paget's disease, and osteoporosis because of their inhibitory effect on osteoclastic bone resorption. The drugs are concentrated in osteoclasts and bound into bone matrix by osteoblasts, where they remain active in bone for many years, being slowly released on bone turnover. The osteoclast inhibition also delays bone healing.

Clinical features: The majority of patients affected are elderly and have metastatic malignant disease because this is the main indication for the causative drugs. As with osteoradionecrosis, the mandible is more commonly affected than the maxilla. A striking presentation is painless exposed bone. Some patients may experience no acute symptoms or infection for prolonged periods.

Once infection is introduced, the condition develops into acute or chronic osteomyelitis depending on the virulence of the organism and resistance of the patient. The drugs cause reduced bone

turnover so that sequestra of necrotic bone separate very slowly and healing is inhibited. Later complications can include oroantral and cutaneous fistulas with suppuration.

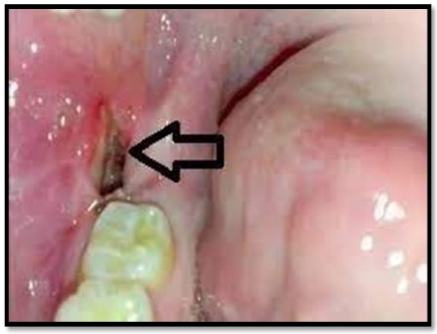
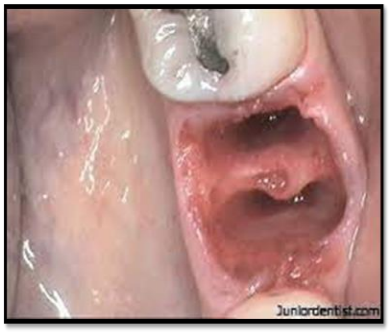


Management:

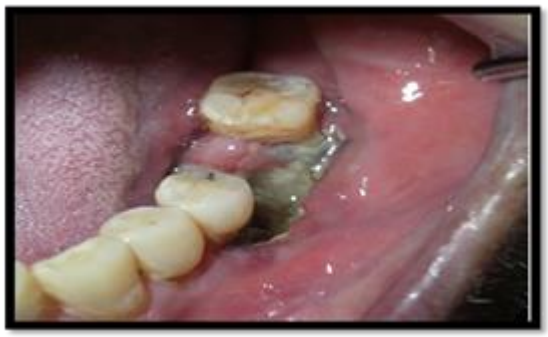
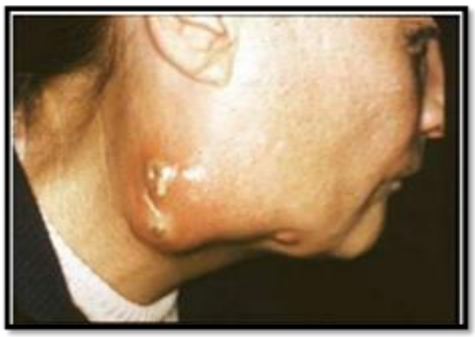
Prevention of infection is paramount. Potential problems should be eliminated before bisphosphonate treatment, infective foci eliminated and teeth of dubious prognosis removed. Some authorities also suggest removal of tori and sharp ridges if prone to denture trauma. Caries and periodontitis must be controlled. Ideally, all surgical dentistry should be avoided for as long as possible after drug administration. If extractions cannot be delayed, they are probably best followed by postoperative antibiotics and chlorhexidine rinses until the sockets are fully epithelialised. Unfortunately, these precautions are not always successful, and sometimes extraction of a tooth reveals an apparently already non-vital socket that does not bleed.

Lab.7

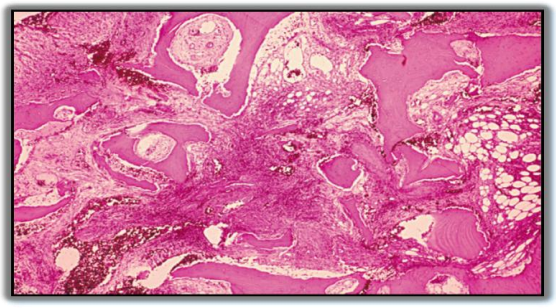
Inflammatory diseases of bone

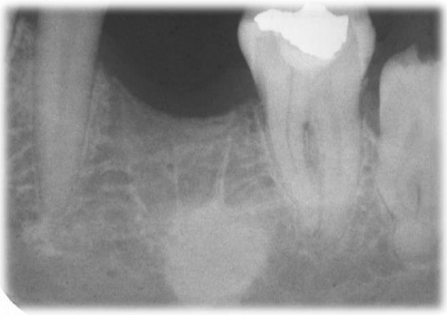
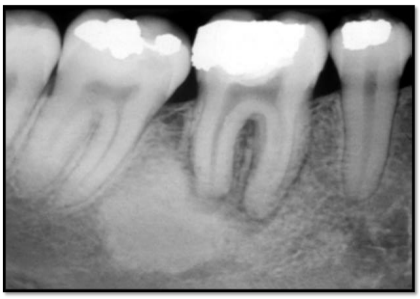
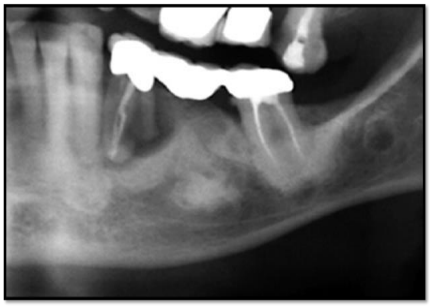
Alveolar ostities (Dry socket)

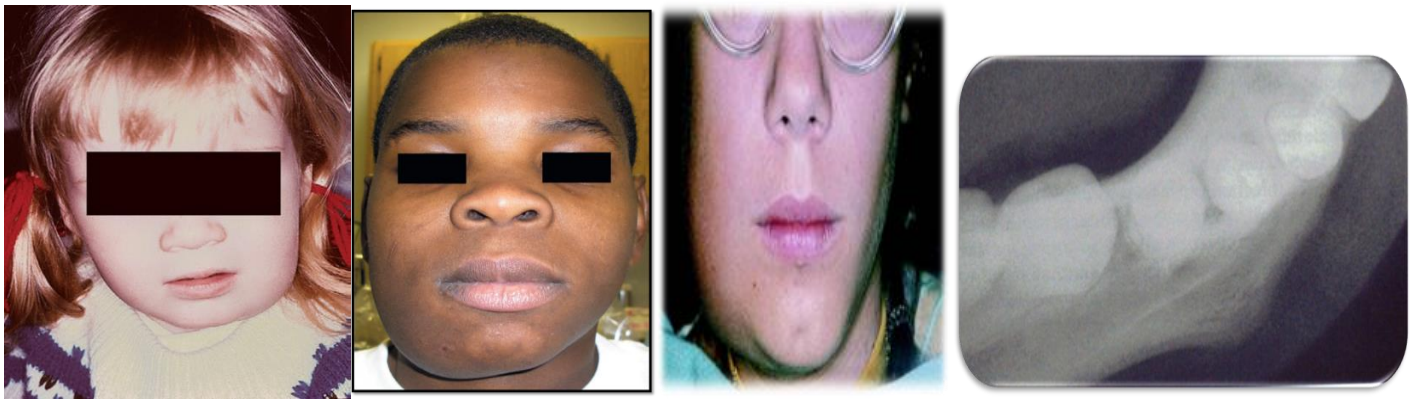
Acute osteomyelitis

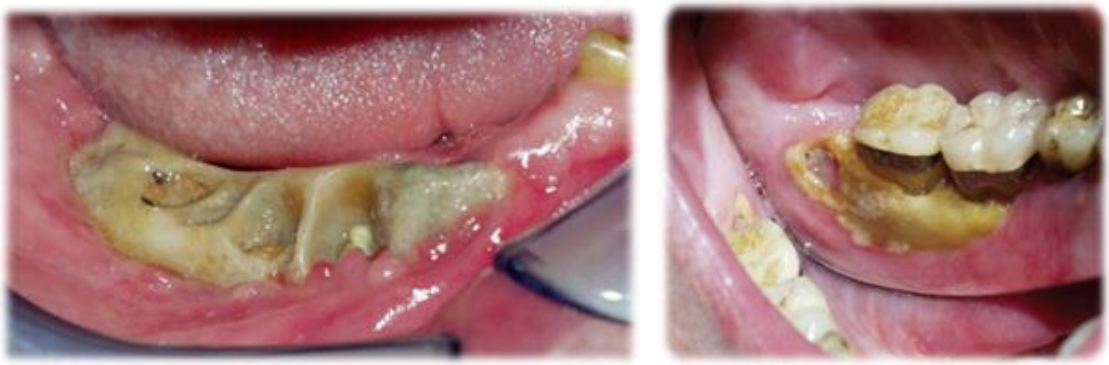
Chronic osteomyelitis

Focal sclerosing osteomyelitis



(Garré's Osteomyelitis)



Bisphosphonate-Associated Osteonecrosis

Oral Pathology

Lec.8

Fibro-osseous Lesions

A group of lesions affecting the *craniofacial skeleton* and characterized microscopically by *fibrous stroma* containing various combinations of bones and/or cementum-like material fall under the term ***benign fibro-osseous lesions***. They include a wide variety of lesions of *developmental*, *dysplastic*, and *neoplastic* origins with different clinical and radiographic presentation & behavior. Because of the histologic similarities between these diverse diseases, proper diagnosis requires ***clinical findings***, ***radiographic features***, ***surgical notes*** and ***histopathologic correlation*** to establish a specific diagnosis.

Commonly included among the fibro-osseous lesions of the jaw are the following:

1. Fibrous dysplasia.
2. Ossifying fibroma.
3. Juvenile Ossifying fibroma.
4. cemento-osseous dysplasia.

The conditions mentioned above have different clinical courses and outcomes, hence different treatment modalities ranging from non to surgical excision. For this reason, a specific diagnosis is critical.

Fibrous Dysplasia (FD):

Is a developmental skeletal tumor like condition characterized by replacement of normal bone by poorly organized & inadequately mineralized, immature, woven bone & fibrous connective tissue. The disease may affect a single bone (***monostotic***) or multiple bones (***polyostotic***). Polyostotic FD is less common, occurring in only 25% to 30% of cases. A few of these cases (≈3%) may be associated with skin pigmentation & endocrine abnormalities, a condition known as the ***McCune-Albright syndrome***, which is more common in females.

- **Etiology & Pathogenesis:**

The nature of this condition has not been firmly established. The name dysplasia was originally intended to indicate that the condition represented a dysplastic growth resulting from deranged mesenchymal cell activity or a defect in the control of bone cell activity. Although FD has been

considered as a developmental tumor-like condition; genetic studies, however, has provided evidence that it may be better classified as a neoplastic process. FD is a sporadic condition that results from a postzygotic mutation in the **GNAS1** (guanine nucleotide binding protein, α-stimulating activity polypeptide 1) gene.

Clinically FD may manifest as a localized process, as a condition involving multiple bones, or as multiple bone lesions in conjunction with cutaneous & endocrine abnormalities depending on the point in time during fetal or postnatal life that the mutation of GNAS1 occurs.

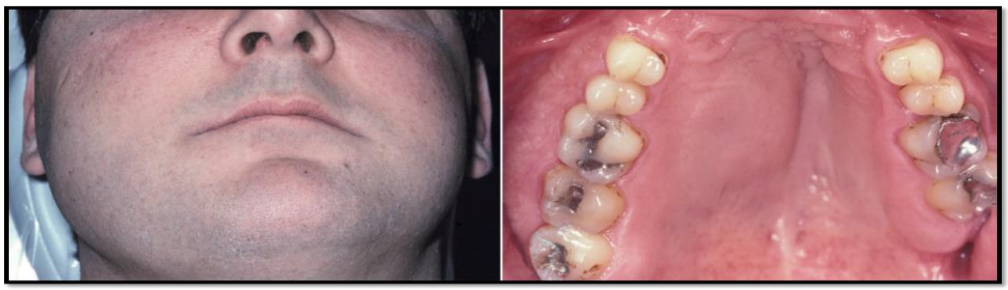
1. Mutation occurs in *early embryonic life* ⟶ mutation in one of undifferentiated stem cells ⟶ osteoblasts, melanocytes and endocrine cells ⟶ clinically presented as ***multiple bone lesions, cutaneous pigmentation& endocrine disturbances***.
2. Mutation occurring during *later stages of embryonic development of the skeletal system* ⟶ the mutated cells that participate in the skeleton formation ⟶ ***multiple bone involvements***.
3. Mutation during *postnatal life* ⟶mutated cells confines to one site ⟶ FD of a ***single bone***.

- **Clinical Features of FD:** The condition presents commonly an asymptomatic, slow enlargement of the involved bone. FD may involve a single bone or several bones concomitantly. Monostotic FD is the term used to describe the process in one bone. Polyostotic FD applies to cases in which more than one bone is involved.

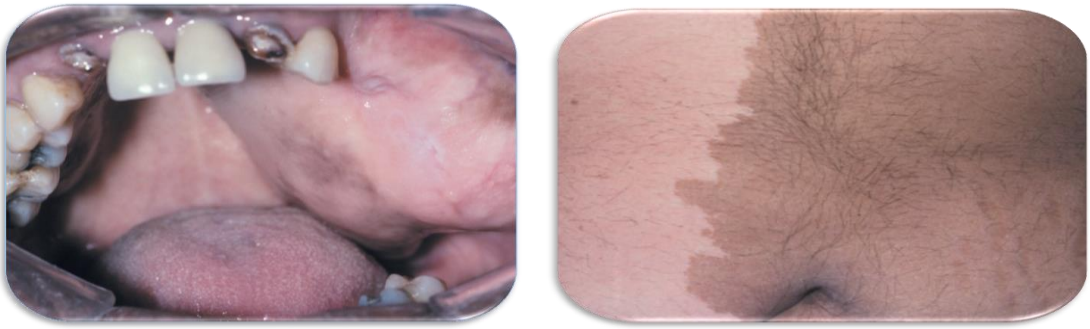
-**McCune-Albright syndrome** consists of polyostotic FD, cutaneous melanotic pigmentations (*café-au-lait macules*) and endocrine abnormalities. The most commonly reported endocrine disorder consists of precocious sexual development in girls, acromegaly, hyperthyroidism, hyperparathyroidism, and hyperprolactinemia.

-**Jaffe-Lichtenstein syndrome** is characterized by multiple bone lesions of FD & skin pigmentations.

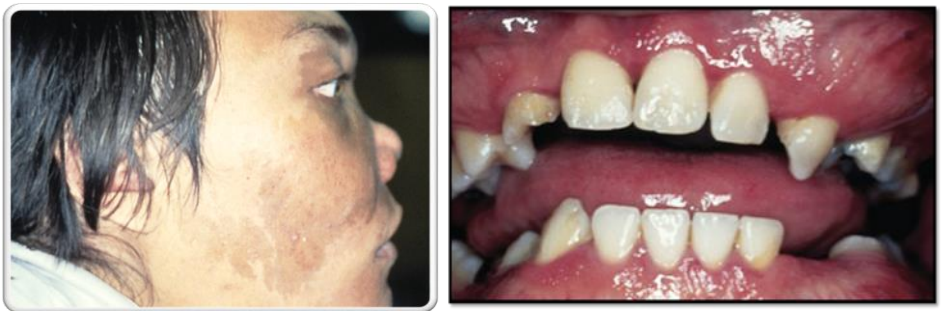
Monostotic FD is much more common than the polyostotic form, accounting for as many as 80% of cases. Jaw involvement is common in this form of disease. Other bones that are commonly affected are the ribs & femur. FD occurs more often in the maxilla than in the mandible. Maxillary lesions may extend to involve the maxillary sinus, zygoma, sphenoid bone and the floor of the orbit. This form of the disease, with the involvement of several adjacent bones, has been referred to as ***craniofacial FD***. The most common site of occurrence with mandibular involvement is the body portion.



Jaw involvement is usually slow & painless, typically a unilateral swelling. Teeth displacement may occur, with malocclusion and interference with tooth eruption, without tooth mobility.



The condition characteristically has its onset during the ***1st&2nddecade of life***. Monostotic FD usually exhibits an equal sex distribution & the polyostotic form tends to occur more commonly in females.



A B

Polyostotic fibrous dysplasia. (A) Clinical appearance of patient exhibiting disproportionate bone growth caused by multiple fibrous lesions of the craniofacial bones and cafau lait pigmentations. (B) Expansible lesions of the mandible and maxilla are evident in all quadrants.

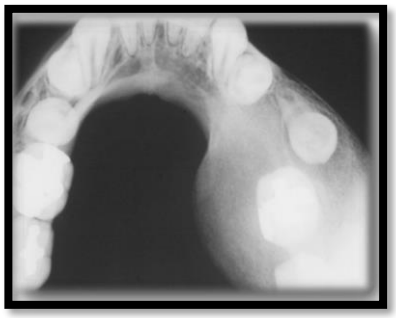
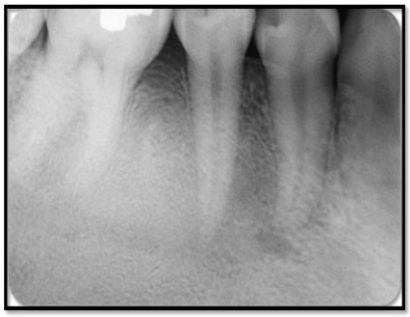
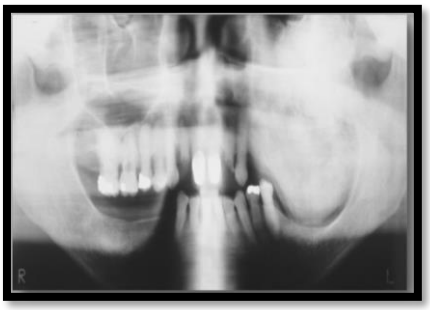
- **Radiographic Findings:**

FD has a variable radiographic appearance that ranges from a radiolucent lesion to a uniformly radiopaque mass. Classical presentation is ***ground-glass*** effect, which results from the superimposition of poorly calcified bone trabeculae arranged in a disorganized pattern

Radiographically, the lesions of FD are not well demarcated. The margins blend into the adjacent normal bone so that the limits of the lesion may be difficult to define.

- Involvement of the ***mandible*** results in:
  - Expansion of the lingual & buccal plates.
  - Bulging of the lower border.
  - Super displacement of the inferior alveolar canal.
  - Periapical (PA) radiographs: narrowing of the periodontal ligament (PDL) space with ill-defined Lamina dura.
- Involvement of the ***maxilla*** results in:
  - Displacement of the sinus floor superiorly.
  - Obliteration of the maxillary sinus.
  - Increased density of the bone of the skull.

*An important feature of FD is the poorly defined radiographic and clinical margins of the lesion that blend into the surrounding normal bone.

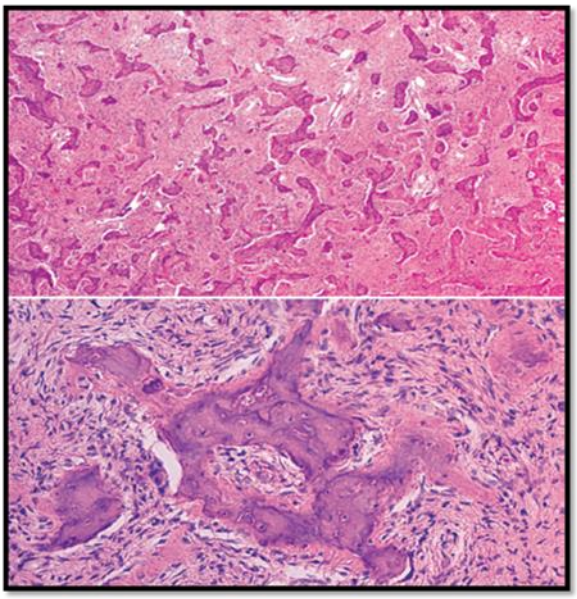




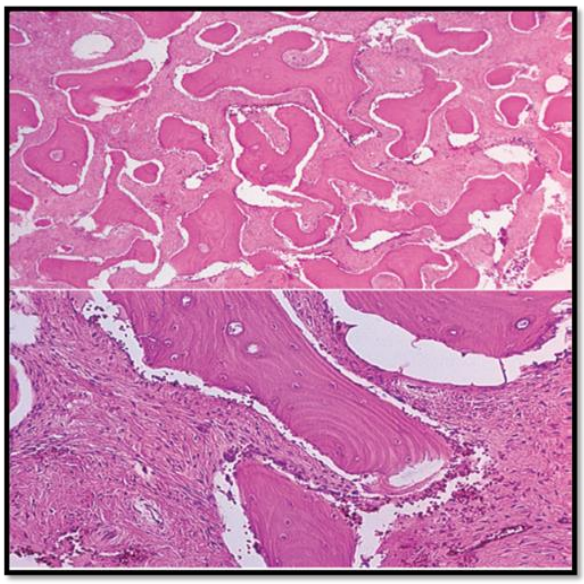
- **Lab Findings:** Serum calcium, Phosphorus & Alkaline phosphatase are ***normal*** in *monostotic FD*, but ***altered*** in *McCune-Albright syndrome*.

Histopathology: FD consists of a slight to moderate cellular fibrous connective tissue stroma that contains foci of irregularly shape

- d trabeculae of immature bone. The bone trabeculae assume irregular shapes linked to ***Chinese characters*** and they do not display any functional orientation, without osteoblastic activity at the bone trabeculae margins.

A, irregularly shaped trabeculae of woven bone in a fibrous stroma.
B, Medium-power view showing peripheral osteoid without osteoblastic rimming.

A-B 

C-D 

- Mature Fibrous Dysplasia. (C), This long-standing lesion shows separate, broad trabeculae of bone within fibrous connective tissue. (D), Note the lamellar maturation of the bone.

- **Treatment & Prognosis:** After a variable period of prepubertal growth, FD stabilizes, although a slow advance may be noted into adulthood.

-Small lesions → No treatment

-Large lesions → Cosmetic or functional deformity

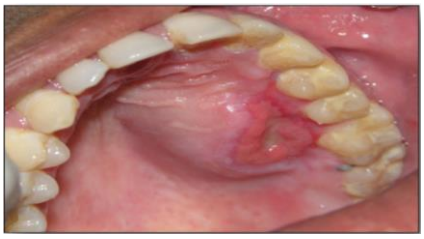
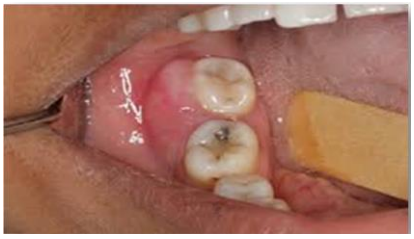
↓

Surgical recontouring

Malignant transformation is a rare complication of FD (less than 1%), usually in the polyostotic type. Many of them (osteosarcoma) were treated by radiation.

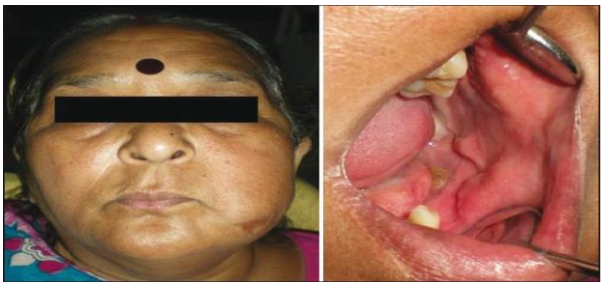
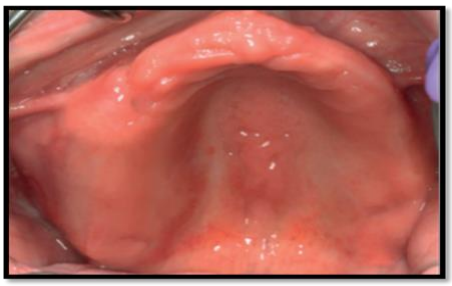
Ossifying Fibroma:

OF is a benign neoplasm of bone that has the potential for excessive growth, bone destruction & recurrence. It is composed of a fibrous connective tissue stroma in which new bone is formed. OF is a true neoplasm with a significant growth potential. It has been suggested that the origin is odontogenic or from periodontal ligament. Recently, mutations in a tumor suppressor gene were identified.

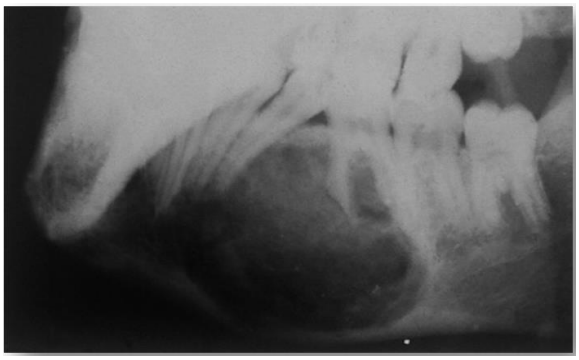
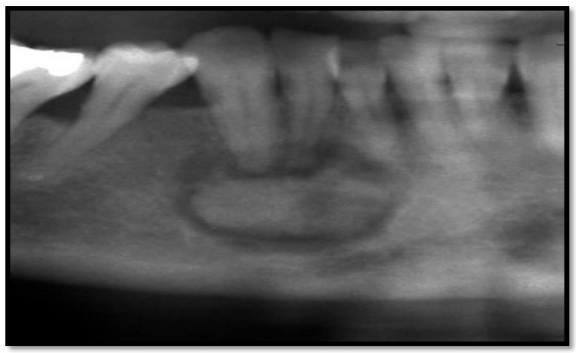
- **Clinical Features:**

The epidemiology of Ossifying fibroma is unclear because many previous diagnosed cases were confused with focal cemento-osseous dysplasia (COD). For that reason, what was thought to be OF, a common neoplasm, is now considered to be uncommon because most of the cases were in reality focal COD. tends to occur during the 3rd& 4th decades of life, in females more than in males. It is a slow growing asymptomatic & expansile lesion. OF may be seen in the jaw & craniofacial bones. Lesions in the jaw arise in the tooth-bearing region, mostly in the molar & premolar area. The tumor may cause expansion of the buccal and lingual cortical plates; however, perforation is very rare. OF is mostly a solitary lesion, although multiple lesions have been reported.

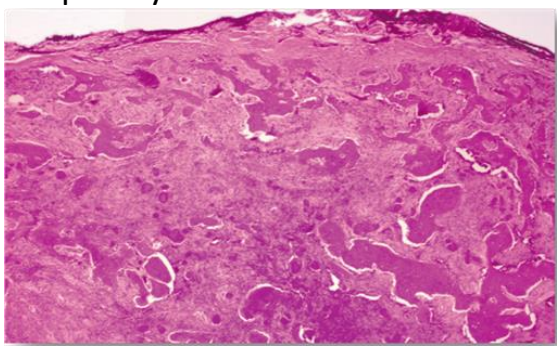



- **Radiographic Findings of COF:**

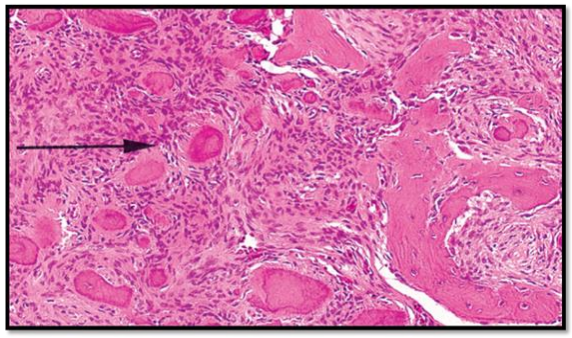
Well circumscribed, sharply demarcated border is the most common presenting radiographic feature, although OF may present as relatively lucent or opaque depending on the density of the calcification present. Also they may be unilocular or multilocular, mixed radiolucent-radiopaque image may be seen. The roots of the teeth present may be displaced & less commonly resorption is seen.

- **Histopathology:** Cementifying fibroma, cemento-ossifying fibroma (COF), ossifying fibroma are terms used to describe the same condition, since the origin is the stem cells in the periodontal ligament which may give rise to both cementoblasts & osteoblasts forming both cementum & bone which cannot be differentiated on H&E stain. The last term (COF) is the one used by WHO classification. COF is composed of fibrous connective tissue with well-differentiated spindle fibroblasts. Cellularity is uniform but may vary from one lesion to the next. Bone trabeculae or islands are evenly distributed throughout the fibrous stroma. The bone is immature & often surrounded by osteoblast (***osteoblast rimming***). Osteoblasts are infrequently seen.



- **(A)** well-circumscribed solid tumor mass. Trabeculae of bone and droplets of cementum-like material can be seen forming within a background of cellular fibrous connective tissue.



(B) High-power photomicrograph showing a mixture of woven bone and cementum-like material.

- **Treatment & Prognosis:** Surgical removal using ***curettage*** or ***enucleation***. The lesion can typically be separated easily from the surrounding bone. Recurrence is rare.

Juvenile Ossifying Fibroma:

Is a well circumscribed rapidly growing neoplasm lack the continuity with adjacent normal bone. Lesions are circumscribed radiolucencies in some cases contain central radio-opacities (Ground glass) opacification may be observed. Those are present within a sinus may appear

radiodense and create a clouding that could be confused with sinusitis. Two different neoplasm have been reported:

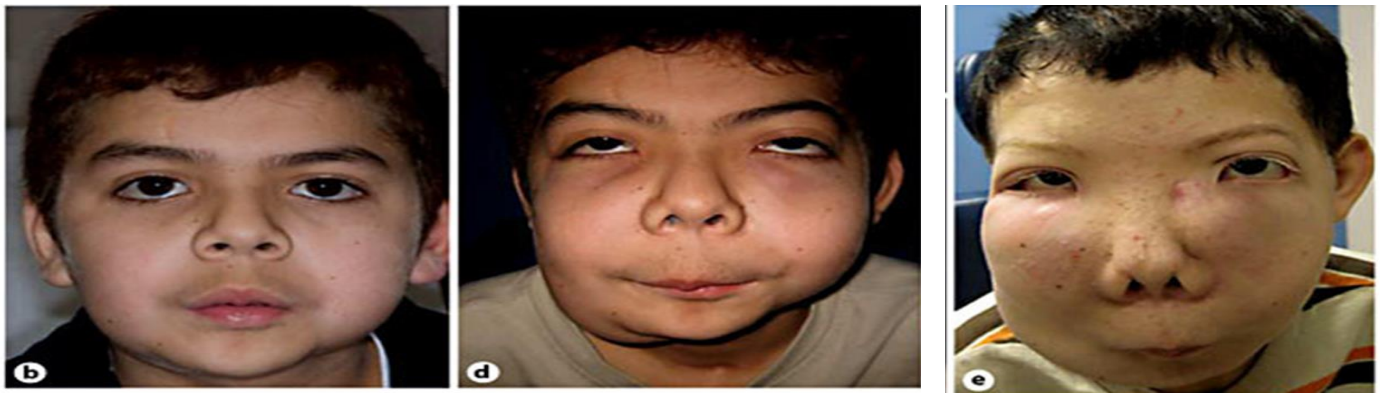
1- **Trabecular**

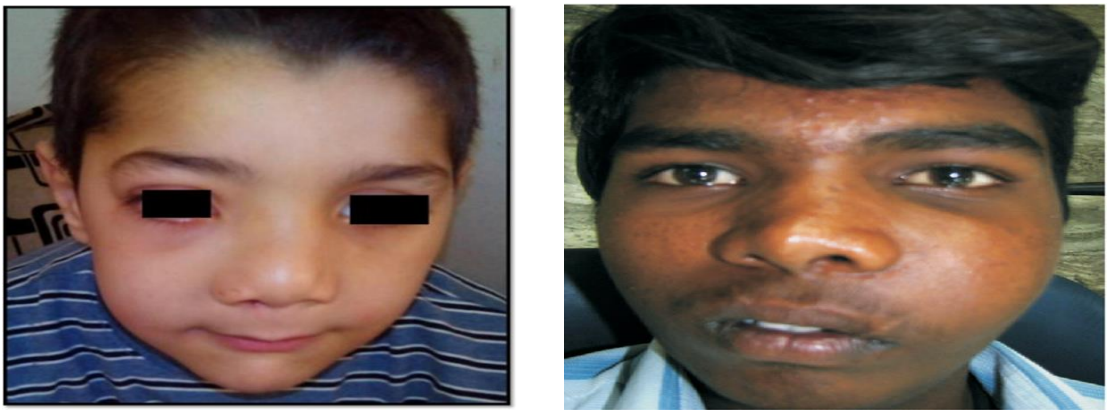
2- **Psammomatoid**.

The latter neoplasm occurs more than the trabecular type in a ratio of approximately 4:1

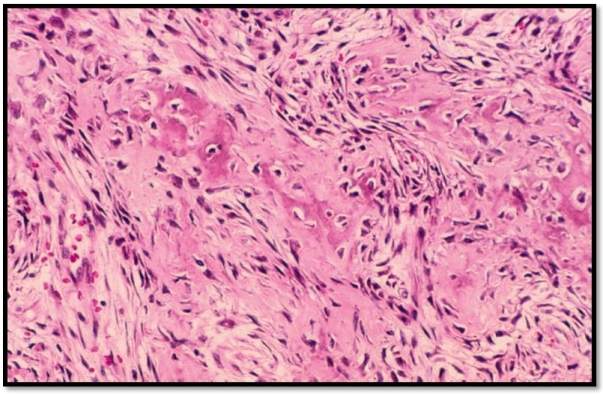
The trabecular variant arises primarily in the jaws, whereas the psammomatoid variant predominantly involves the paranasal sinuses and orbital region. In both variants, gnathic involvement favors the maxilla. Most often arise in children, adolescents, and young adults. The average age at diagnosis is somewhat younger for the trabecular variant (range from 8 1/2 to 12 years) than the psammomatoid variant (range from 16 to 33 years). Small lesions may be discovered incidentally during routine radiographic examination, whereas larger lesions tend to cause painless swelling and obvious facial enlargement. Pain and paresthesia are infrequent findings. Those are present within a sinus may appear radiodense and create a clouding that could be confused with sinusitis.

Lesions are circumscribed radiolucencies in some cases contain central radio-opacities (Ground glass) opacification may be observed.





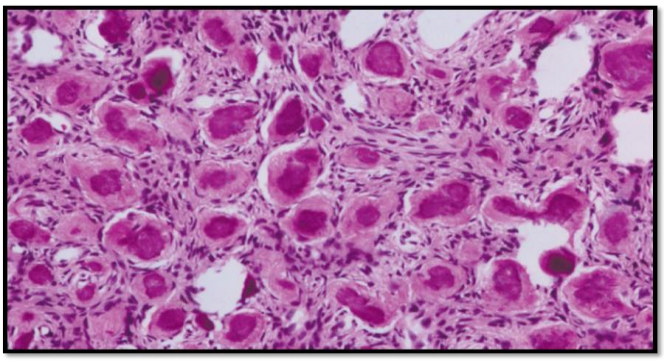
- **Histopathology:** Both patterns are none capsulated but well demarcated from the surrounding bone. Tumors consist of cellular fibrous connective tissue with variants areas of loose and other are so cellular, mitotic figures are found but rare, areas of hemorrhage and small clusters of multinucleated giant cells are usually seen. The trabecular type shows irregular strands of highly cellular osteoid encasing plump osteocytes. These strands are lined by plump osteoblast and in other areas by giant cells.



Trabecular Variant.

Trabeculae of cellular woven bone are present in a cellular fibrous stroma.

-In psammomatoid pattern concentric lamellated and spherical ossicles that have basophilic centers with peripheral eosinophilic osteoid rims.



Psammomatoid Variant. Cellular fibrous connective tissue containing spherical ossicles with basophilic centers and peripheral eosinophilic rims.

Treatment and Prognosis: For small lesions, complete local excision or thorough curettage appears adequate, while for large or aggressive lesions, wider resection may be required. Recurrence rates of 30% to 58% have been reported for juvenile ossifying fibromas.

Cemento-osseous Dysplasia (COD):

The most common fibro-osseous lesion encountered in clinical practice. These poorly understood diseases are non-neoplastic disturbances of growth and remodeling of bone and cementum, Represents a reactive or dysplastic process rather than a neoplastic one. Some investigators have

suggested that cemento-osseous dysplasia originates from the periodontal ligament. Others believe this condition represents a defect in extraligamentary bone remodeling that may be triggered by local injury or, possibly, an underlying hormonal imbalance.

COD includes:

- Periapical COD.
- Focal COD.
- Florid COD.

All the 3 disease processes have the same features, only distinguished on the basis of the extent of involvement of the affected portions of the jaw.

1. Periapical COD:

Represents a reactive or dysplastic process rather than a neoplastic one. It may represent an unusual response of periapical bone & cementum to some undetermined local factor.

- When not associated with a tooth apex ⟶ ***Focal COD***.

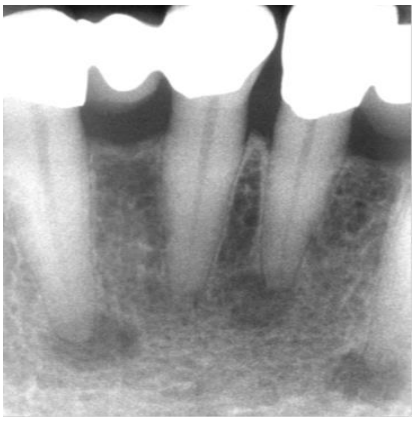
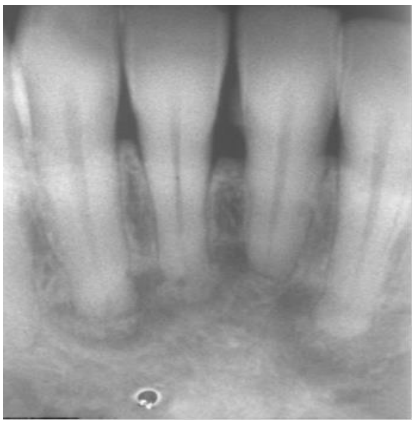
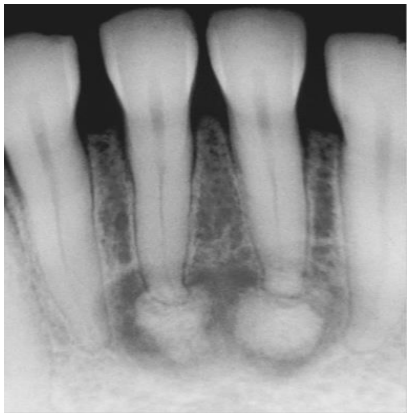
- **Clinical Features:**

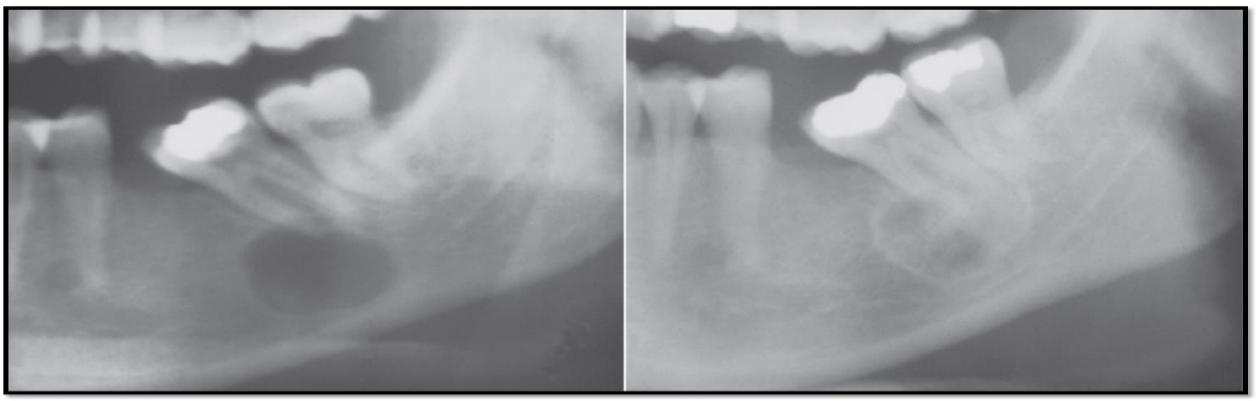
A common phenomenon, that occurs at the apex of vital teeth. A biopsy is unnecessary because the condition is usually diagnosed by clinical & radiographic features. Females are affected more than males. PACOD occurs in females at middle age (around 40 years) & rarely before the age 20. The mandible, especially the anterior periapical region, is far more commonly affected than other areas. More often, the apices of two or more teeth are affected.

- *To be differentiated from* ***Periapical granuloma*** ⟶ ***vitality test***.

Radiographically:

- The condition appears 1st as a periapical lucency that is continuous with the periodontal ligament space. (A)
- As the condition progresses, the lucent lesion develops into a mixed or mottled pattern because of bone repair. (B)
- The final stage appears as a solid, opaque mass that is surrounded by a thin, lucent ring (after months – years). (C)

A  B  C 



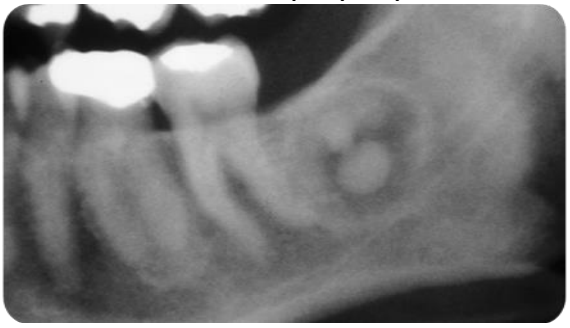
A

Focal Cemento-Osseous Dysplasia.

B

A) A radiolucent area involves the edentulous first molar area and the apical area of the second molar.

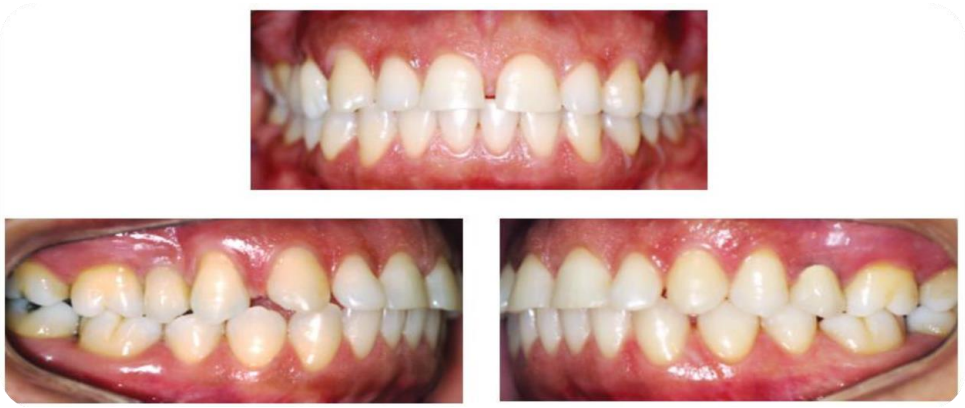
B) Radiograph of the same patient taken 9 years later showing a mixed radiolucent and radiopaque pattern.



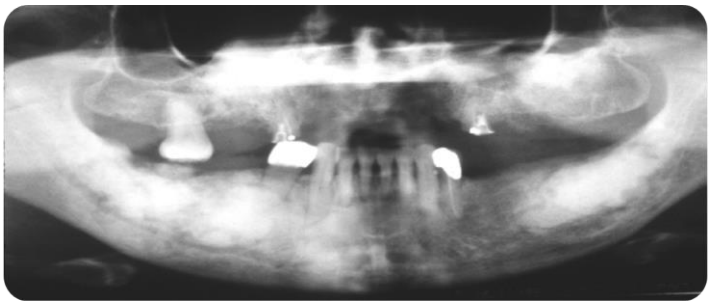
2-*Florid COD:*

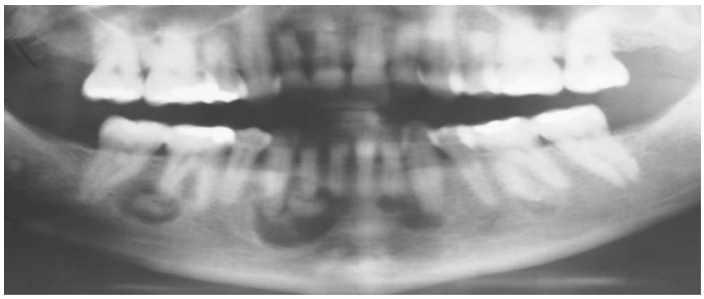
The FCOD is an exuberant[1] form of PACOD. FCOD represents the severe end of the spectrum of this unusual process. The patient is asymptomatic except when complication of

osteomyelitis occurs. Females are more commonly affected (**black women**); between 25-60 years of age. The condition is typically bilateral & may affect all four quadrants.



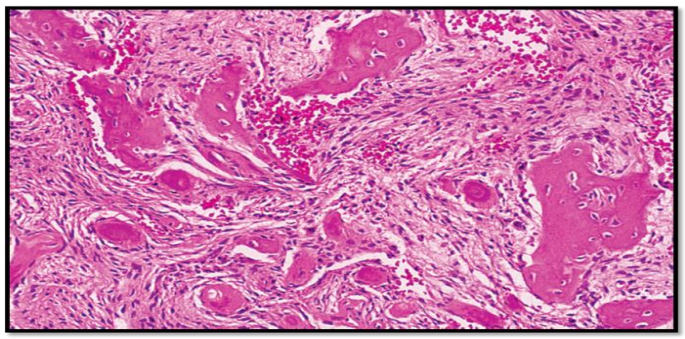
Radiographically, FCOD appears as diffuse radiopaque masses throughout the alveolar segment of the jaw. A ***ground-glass*** or cyst-like appearance may also be seen.



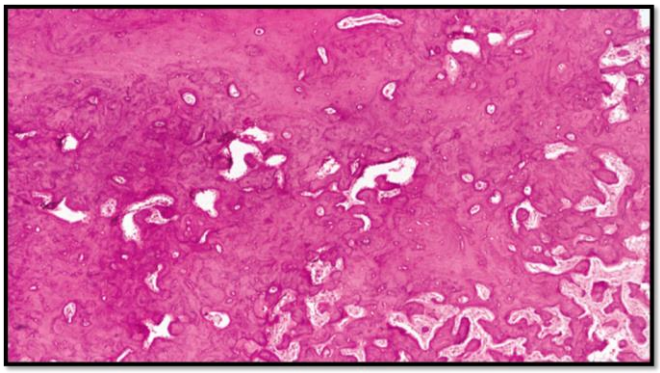


• Histopathology of COD:

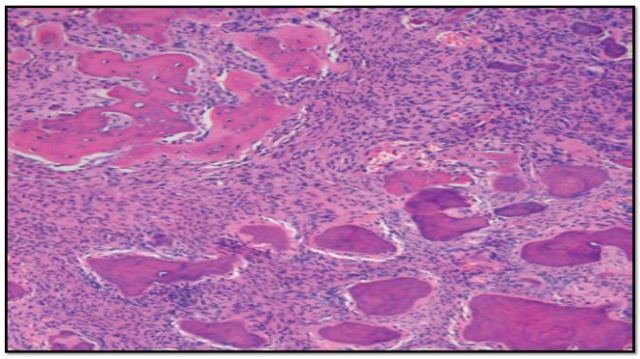
All 3 types show a mixture of benign fibrous tissue, bone, and cementum. The calcified tissue is arranged in trabeculae, spicules or larger irregular masses. Numerous small blood vessels & free hemorrhage is typically noted throughout the lesion. The proportion of the mesenchymal component to the mineralized material is variable depending on the stage and from area to area in the same lesion.



Spicules of bone and cementum-like hard tissue within moderately cellular fibrous connective tissue. Note the hemorrhage around the bony trabeculae.



Late-stage lesion showing a sclerotic mass of cemento-osseous material.



Cemento-osseous dysplasia. A very cellular fibrous tissue containing trabeculae of woven and sclerotic bone and islands of dense basophilic cementum-like bone.

Treatment:

-No treatment.

-For the asymptomatic patient, the best management consists of regular recall examinations with prophylaxis and oral hygiene reinforcement to control periodontal disease and prevent tooth loss

FCOD → sclerotic stage → decrease of vascularity → prone to necrosis & osteomyelitis → instruction for good oral hygiene to prevent infection.

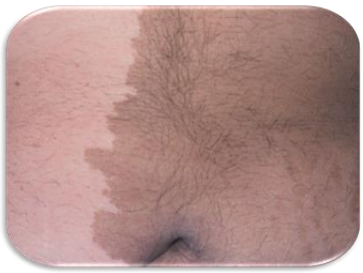
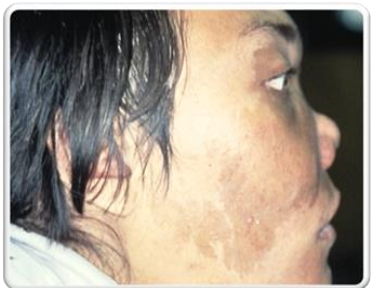
-Management of the symptomatic patient who has developed secondary osteomyelitis is more difficult.

↓

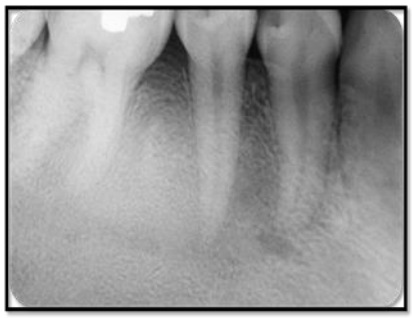
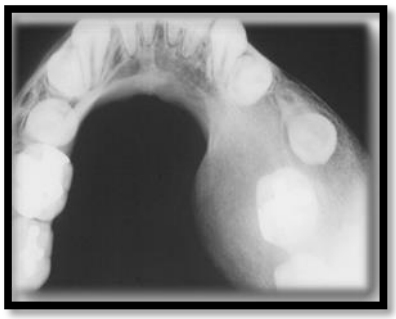
Antibiotics + Saucerization

Lab.8

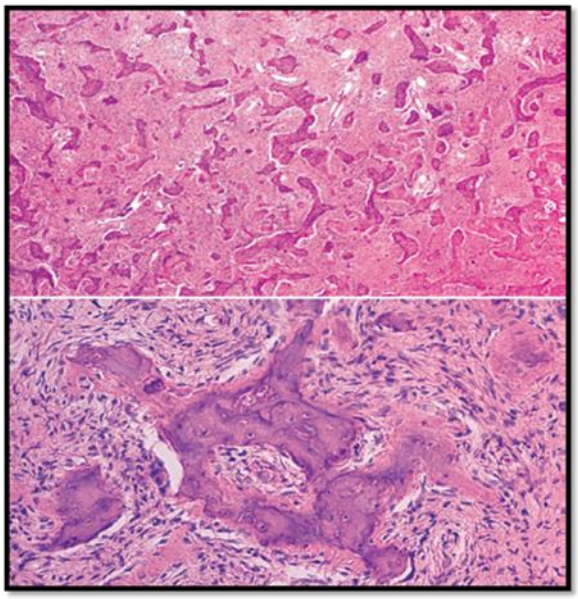
Fibro-osseous dysplasia

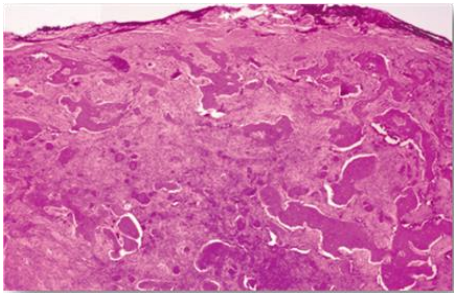
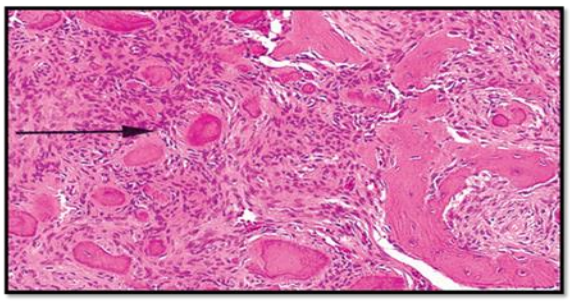
Fibrous dysplasia

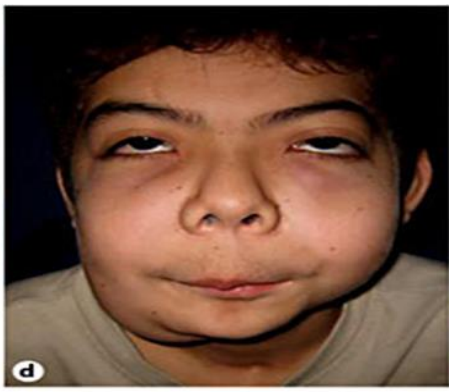
fibrous dysplasia



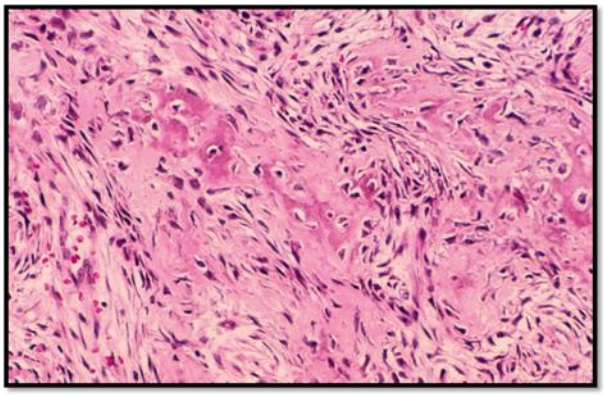
fibrous dysplasia

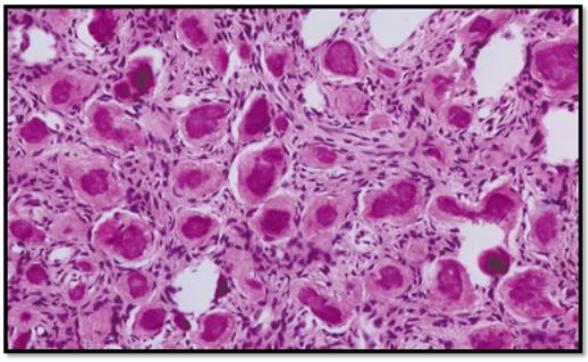
Ossifying fibroma

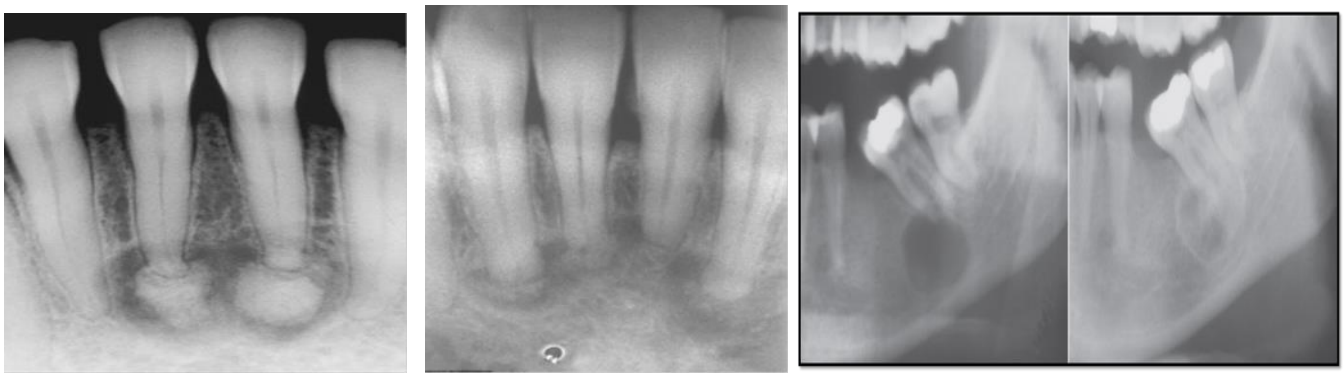
Juvenile ossifying fibroma



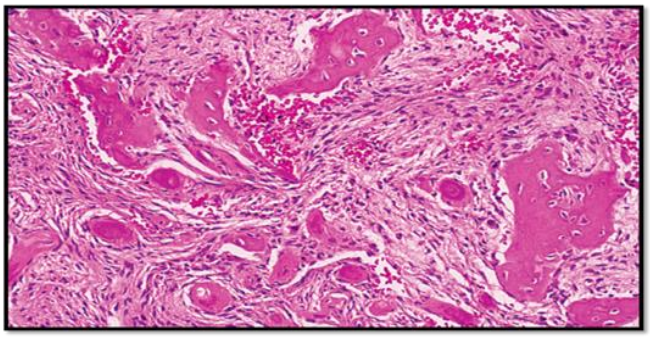
Trabecular variant (juvenile ossifying fibroma)



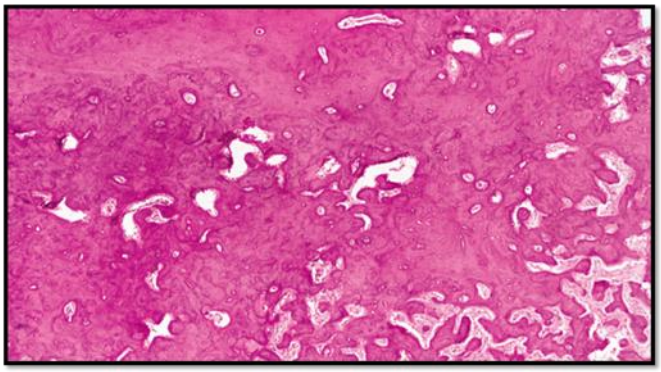
Psammomatoid variant (juvenile ossifying fibroma_



Focal cemento-osseous dysplasia



Early stage of cemento-osseous dysplasia

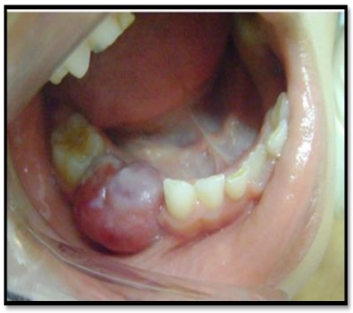


Late stage of cemento-osseous dysplasia

Oral pathology

Lec.9

Giant cell lesions



Giant cell lesions of the jaw include: -

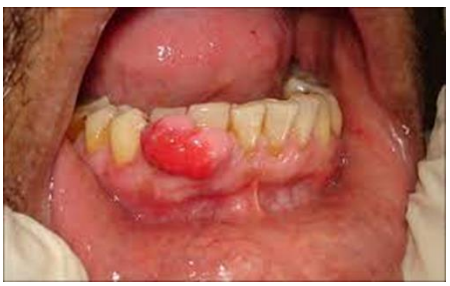
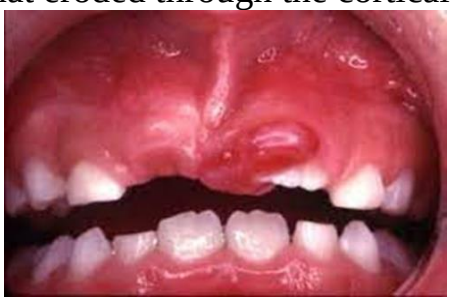
1-Giant cell granuloma (central-peripheral)
2- Cherubism
3- Aneurysmal bone cyst
4-Brown tumor of hyperparathyroidism

Peripheral giant cell granuloma(giant cell epulis):

The peripheral giant cell granuloma is a relatively common tumor like growth of the oral cavity. It probably does not represent a true neoplasm but rather is a reactive lesion caused by local irritation or trauma. In the past it often was called a peripheral giant cell reparative granuloma, but any reparative nature appears doubtful. Some investigators believe that the giant cells show immunohistochemical features of osteoclasts, whereas other authors have suggested that the lesion is formed by cells from the mononuclear phagocyte system. The peripheral giant cell granuloma bears a close microscopic resemblance to the central giant cell granuloma, and some pathologists believe that it may represent a soft tissue counterpart of this central bony lesion.

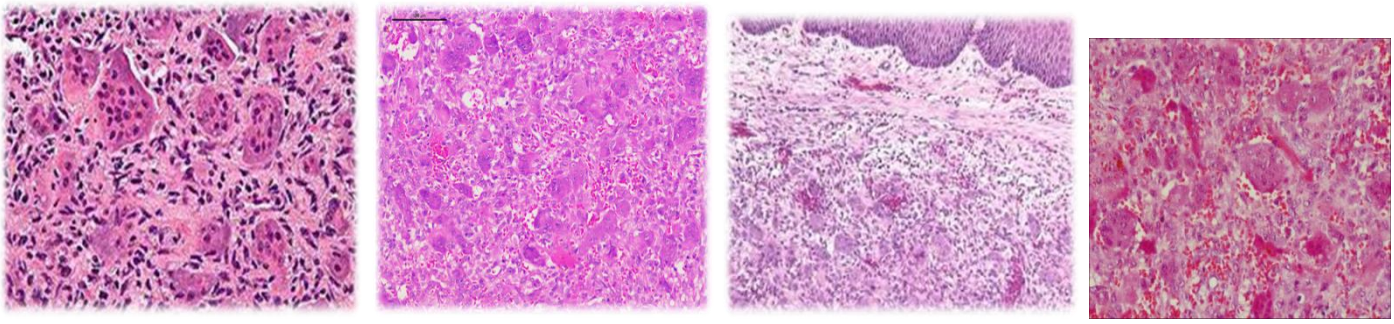
Clinical and Radiographic Features:

The peripheral giant cell granuloma occurs exclusively on the gingiva or edentulous alveolar ridge, presenting as a red or reddishblue nodular mass. Most lesions are smaller than 2cm in diameter although larger ones are seen occasionally. The lesion can be sessile or pedunculated and mayor may not be ulcerated. The clinical appearance is similar to the more common pyogenic granuloma of the gingiva. Although the peripheral giant cell granuloma often is more bluishpurple compared with the bright red of atypical pyogenic granuloma. Peripheral giant cell granulomas can develop at almost any age but show peak prevalence in the fifth and sixth decades of life. Approximately 60% of cases occur in females. It may develop in either the anterior or posterior regions of the gingiva or alveolar mucosa and the mandible is affected slightly more often than the maxilla. Although the peripheral giant cell granuloma develops within soft tissue. "cupping" resorption of the underlying alveolar bone sometimes is seen. On occasion, it may be difficult to determine whether the mass arise as a peripheral lesion or as a central giant cell granuloma that eroded through the cortical plate into the gingival soft tissues.


Histopathologic Features:

Microscopic examination of a peripheral giant cell granuloma" shows a proliferation of multinucleated giant cells within a back ground of plump ovoid and spindle-shaped mesenchymal cells. The giant cells may contain only a few nuclei or up to several dozen. Some of these cells may have large vesicular nuclei, others demonstrate small pyknotic nuclei. Mitotic figures are fairly common in the background mesenchymal cells. Abundant hemorrhage is characteristically found throughout the mass which often results in deposits of hemosiderin pigment especially at the periphery of the lesion. The overlying mucosal surface is ulcerated in about 50% of cases. A zone of dense fibrous connective tissue usually separates the giant cell proliferation from the mucosal surface. Adjacent acute and chronic inflammatory cells are frequently present. Areas of reactive bone formation or dystrophic calcifications are not unusual.



Treatment and Prognosis

The treatment of the peripheral giant cell granuloma consists of local surgical excision down to the underlying bone. The adjacent teeth should be carefully scaled to remove any source of irritation and to minimize the risk of recurrence. Approximately 10% of lesions are reported to recur and reexcision must be performed. On rare occasions, lesions indistingushable from peripheral giant cell granulomas have been seen in patients with hyper parathyroidism. They apparently represent the so-called osteoclastic brown tumors associated with this endocrine disorder. However; the brown tumors of hyperparathyroidism are much more likely to be intraosseous in location and mimic a central giant cell granuloma.

Central giant cell granuloma (giant cell lesion; giant cell tumor):

The giant cell granuloma is considered widely to be a non-neoplastic lesion, although formerly designated as "giant cell reparative granuloma," there is little evidence that the lesion represents a reparative response. Some lesions demonstrate aggressive behavior similar to that of a neoplasm. Most oral and maxillofacial pathologists have dropped the term "reparative"; today, these lesions are designated as giant cell granuloma or by the more non-committal term, giant cell lesion. Whether or not true giant cell tumors occur in the jaws is uncertain and controversial.

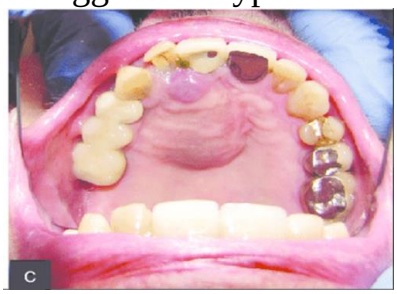
Clinical and Radiographic Features

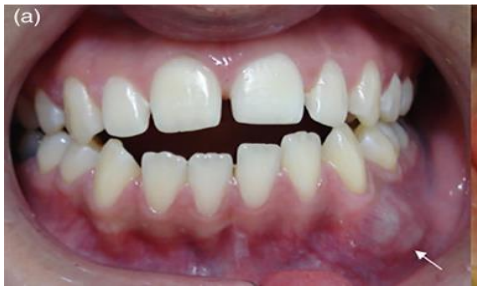
Giant cell granulomas may be encountered in patients ranging from 2 to 80 years of age, although more than 60% of all cases occur before age 30. Although the sex ratio varies in different reviews, a majority of giant cell granulomas are noted in females, and approximately 70% arise in the mandible. Lesions are more common in the anterior portions of the jaws, and mandibular lesions frequently cross the midline. Most giant cell granulomas of the jaws are asymptomatic and first come to attention during a routine radiographic examination or as a

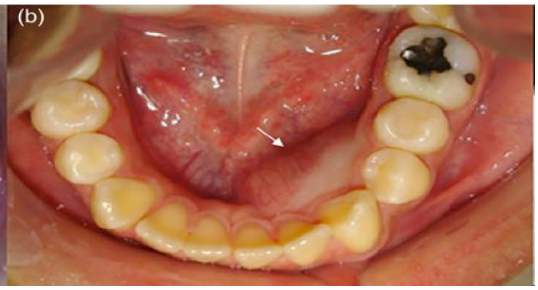
result of painless expansion of the affected bone. A minority of cases, however, may be associated with pain, paresthesia, or perforation of the cortical bone plate, occasionally resulting in ulceration of the mucosal surface by the underlying lesion. Based on the clinical and radiographic features, several groups of investigators have suggested that central giant cell lesions of the jaws may be divided into two Categories:

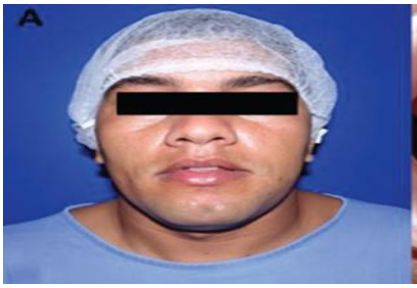
1. Nonaggressive lesions make up most cases, exhibit few or no symptoms, demonstrate slow growth, and do not show cortical perforation or root resorption of teeth involved in the lesion.

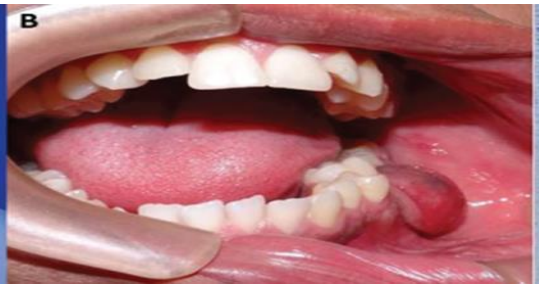
2. Aggressive lesions are characterized by pain, rapid growth, cortical perforation and root resorption. They show a marked tendency to recur after treatment, compared with the nonaggressive types.

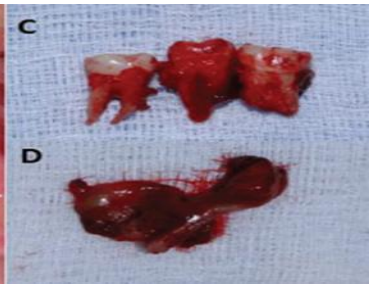




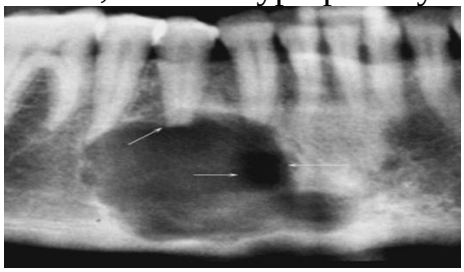
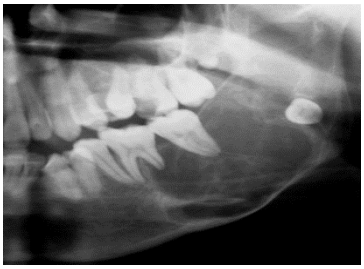
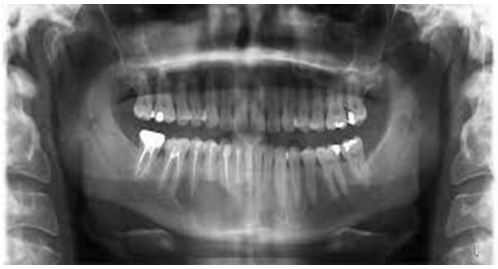






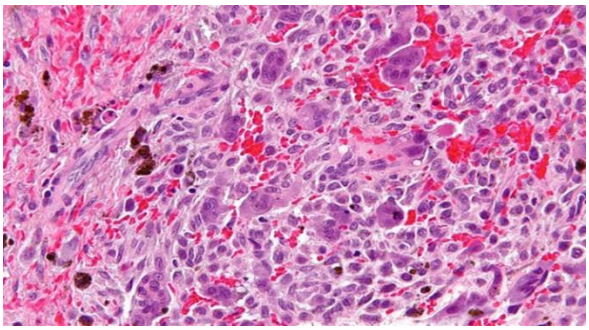


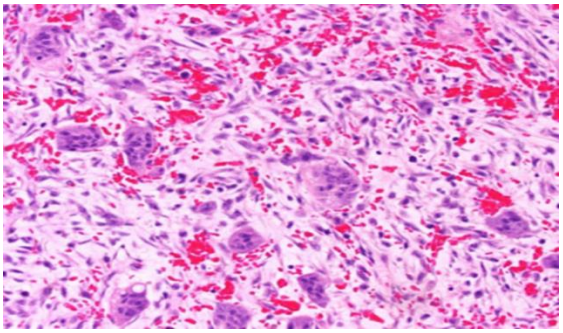
Radiographically: central giant cell lesions appear as radiolucent defects, which may be unilocular or multilocular. The defect is usually well delineated, but the margins are generally non corticated. The lesion may vary from a 5 X 5 mm incidental radiographic finding to a destructive lesion greater than 10 cm in size. The radiographic findings are not specifically diagnostic. Small unilocular lesions may be confused with periapical granulomas or cysts. Multilocular giant cell lesions cannot be distinguished radiographically from ameloblastoma or other multilocular lesions. Areas histopathologically identical to giant cell granuloma have been noted aneurysmal bone cysts and intermixed with central odontogenic fibromas. Because giant cell granulomas are histopathologically identical to brown tumors, hyperparathyroidism should be ruled out in all instances. In addition, multifocal involvement in childhood suggests cherubism and warrants further investigation. Most giant cell granulomas are single lesions rarely multifocal involvement is seen in patients who demonstrate no evidence of an associated disease, such as hyperparathyroidism or cherubism.

Histopathologic Features:

Giant cell lesions of the jaw show a variety of features. Common to all is the presence of few-many multinucleated giant cells in a background of ovoid to spindle shaped mesenchymal cells. There is evidence that these giant cells represent osteoclasts, although others suggest the cells may be aligned more closely with macrophages. The giant cells may be aggregated focally in the lesional tissue or may be present diffusely throughout the lesion. These cells vary considerably in size and shape from case to case. Some are small and irregular in shape and contain only a few nuclei. In other cases, the giant cells are large and round and contain 20 or more nuclei. In some cases, the stroma is loosely arranged and edematous; In other cases, it may be quite cellular. Areas of erythrocyte extravasation and hemosiderin deposition often are prominent. Older lesions may show considerable fibrosis of the stroma. Foci of osteoid and newly formed bone are occasionally present within the lesion. Correlation of the histopathologic features with clinical behavior remains debatable, but lesions showing large, uniformly distributed giant cells and a predominantly cellular stroma appear more likely to be clinically aggressive with a greater tendency to recur after surgical treatment.





Treatment and Prognosis

Central giant cell lesions of the jaws are usually treated by thorough curettage. In reports of large series of cases, recurrence rates range from 2% to 50% or greater. Most studies indicate a recurrence rate of about 15% to 20%. Those lesions considered on clinical and radiologic grounds to be potentially aggressive show a higher frequency of recurrence. Recurrent lesions often respond to further curettage, although some aggressive lesions require more radical surgery for cure. In patients with aggressive tumors, three alternatives surgery-(1) corticosteroid's (2) calcitonin, and (3) interferon alfa-2a-.

In spite of the reported recurrence rate, the long term prognosis of giant cell granulomas is good and metastases do not develop.

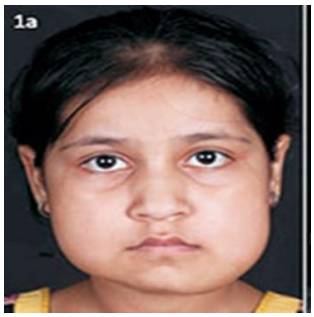
CHERUBISM

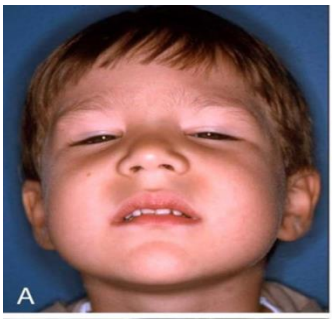
Cherubism is a rare developmental jaw condition that is generally inherited as an autosomal dominant trait with high penetrance but variable expressivity. The gene for cherubism was mapped to chromosome 4p 16. Although genetic heterogeneity is possible, these findings were discovered in widely separated cohorts. Sporadic cases do occur and are thought to represent spontaneous mutations. The name cherubism was applied to this condition because the facial

appearance is similar to that of the plump-cheeked little angels (cherubs) depicted in Renaissance paintings, although cherubism also has been called "familial fibrous dysplasia," this term should be avoided because cherubism has no relationship to fibrous dysplasia of bone.

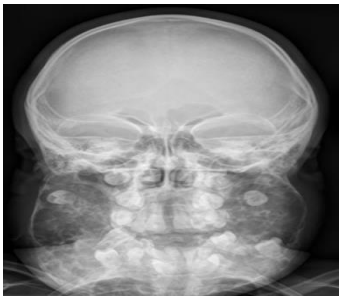
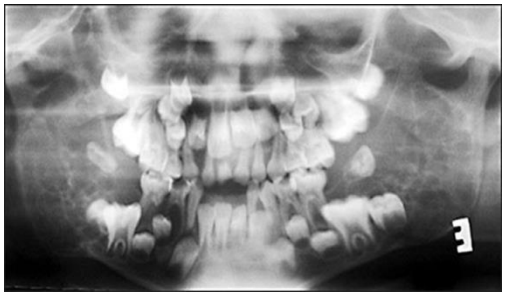
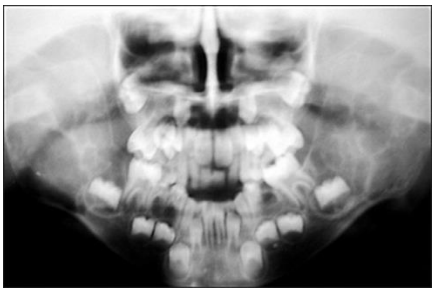
Clinical and Radiographic Features: Although some examples of cherubism may develop as early as 1 year of age, the disease usually occurs between the ages of 2 and 5 years. In mild cases, the diagnosis may not be made until the patient reaches 10 to 12 years of age. The clinical alterations typically progress until puberty, then stabilize and slowly regress. The cherub like facies arises from bilateral involvement of the posterior mandible that produces angelic chubby checks. In addition, there is an "eyes upturned to heaven" appearance that is due to a wide rim of exposed sclera noted below the iris. This latter feature is due to involvement of the infraorbital rim and orbital floor that tilts the eyeballs upward, and to stretching of the upper facial skin that pulls the lower lid downward. On occasion, affected patients also reveal marked cervical lymphadenopathy. The mandibular lesions typically appear as a pain less, bilateral expansion of the posterior mandible that tends to involve the angles and ascending rami. The bony expansion is usually bilaterally symmetrical: in severe cases most of the mandible is involved. Milder maxillary involvement occurs in the tuberosity areas; in severe cases, the entire maxilla can be affected. Extensive bone involvement causes a marked widening and distortion of the alveolar ridges. In addition to the aesthetic and psychologic impact. the enlargements may cause tooth displacement or failure of eruption, impair mastication, create speech difficulties, or rarely lead to loss of normal vision or hearing. Although there have been rare reports of unilateral cherubisrn, it is difficult to accept these as examples of this disease unless there is a strong family history.





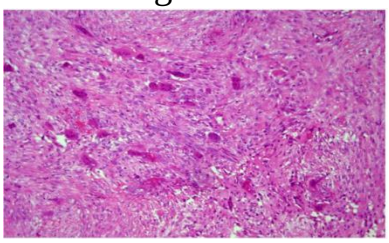
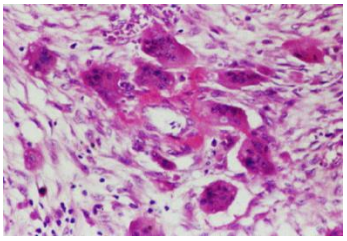
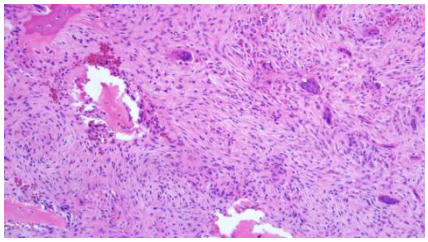


Radiographically; the lesions are typically multilocular expansile radiolucencies. The appearance is virtually diagnostic as a result of their bilateral location. Less commonly, the lesions appear as unilocular radiolucencies. Although cherubism typically involves only the jaws involvement also has been reported rarely in other bones such as the ribs and humerus. No unusual biochemical findings have been reported in patients with cherubism. If laboratory results do not suggest the diagnosis of with multiple symmetric giant cell granulomas represent examples of cherubism. However, it has been suggested that the bony lesions of cherubism represent a phenotypic picture common to a number of disease processes that arise from multiple distinct Initiating pathogenetic events.

Histopathologic Features:

The microscopic findings of cherubism are essentially similar to those of isolated giant cell granulomas, and they seldom permit a specific diagnosis of cherubism in the absence of clinical and radiologic information. The lesional tissue consists of vascular fibrous tissue containing variable numbers of multinucleated giant cells. The giant cells tend to be small and usually aggregated focally. Foci of extravasated blood are commonly present. The stroma in cherubism often tends to be more loosely arranged than that seen in giant cell granulomas; in some cases, cherubism reveals eosinophilic, cuff like deposits surrounding small blood vessels throughout the lesion. The eosinophilic cuffing appears to be specific for cherubism. However, these deposits are not present in many cases, and their absence does not exclude a diagnosis of cherubism. In older, resolving lesions of cherubism, the tissue becomes more fibrous, the number of giant cells decreases, and new bone formation is seen.

Treatment and Prognosis:

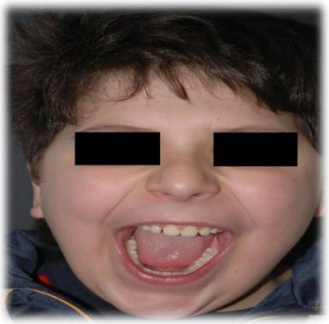
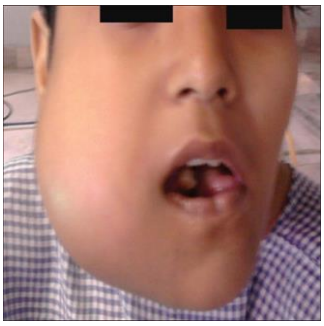
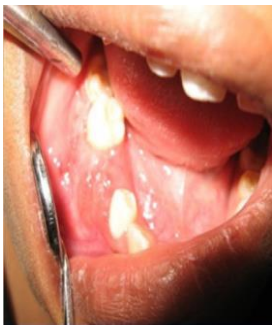
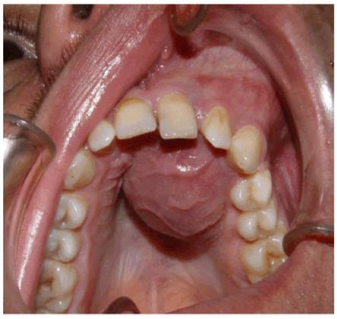
The prognosis in any given case is unpredictable. In most instances, the lesions tend to show varying degrees of remission and involution after puberty. By the fourth decade, the facial features of most patient's approach normalcy. In spite of the typical scenario, some patients demonstrate very mild alterations, whereas others reveal grotesque changes that often are very slow to resolve. In occasional patients, the deformity can persist. The question of whether to treat or simply observe a patient with cherubism is difficult. Excellent results have been obtained in some cases by early surgical intervention with curettage of the lesions. Conversely, early surgical intervention sometimes has been followed by rapid regrowth of the lesions and worsening deformity. A course limited only to observation may result in extreme and sometimes grotesque facial deformity, with associated psychologic problems and functional deformity that may necessitate extensive surgery; several investigators have suggested the use of calcitonin in severe cases, but such therapy a waits further study. Radiation therapy is contraindicated because of the risk of development of post-irradiation sarcoma. The optimal therapy for cherubism has not been determined.

ANEURYSMAL BONE CYST

Aneurysmal bone cyst is an intraosseous accumulation of variable-sized. Blood filled spaces surrounded by cellular fibrous connective tissue that often is admixed with trabeculae of reactive woven bone. The cause and pathogenesis of the aneurysmal bone cyst are poorly understood. Several investigators have proposed that aneurysmal "bone cyst arises from a traumatic event. Vascular malformation or neoplasm that disrupts the normal osseous hemodynamics and leads to an enlarging hemorrhagic extravasation. As a corollary of this theory others have suggested that aneurysmal cyst and giant cell granuloma are closely related. An aneuyismal bone cyst may form when an area of hemorrhage maintains connection with the disrupted feeding vessels; subsequently; giant cell granuloma like areas can develop after loss of connection with the original vascular source. Some authors have presented large series of cases involving the extragnathic skeleton and claim that none of the cases has shown evidence of a preexisting lesion. Others have reported similar large series and contend that a preexisting lesion may be evident in one third of cases. It is likely that the aneurysmal bone cyst may occur either as a primary lesion or as a result of disrupted vascular dynamics in a preexisting intra bony lesion.

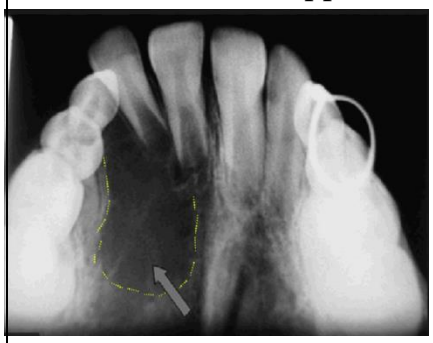
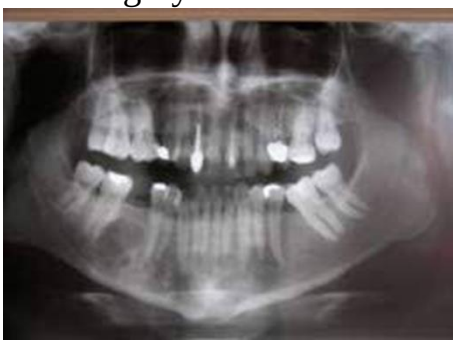
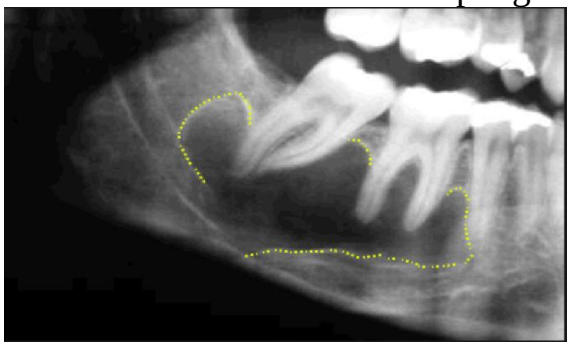
Clinical and Radiographic Features:

Aneurysmal bone cysts are located most commonly in the shaft of a long bone or in the vertebral column in patients younger than age 30. Gnathic aneurysmal bone cysts are uncommon, with approximately 2% reported from the jaws. Within the jaws, a wide age range is noted, but most cases arise in children and young adults with an approximate mean age of 20 years. No significant sex predilection is noted. A mandibular predominance is noted, and the vast majority arises in the posterior segments of the jaws. The most common clinical manifestation is a swelling that has usually developed rapidly. Pain often is reported; paresthesia compressibility and crepitus are rarely seen. On occasion, malocclusion, mobility, migration, or resorption of involved teeth may be present. Maxillary lesions often bulge into the adjacent tissue; nasal obstruction, nasal bleeding, proptosis, and diplopia are noted uncommonly.

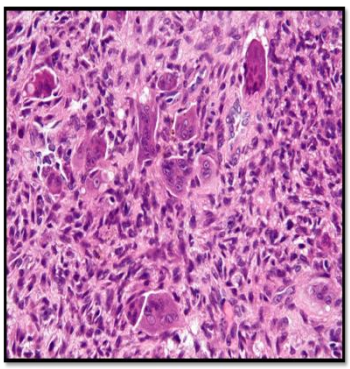
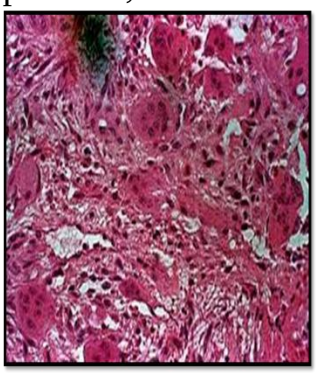
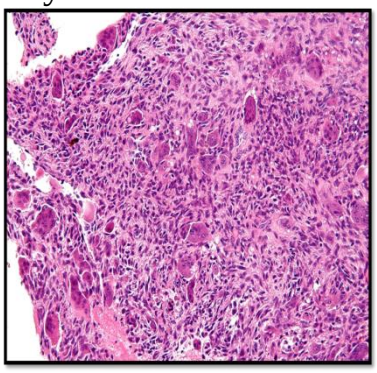
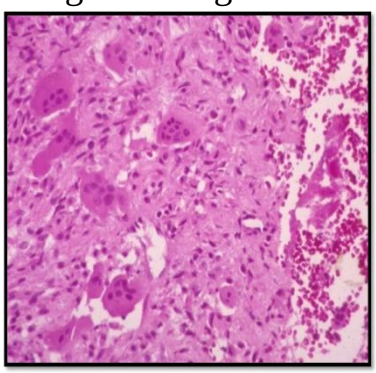
Radiographic study shows a unilocular or multilocular radiolucent lesion often associated with marked cortical expansion and thinning. The radiographic borders are variable and may be well defined or diffuse. Frequently, a ballooning or "blow-out" distention of the contour of the affected bone is described. Uncommonly, small radiopaque foci, thought to be small trabeculae of reactive bone, are noted within the radiolucency. At the time of surgery, intact periosteum and a thin shell of bone are typically found covering the lesion. Cortical perforation may occur, but spread into the adjacent soft tissue has not been documented. When the periosteum and bony

shell are removed, dark venous blood frequently wells up and venous like bleeding may be encountered. The appearance at surgery has been likened to that of a "blood-soaked sponge."

Histopathologic Features:

Microscopically, the aneurysmal bone cyst is characterized by spaces of varying size, filled with unclotted blood surrounded by cellular fibroblastic tissue containing multinucleated giant cells and trabeculae of osteoid and woven bone. On occasion, the wall contains an unusual lacelike pattern of calcification that is uncommon in other intraosseous lesions. The blood-filled spaces are not lined by endothelium. In approximately 20% of the cases, aneurysmal bone cyst is associated with another pathosis, most commonly a fibro-osseous lesion or giant cell granuloma.

Treatment and Prognosis

Aneurysmal bone cysts of the jaws are usually treated by curettage or enucleation, sometimes supplemented with cryosurgery. The vascularity of gnathic lesions is typically low flow, a removal of the bulk of the lesion is usually sufficient to control the bleeding. Rare cases require more extensive surgical resection. In most instances, the surgical defect heals within 6 months to 1 year and does not necessitate bone grafting. Irradiation is contraindicated. The reported recurrence rates are variable and have been as low as 8% and as high as 60%. Most recurrent examples arise from inadequate or subtotal removal upon initial therapy. On occasion, recurrence may be related to incomplete removal of a coexisting lesion such as an osteoblastoma or ossifying fibroma. Overall, in spite of recurrences, the long-term prognosis appears favorable.

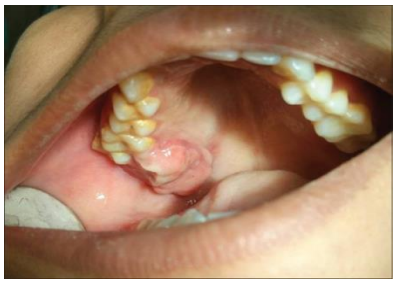
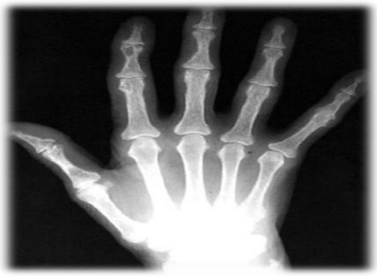
Hyperparathyroidism

Excess production of parathyroid hormone (PTH) results in the condition known as hyperparathyroidism. PTH normally is produced by the parathyroid glands in response to a decrease in serum calcium levels. Primary hyperparathyroidism is the uncontrolled production of PTH, usually as a result of a parathyroid adenoma (80% to 90% of cases) or parathyroid hyperplasia (10% to 15% of cases). Infrequently (in less than2% of cases), a parathyroid

carcinoma may be the cause of primary hyperparathyroidism. Secondary hyperparathyroidism develops when PTH is continuously produced in response to chronic low levels of serum calcium, a situation usually associated with chronic renal disease. The kidney processes vitamin D. which is necessary for calcium absorption from the gut, therefore in a patient with chronic renal disease, active vitamin D is not produced and less calcium is absorbed from the gut, resulting in lowered serum calcium levels.

Clinical and Radiographic Features

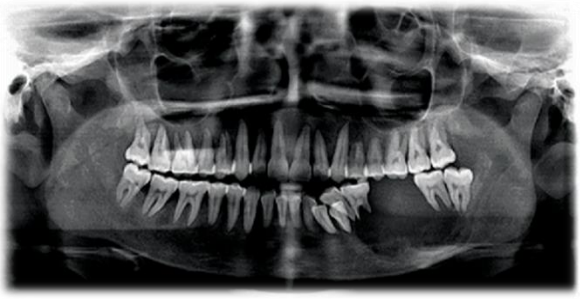
Most patients with primary hyperparathyroidism are older than 60 years of age. Women have this condition two to four times more often than men. Patients with the classic triad of signs and symptoms of hyperparathyroidism are described as having "stones, bones and abdominal groans." Stones refer to the fact that these patients, particularly those with primary hyperparathyroidism, have a marked tendency to develop renal calculi (kidney stones, nephrolithiasis) because of the elevated serum calcium levels. Metastatic calcifications are also seen, frequently involving other soft tissues such as blood vessel walls, subcutaneous soft tissues, the sclera the dura and the regions around the joints.

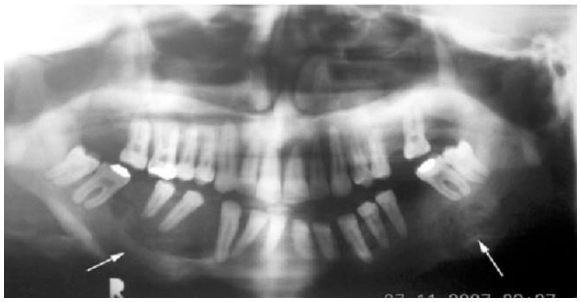




Bones refers to a variety of osseous changes that may occur in conjunction with hyperparathyroidism. One of the first clinical signs of this disease is seen radiographically as subperiosteal resorption of the phalanges of the index and middle fingers. Generalized loss of the lamina dura surrounding the root s of the teeth is also seen as an early manifestation of the condition. Alterations in trabecular pattern characteristically develop next. A decrease intrabecular density and blurring of the normal trabecular pattern occur; often a "g round glass" appearance results with persistent disease other osseous lesions develop, such as the so-called **brown tumor** of hyperparathyroidism. This lesion derives its name from the color of the t issue specimen which is usually a dark reddish-brown because of the abundant hemorrhage and hemosiderin deposition within the tumor.

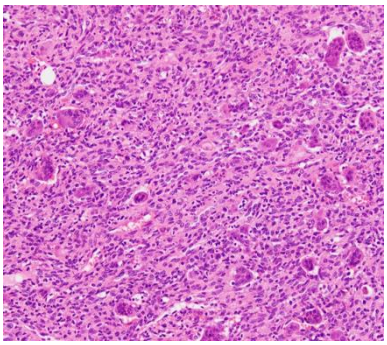
“Abdominal groans” refers to the tendency for the development of duodenal ulcers.

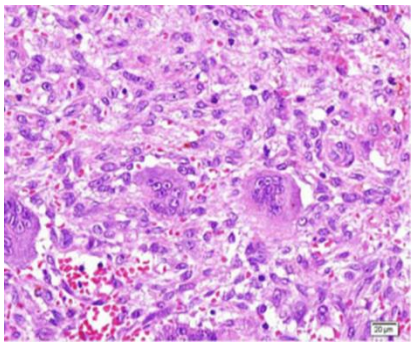
Radiographicaly: These lesions appear radiographically as well-demarcated unilocular or multilocular radio lucencies. They commonly affect the mandible clavicles ribs and pelvis. They may be solitary but are often multiple, and longstanding lesions may produce significant cortical expansion. Typically, the other osseous changes are observable if brown tumors are present. The most severe skeletal manifestation of chronic hyperparathyroidism has been called osteitis fibrosa cystica, a condition that develops from the central degeneration and fibrosis of long standing brown tumors. In patients with secondary hyperparathyroidism caused by end-stage renal disease (renal osteodystrophy), striking enlargement of the jaws has been known to occur

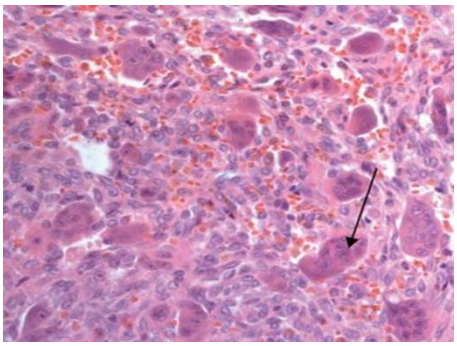




Histopathologic Features: The brown tumor of hyperparathyroidism is histopathologically identical to the central giant cell granuloma of the jaws, a benign tumor like lesion that usually affects teenagers and young adults. Both lesions are characterized by a proliferation of exceedingly vascular granulation tissue, which serves as a background for numerous multinucleated osteoclast- type giant cells, some lesions may also show a proliferative response characterized by a parallel arrangement of spicules of woven bone set in a cellular fibroblastic background with variable numbers of multinucleated giant cells. This patter n is often associated with secondary hyperparathyroidism related to chronic renal disease (renal osteodystrophy).





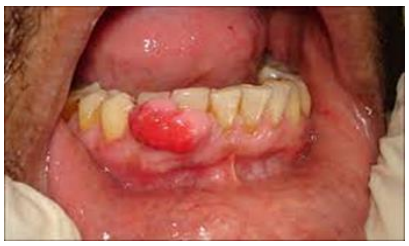
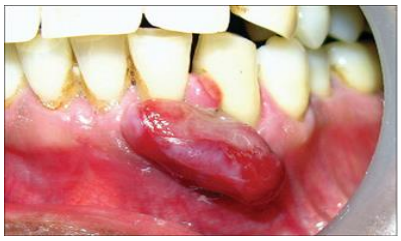
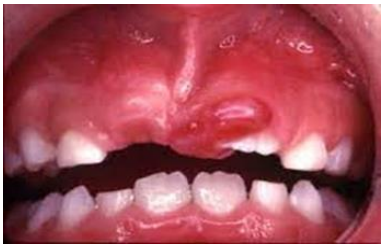


Treatment and Prognosis:

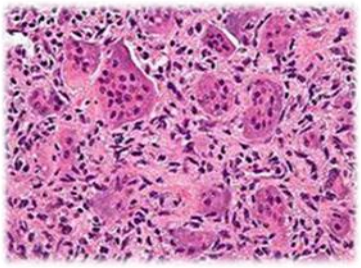
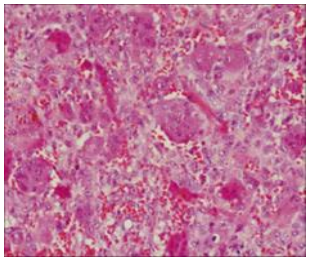
In primary hyperparathyroidism, the hyperplastic parathyroid tissue or the functional tumor must be removed surgically to reduce PTH levels to normal. Secondary hyperparathyroidism may evolve to produce signs and symptoms related to renal calculi or renal osteodystrophy. Restriction of dietary phosphate, use of phosphatebinding agents and pharmacologic treatment with an active vitamin D metabolite (e.g.,calcitriol) may avert problems. Exposure to aluminum salts. Which inhibit bone mineralization, should be eliminated also Patients who do not respond to medical therapy may require parathyroidectomy. Renal transplantation is the ideal treatment because it usually restores the normal physiologic processing of vitamin D, as well as phosphorus and calcium reabsorption and excretion.

Lab.9

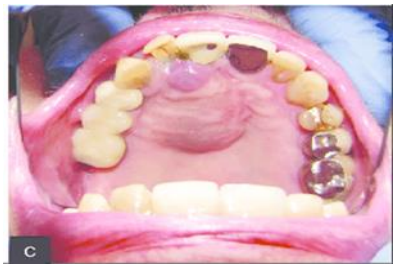
Giant cell lesions

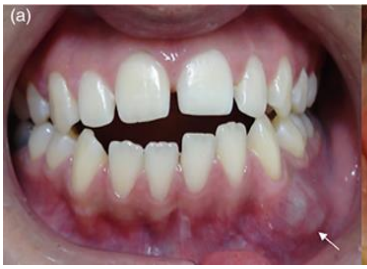




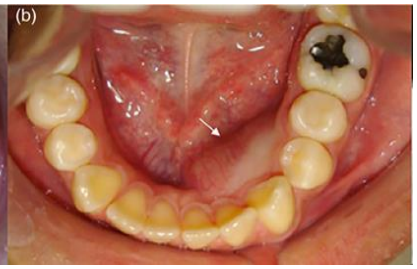
Peripheral giant cell granuloma (giant cell epulis)

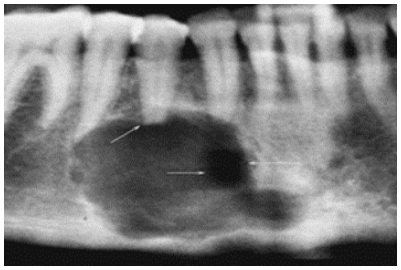
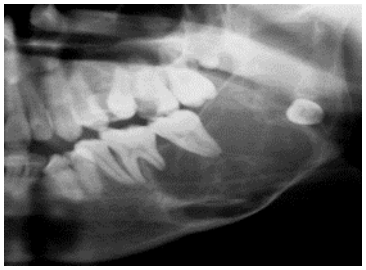
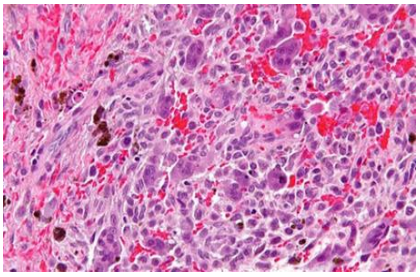



Giant cell granuloma



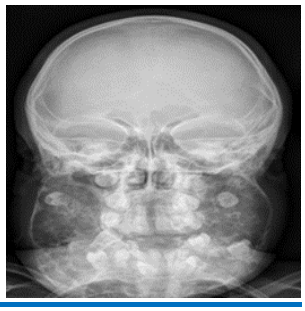




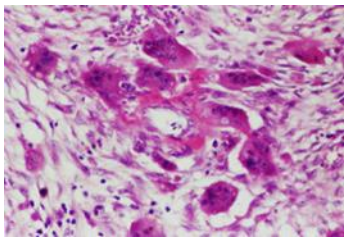
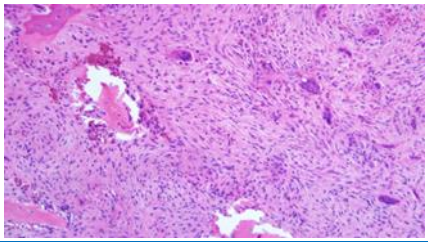




Central giant cell granuloma





Cherubism

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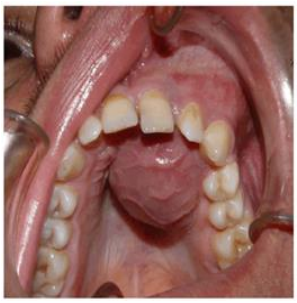
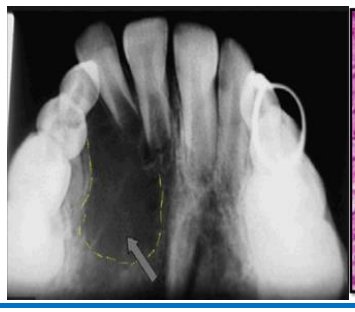
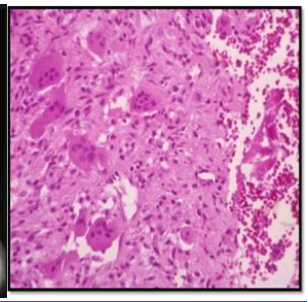
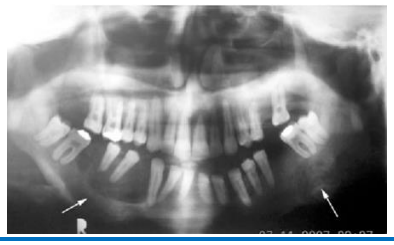
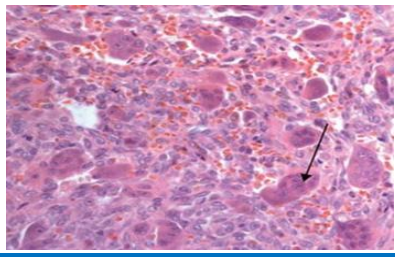




Aneurysmal bone cyst

Brown tumor (Parahyperthyrodism)

Oral pathology

Lec. 10

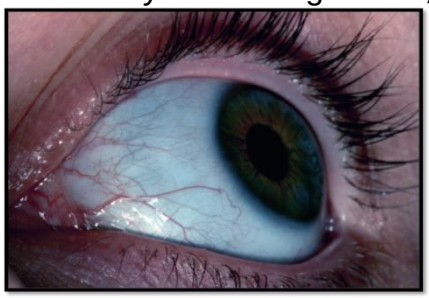
Metabolic and Genetic diseases of bone

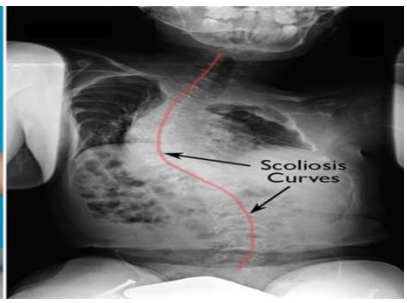
Osteogenesis imperfect

Osteogenesis imperfect comprises a heterogeneous group of heritable disorders characterized by impairment of collagen maturation. Except on rare occasions, the disorder arises from heterozygosity for mutations in one of two genes that guide the formation of type I collagen: the COLIA1 gene on chromosome 17 and the COLIA2 geneon chromosome 7. Collagen forms a major portion of bone, dentin, sclerae, ligaments, and skin: osteogenesis imperfecta demonstrates a variety of changes that involve these sites. Several different forms of osteogenesis imperfect are seen, and they represent the most common type of inherited bone disease. Abnormal collagenous maturation results in bone with *a* thin cortex, fine trabeculation, and diffuse osteoporosis. Upon fracture healing will occur but may be associated with exuberantcallus formation.

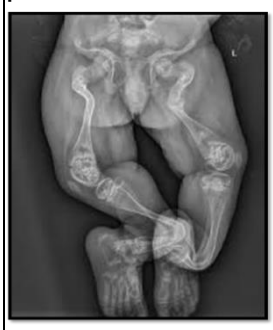
Clinical and Radiographic Features

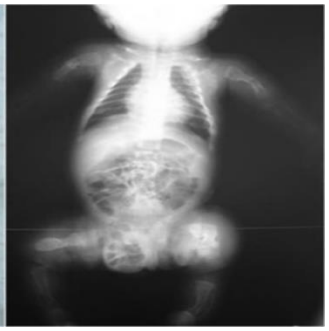
Osteogenesis imperfect is a rare disorder that affects one in 8000 individuals, with many being stillborn ordying shortly after birth. Both autosomal dominant and recessive hereditary patterns occur, and many cases are sporadic. The severity of the disease varies widely, even in affected members of a single family. In addition to bone fragility, some affected individuals also have blue sclera, altered teeth, hypoacusis (hearing loss), long bone and spine deformities, and joint hyper extensibility. The radiographic hallmarks of osteogenesis imperfect include osteopenia, angulation or deformity of the long bones, multiple fractures, and wormian bones in the skull.

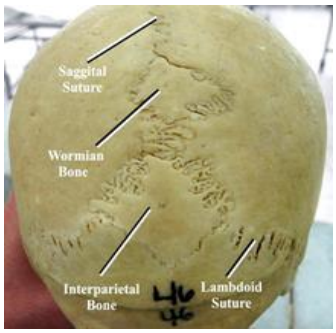




Wormian bones consist of ten or more sutural bones that are 6X 4 mm in diameter or larger and arranged in a mosaic pattern. Wormian bones are not specific and can be seen in other processes, such as cleidocranial dysplasia.

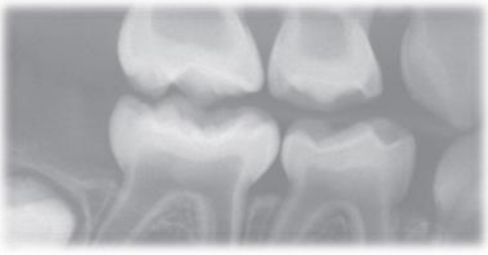
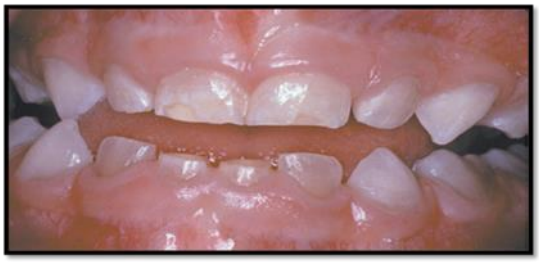






Several distinctive findings are noted in the oral cavity. Dental alterations that appear clinically and radiographically identical to dentinogenesis imperfecta are occasionally noted. In affected patients; both dentitions are involved and demonstrate blue to brown translucence. Radiographs typically reveal premature pulpal obliteration, although shell teeth rarely may be seen. Although the altered teeth closely resemble dentinogenesis imperfecta, the two diseases are the result of different

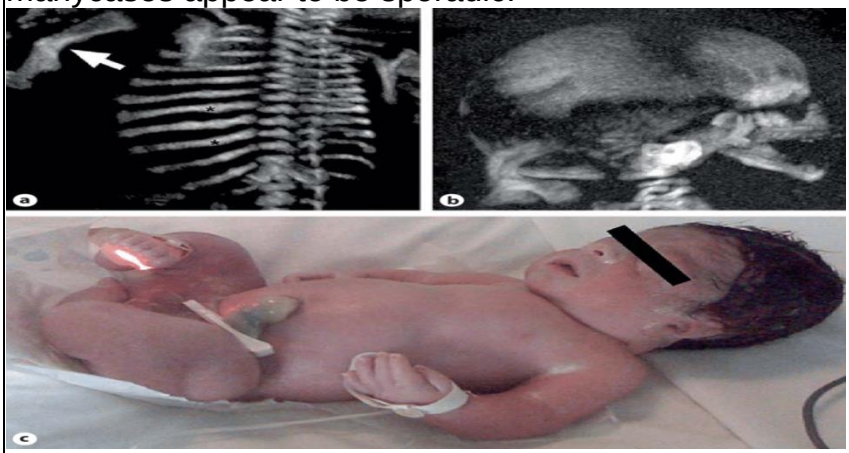
mutations and should be considered as separate processes.Such dental defects in association with the systemic bone disease should be termed opalescent teeth, reserving the diagnosis of dentinogenesis imperfect for those patients with alterations isolated to the teeth.In addition, patients with osteogenesis imperfect demonstrate an increased prevalence of class III malocclusion that is caused by maxillary hypoplasia, with or without mandibular hyperplasia. On rare occasions, panoramic radiographs may reveal multifocal radiolucencies, mixed radiolucencies, or radiopacities that resemble those seen in florid cemento-osseous dysplasia. When predominantly radiopaque, these areas are sensitive to inflammation and undergo sequestration easily. In these patients, marked coarseness also is noted in the remainder of the skeleton.

Four major types of osteogenesis imperfecta arc recognized, each having several subtypes.

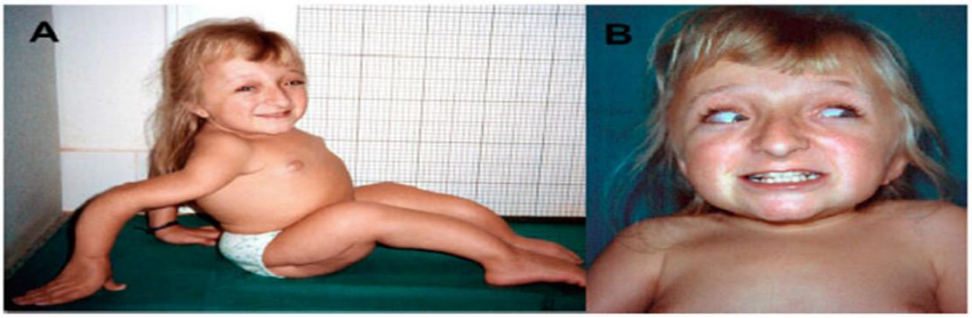
1-Type I osteogenesis imperfecta. Type I is the most common and mildest form. Affected patients have mild to moderately severe bone fragility. Fractures are present at birth in about 10% of cases, but there is great variability in frequency and age of onset of fractures, with10% of patients not demonstrating fractures. Most fractures occur during the preschool years and are less common after puberty. Hearing loss commonly develops before age 30 and most older patients have hearing deficits. Hypermobile joints and easy bruising becauseof capillary fragility are not rare. Some affected patients have normal teeth, but others show opalescent dentin. The sclera is distinctly blue at all ages and aid in classification. Osteogenesis imperfecta type I is inherited as an autosomal dominant trait.

2-Type II osteogenesis imperfect: Osteogenesis imperfect type II is the most severe form and exhibits extreme bone fragility and frequent fractures, which may occur during delivery. Many patients are stillborn and 90% die before 4 weeks of age. Blue sclera are present, opalescent teeth may be present both autosomal recessive and dominant patterns may occur, and manycases appear to be sporadic.



3-Type III osteogenesis imperfecta, Type III is the most severe form noted in individuals beyond the perinatal period and demonstrates moderately severe to severe bone fragility. The sclerae are normal or pale blue or grayat birth; if discoloration is present, it fades as the child grows older. Ligamentous laxity and hearing loss are common. Fractures may be present at birth, but there is a low mortality in Infancy. Although one third survives into adulthood, the majority of affected

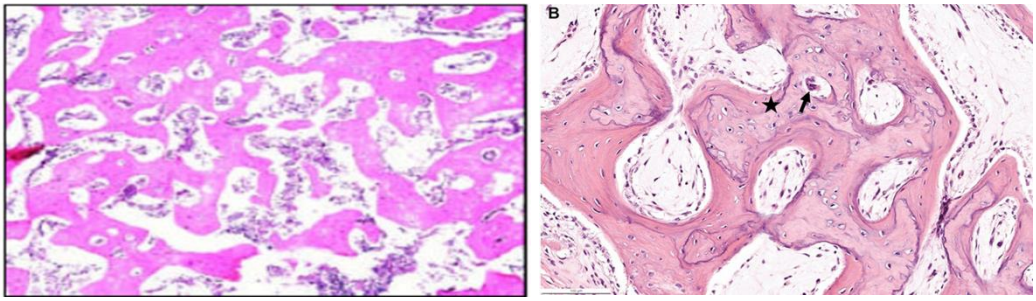
individuals die during childhood, usually from cardiopulmonary complications caused by kyphoscoliosis. Some patients have opalescent dentin whereas others have normal teeth, both autosomal dominant and recessive hereditary patterns are noted.



4-Type IV osteogenesis imperfecta. Type IV is associated with mild to moderately severe bone fragility. The sclera may be pale blue in early childhood. but the blue color fades later in life. Fractures are present at birth in about 50% of these patients. The frequency of fractures decreases after puberty and some individuals never experience bone fracture at any time. Some of the patients have opalescent dentin: others have normalteeth. This variant appears to be inherited as an autosomal dominant trait.

Histopathologic Features

Upon histopathologic examination, cortical bone appears attenuated. Osteoblasts are present, but bone matrix production is reduced markedly. The bone architecture remains immature throughout life and there is a failure of woven bone to become transformed to lamellar bone.



Treatment and Prognosis

There is no treatment for osteogenesis imperfecta, Management of the fractures may be a major problem. Patients with opalescent dentin usually show severe attrition of their teeth, leading to tooth loss. Treatment of the dentition is similar to that employed for dentinogenesis imperfecta, but use of implants is questionable because of the deficient quality of the supporting bone.

In patients with significant malocclusion, orthognathic surgery may be performed but associated medical problems make presurgical planning paramount. Although highly variable occasional patients have associated bleeding disorders. Cardiac malformations, and an increased risk of hyperthermia. The prognosis varies from relatively good to very poor. Some patients have little to no disability, whereas others have severe crippling as a result of the fractures. In severe forms, death occurs *in utero,* during delivery or early in childhood.

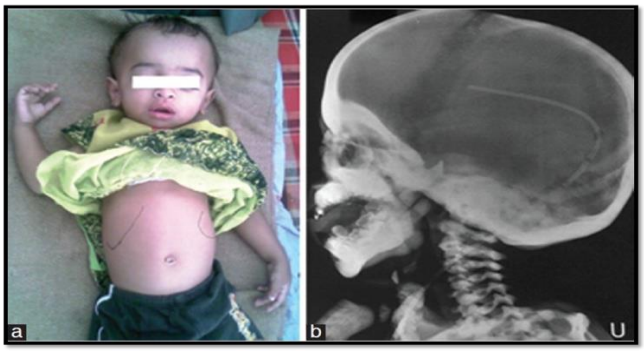
Osteopetrosis (albers-schonbergdisease; marble bone disease)

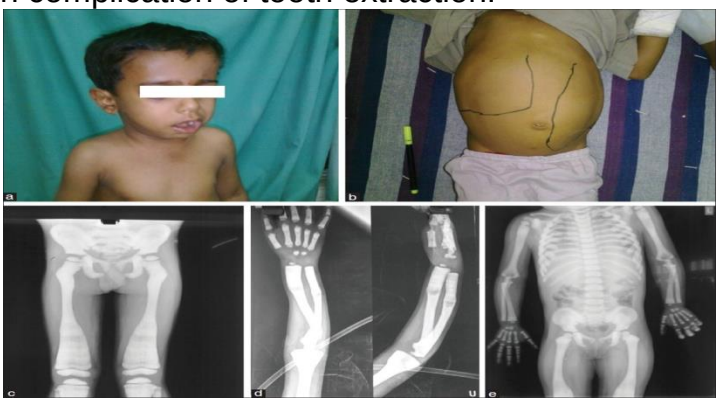
Osteopetrosis is a group of rare hereditary skeletal disorders characterized by a marked increase in bone density resulting from a defect in remodeling caused by failure or normal osteoclast function. The number of osteoclasts present is often increased; however, because of their failure to function normally, bone is not resorbed. Defective osteoclastic bone resorption, combined with continued bone formation and endochondral ossification, results in thickening of cortical bone and sclerosis of the cancellous bone. Although a number or types have been identified, these pathoses group into two major clinical patterns :(1) infantile and (2) adult osteopetrosis. Although the exact

prevalence has not been determined, it is estimated to be 1 in 100,000 to 1 in 500,000. The clinical severity of the disease varies widely, even within the same pattern of osteopetrosis.

Clinical and Radiographic Features

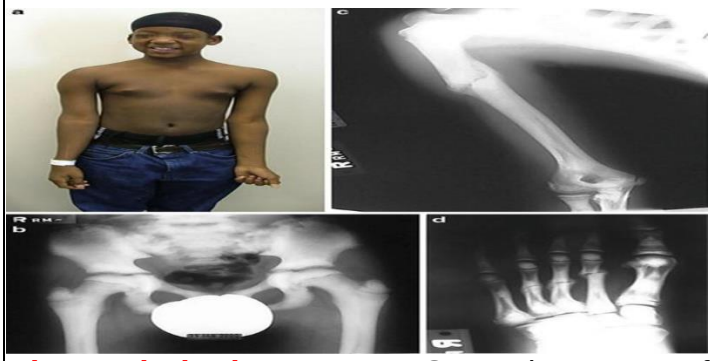
Infantile osteopetrosis: Patients discovered with osteopetrosis at birth or in early infancy usually have severe disease that is termed malignant osteopetrosis. In most cases, infantile osteopetrosisis inherited as an autosomal recessive trait and leads to a diffusely sclerotic skeleton, Marrow failure, frequent fractures, and evidence of cranial nerve compression are common. The initial signs of infantile osteopetrosis often are normocytic anemia with hepatosplenomegaly resulting from compensatory extramedullary hematopoiesis. Increased susceptibility to infection is common as a result of granulocytopenia. Facial deformity develops in many of the children, manifesting as a broad face, hypertelorism, snub nose, and frontal bossing. Tooth eruption almost always is delayed. Failure of resorption and remodeling of the skull bones produces narrowing's of the skull foramina that press on the various cranial nerves and result in optic nerve atrophy and blindness, deafness, and facial paralysis. Inspite of the dense bone, pathologic fractures are common. Osteomyelitis of the jaws is a common complication of tooth extraction.

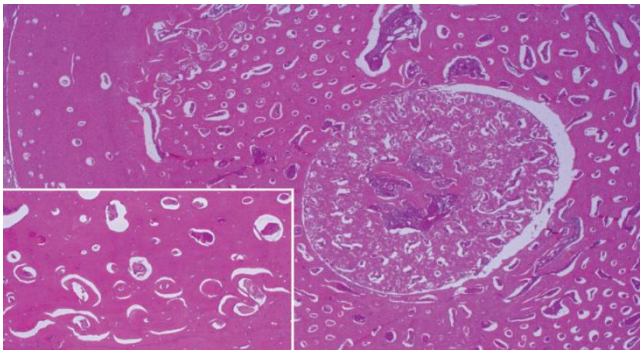




Radiographically There is a widespread increase in skeletal density with detects in metaphyseal remodeling, the radiographic distinction between cortical and cancellous bone is lost. In dental radiographs, the roots of the teeth often are difficult to visualize because of the density of the surrounding bone. Less severe variants of infantile osteopetrosis exist and have been termed intermediate osteopetrosis. Affected patients often are asymptomatic at birth but frequently exhibit fractures by the end of the first decade.

Adult osteopetrosis: Adult osteopetrosis is usually discovered later in life and exhibits less severe manifestations. In most patients, this pattern is inherited as an autosomal dominant trait and has been termed benign osteopetrosis. The axial skeleton usually reveals significant sclerosis whereas the long bones demonstrate little or no defects. Approximately 40% are asymptomatic, and marrow failure is rare. Occasionally; the diagnosis is discovered initially on review of dental radiographs that reveal a diffuse increased radiopacity of the medullary portions of the bone. In symptomatic patients, bone pain is frequent. Two major variants of adult osteopetrosis are seen. In one form, cranial nerve compression is common, although fractures occur rarely. In contrast, the second pattern demonstrates frequent fractures, but nerve compression is uncommon. When the mandible is involved, fracture and osteomyelitis after tooth extraction are significant complications.





Histopathologic Features Several patterns of abnormal endosteal bone formation have been described. These include the following:

- Tortuous lamellar trabeculae replacing the cancellous portion of the bone
- Globular amorphous bone deposition in the marrow spaces
- Osteophytic bone formation.
- Numerous osteoclasts may be seen, but there is no evidence that they function because Howship's lacunae are not visible.

Treatment and Prognosis

Because of the mild severity of the disease, adult osteopetrosis is usually associated with long-term survival.

1-Bonemarrow transplantation is the only hope for permanent cure.

2-Interferon gamma-l b, often in combination with calcitriol, has been shown to reduce bone mass, decrease the prevalence of infections, and lower the frequency of nerve compression.

3-administration of corticosteroids to increase circulating red blood cells and platelets, parathormone, macrophagecolony stimulating factor, and erythropoietin.

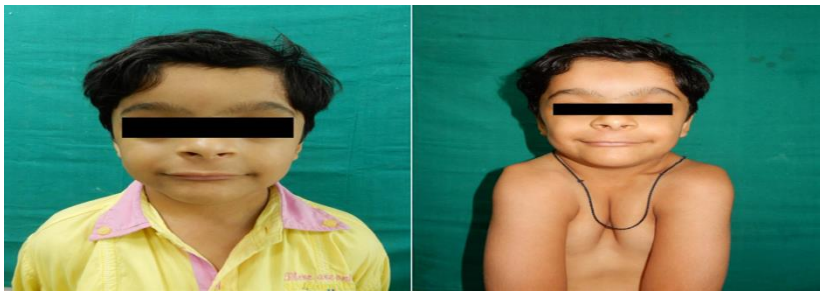
4-Theantibiotics most frequently selected include penicillin. clindamycin. cephalexin. cefotaxime, tobramycin, and gentamicin.

Cleidocranial dysplasia

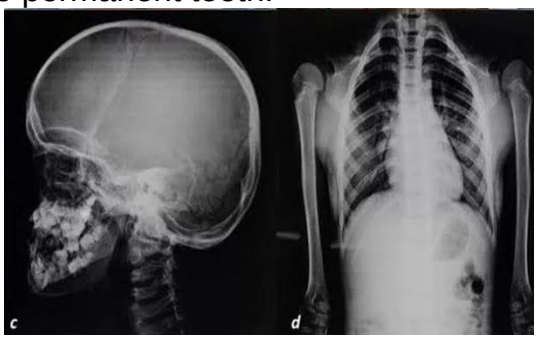
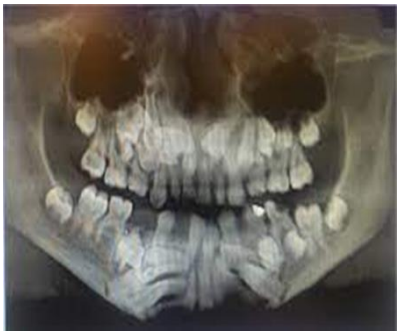
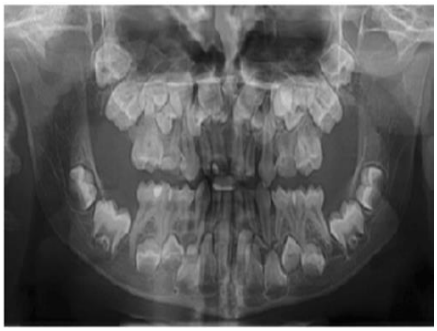
Best known for its dental and clavicular abnormalities, cleidocranial dysplasia is a disorder of bone caused by a defect in the CBFAI gene on chromosome 6p21. This gene normally guides osteoblastic differentiation and appropriate bone formation. The process was initially thought to involve only membranous bones (e.g., clavicles, skull, flat bones) but now is known also to affect endochondral ossification and to represent a generalized disorder of skeletal structures. The disease shows an autosomal dominant inheritance pattern, but as many as 40% of cases appear to represent spontaneous mutations. This condition formerly was known as *cleidocranial dysostosis.*

Clinical and Radiographic Features:

The bone defects in patients with cleidocranial dysplasia chiefly involve the clavicles and skull, although a wide variety of anomalies may be found in other bones. The clavicles are absent, either unilaterally or bilaterally, in about 10% of all cases. More commonly, the clavicles show varying degrees of hypoplasia and malformation. The muscles associated with the abnormal clavicles are under developed. The patient's neck appears long: the shoulders are narrow and show marked drooping. The absence or hypoplasia of the clavicles leads to an unusual mobility of the patient's shoulders. In some instances, the patient can approximate the shoulders in front of the chest.

Although the clavicular defects result in variations of the associated muscles. Function is remarkably good. The appearance of the patient affected by cleidocranial dysplasia often is diagnostic, the patients tend to be of short stature and have large heads with pronounced frontal and parietal bossing. Ocular hypertelorism and abroad base of the nose with a depressed nasal bridge often are noted. On skull radiographs, the sutures and fontanels show delayed closure or may remain open throughout the patient's life, Secondary centers of ossification appear in the suture lines, and many wormian bones may be seen. The gnathic and dental manifestations are distinctive and may lead to the initial diagnosis. The patients often have a narrow, high-arched palate, and there is an increased prevalence of cleft palate. Prolonged retention of deciduous teeth and delay or complete failure of eruption of permanent teeth are characteristic features. Upon review of dental radiographs, the most dramatic finding is the presence of numerous unerupted permanent and supernumerary teeth, many of which frequently exhibit distorted crown and root shapes. The number of supernumerary teeth can be impressive, with reports of some patients demonstrating greater than 60 such teeth. In addition to the dental alterations, review of panoramic radiographs also reveals an increased prevalence of a number of additional osseous malformations. The mandible often demonstrates coarse trabeculation with areas of increased density, narrow ascending rami, and slender, pointed coronoid processes. The maxilla often is associated with a thin zygomatic arch and small or absent maxillary sinuses. Although young patients typically exhibit a relatively normal jaw relationship, as the individuals age, a short lower face height, acute gonial angle, anterior inclination of the mandible, and mandibular prognathism. Clinicians believe that these changes may be from inadequate vertical growth of the maxilla and hypoplastic alveolar ridge development caused by delay or lack of eruption of the permanent teeth.

Histopathologic Features: The reason for failure of permanent tooth eruption in patients with cleidocranial dysplasia is not understood well. Microscopic study of unerupted permanent teeth shows that these teeth lack secondary cementum.

Treatment and Prognosis: No treatment exists for the skull, clavicular, and other bone anomalies associated with cleidocranial dysplasia. Most patients function well without any significant problems. It is not unusual for an affected individual to be unaware of the disease until some professional calls it to his or her attention. Treatment of the dental problems

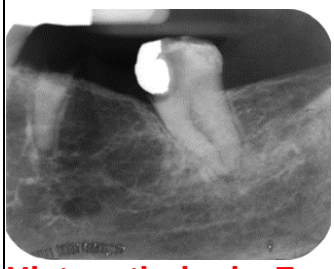
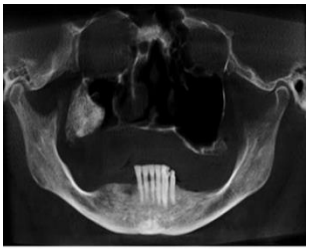
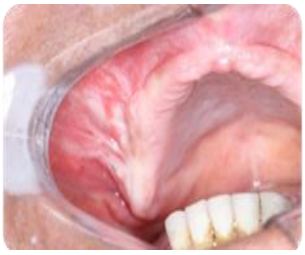
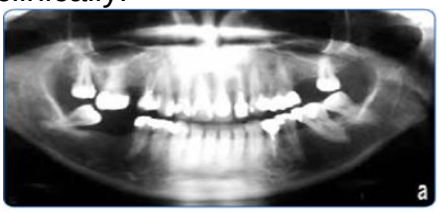
associated with the disease, however, may be a major problem. Therapeutic options include full-mouth extractions with denture construction, auto transplantation of selected impacted teeth followed by prosthetic restoration, or removal of primary and supernumerary teeth followed by exposure of permanent teeth that are subsequently extruded orthodontically, the latter mode of therapy appears to be the treatment of choice; if performed before adulthood, it can prevent the short lower face height and mandibular prognathism.

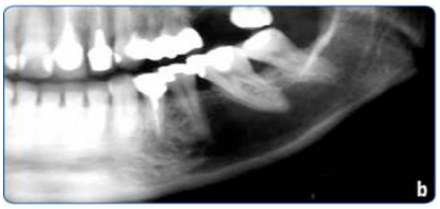
Focal osteoporotic marrow defect

The focal osteoporotic marrow defect is an area of hematopoietic marrow that is sufficient in size to produce an area of radiolucency that may be confused with an intraosseous neoplasm. The area does not represent a pathologic process, but its radiographic features may be confused with a variety of pathoses. The pathogenesis of this condition is unknown. Various theories include the following:

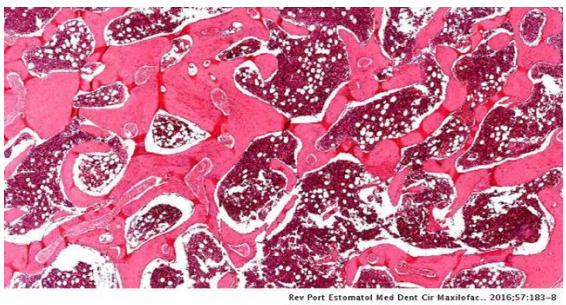
- Aberrant bone regeneration after tooth extraction.
- Persistence of fetal marrow.
- Marrow hyperplasia in response to increased demand for erythrocytes**.**

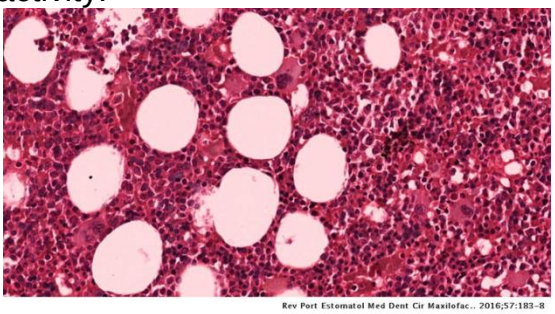
Clinical and Radiographic Features: The focal osteoporotic marrow defect is invariably asymptomatic and is detected as an incidental finding on a radiographic examination. The area appears as a radiolucent lesion, varying in size from several millimeters to several centimeters in diameter. In many instances, when discovered in panoramic radiographs, the area appears radiolucent and somewhat circumscribed; however, upon review of higher detailed periapical radiographs, the defect typically exhibits ill-defined borders and fine central trabeculations. More than 75% of all cases are discovered in adult women. About 70% occur in the posterior mandible, most often in edentulous areas. No expansion of the jaw is noted clinically.



Histopathologic Features: Microscopically, the defects contain cellular hematopoietic marrow. Lymphoid aggregates may be present. Bone trabeculae included in the biopsy specimen show no evidence of abnormal osteoblastic or osteoclastic activity.





Treatment and Prognosis: The radiographic findings, although often suggestive of the diagnosis, are not specific and may simulate those of a variety of other diseases. incisional biopsy, therefore, often is necessary to establish the diagnosis. Once the diagnosis is established, no further

treatment is needed. The prognosis is excellent and no association between focal osteoporotic marrow defects and anemia or other hematologic disorders has been established.

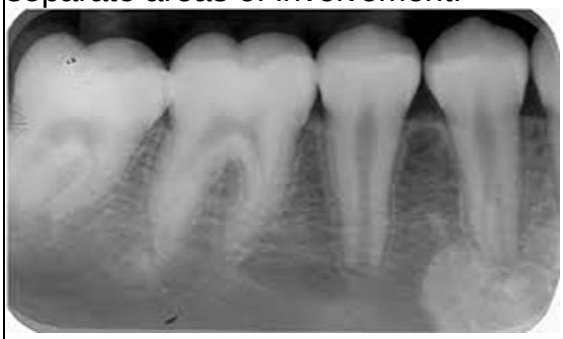
Idiopathic osteosclerosis

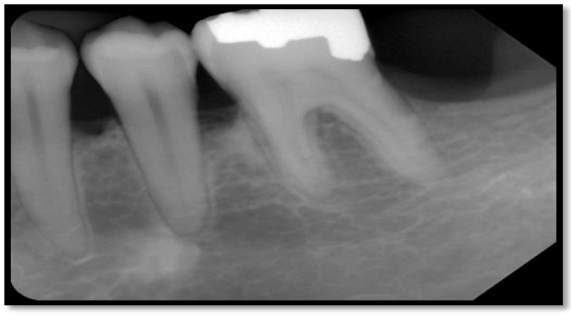
Idiopathic osteosclerosis refers to a focal area of increased radiodensity that is of unknown cause and cannot be attributed to any inflammatory, dysplastic, neoplastic, or systemic disorder. Idiopathic osteosclerosis also has been termed dense bone island, bone eburnation, bone whorl, bone scar, enostosis, and focal periapical osteopetrosis.

These sclerotic areas are not restricted to the jaws, and radiographically similar lesions may be found in other bones. Similar radiopaque foci may develop in the periapical areas of teeth with non-vital or significantly inflamed pulps; these lesions most likely represent a response to a low-grade inflammatory stimulus. Such reactive foci should be designated as condensing osteitis or focal chronic sclerosing osteomyelitis and should not be included under the designation of idiopathic osteosclerosis. Because past studies did not distinguish the idiopathic lesions from those of inflammatory origin, confusion in terminology has resulted.

Clinical and Radiographic Features

Although previous studies often are difficult to interpret because of differences in diagnostic criteria, the prevalence appears to be approximately 5%, with some investigators suggesting a slightly increased frequency in blacks and Asians. No significant sex predilection is seen. Upon review of several studies with long-term follow-up, a pattern has emerged. Although exceptions can be seen, most areas of idiopathic osteosclerosis arise in the late first or early second decade. Once noted, the lesions may remain static, but many reveal a slow increase in size. In almost all cases, once the patient reaches full maturity, all enlargement ceases and the sclerotic area stabilizes. In a smaller percentage, the lesion diminishes or undergoes complete regression. The peak prevalence of osteosclerosis occurs in the third decade, with the attainment of peak bone mass seen in the fourth decade. Idiopathic osteosclerosis in variably asymptomatic, not associated with detectable cortical expansion, and is typically detected during a routine radiographic examination. About 90% of examples are seen in the mandible, most often in the first molar area. The second premolar and second molar areas also are common sites. In most cases, only one focus of sclerotic bone is present. A small number of patients have two or even three separate areas of involvement.

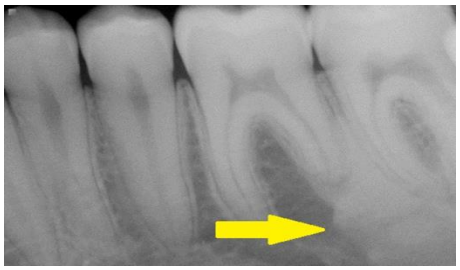


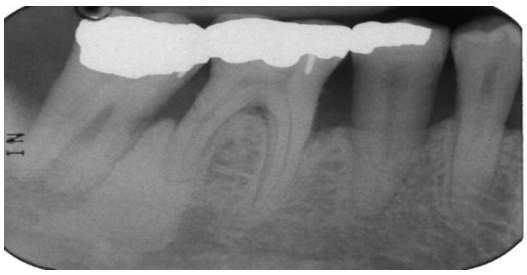


Radiographically

The lesions are characterized by a well-defined, rounded, or elliptic radiodense mass. Although the majority is uniformly radiopaque, occasional large lesions demonstrate a non-homogeneous mixture of increased and reduced radiopacity. This is most likely due to variation in the three-dimensional shape of the lesion and is unrelated to differences in the mineral content of the mass. The lesions vary from 3 mm to more than 2.0 cm in greatest extent. A radiolucent rim does not surround the radiodense area. Most examples of idiopathic osteosclerosis are associated with a root apex. In a lesser number of cases, the sclerotic area may extend into or be located only in the interradicular area is located in the jaw, with no apparent relationship to a tooth. Rarely, the

sclerotic bone may surround all or portions of an impacted tooth. Root resorption and movement of teeth have been noted but are uncommon.





Histopathologic Features: in the few microscopic studies that have been reported, the lesion consists of dense lamellar bone with scant fibro-fatty marrow. Inflammatory cells are inconspicuous or absent.

Diagnosis: Usually a diagnosis of idiopathic osteosclerosis may be made with confidence, based on history, clinical features, and radiographic findings. Biopsy is considered only if associated symptoms or significant cortical expansion is present. Although idiopathic osteosclerosis demonstrates radiographic and histopathologic similarities with a compact osteoma, the lack of cortical expansion and failure of continued growth rule against a neoplastic process. Differentiation from condensing osteitis may be difficult; but in the absence of adeep restoration or caries, a periapical radiodense area associated with a vital tooth is likely to represent idiopathic osteosclerosis.

Treatment and Prognosis If the lesion is discovered during adolescence, periodic radiographs appear prudent until the area stabilizes. After that point, no treatment is indicated for idiopathic osteosclerosis, because there is little or no tendency for the lesions to progress or change in adulthood.

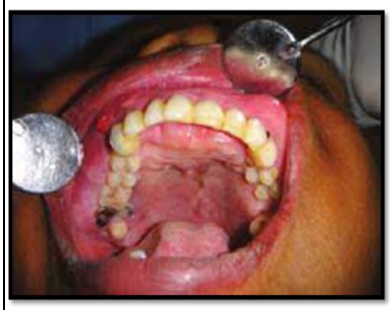
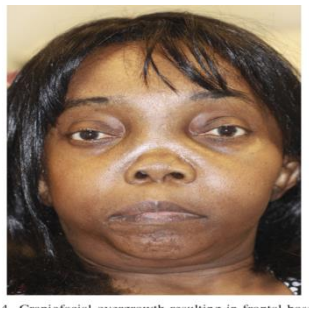
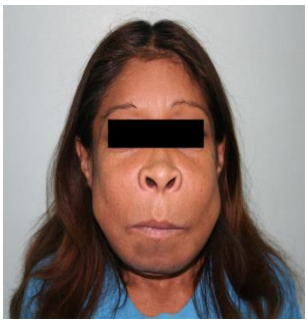
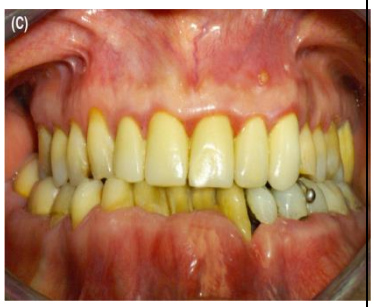
Paget's disease of bone (osteitis deformans)

Paget's disease of bone is a disease characterized by abnormal resorption and deposition of bone, resulting in distortion and weakening of the affected bones. The cause of Paget's disease is unknown, but inflammatory, genetic and endocrine factors may be contributing agents. In some studies, 15% to 30% of affected patients have a positive family history of the disease. The possibility that the disease is the result of a slow virus infection has received considerable attention in recent years, but a viral cause remains unproven, inclusion bodies identified as nucleocapsids from aparamyxo virus have been detected in osteoclasts in patients with Paget's disease, but a cause and effect relationship has not been established.

Clinical and Radiographic Features

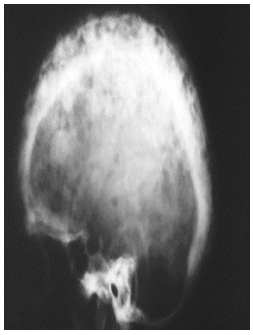
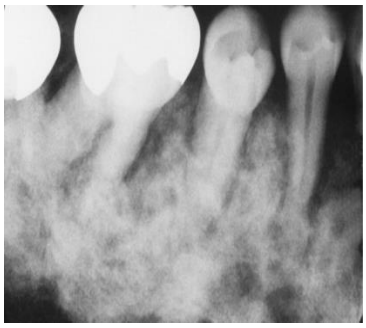
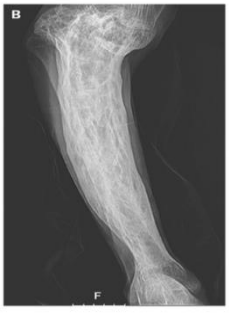
Paget's disease is relatively common, although there is a marked geographic variance in its prevalence. It is more common in Britain than in the United States, whereas it is rare in Africa and Asia. The disease principally affects older people and is rarely encountered in patients younger than 40 years of age. Men are affected more often than women, and whites are affected more than blacks. Reviews have estimated that 1 in 100 to 150 individuals greater than 45 years of age have Paget's disease. Subclinical disease is not rare, and an increased number of cases are being seen as the population ages. Asymptomatic disease often is discovered in radiographs taken for unrelated reasons or from an unexpected elevation in serum alkaline phosphatase. The frequency increases with age and the true prevalence (Including undiscovered subclinical disease) probably range s from 1% in the fifth decade to 10% in the teeth decade. Although the disease may be monostotic (limited to one bone), most cases of Paget's disease are polyostotic (more than one bone is affected). Symptoms vary; and some patients may remain relatively asymptomatic. Bone pain, which may be quite severe, is a common complaint. Affected bones become thickened, enlarged, and weakened. An involvement of weight-bearing bone often leads

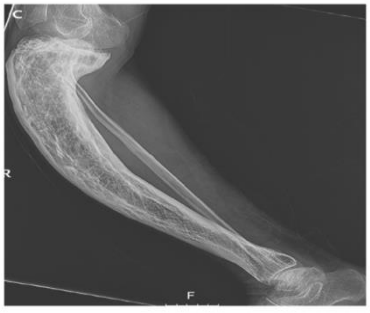
to a bowing deformity, Paget's disease affecting the skull generally leads to a progressive increase in the circumference of the head. Jaw involvement is present in approximately 17% of patients diagnosed with Paget's disease. Maxillary disease, which is far more common than mandibular involvement, results in enlargement of the middle third of the face. In extreme cases, the alteration results in a lion like facial deformity (leontiasisossea). Nasal obstruction, enlarged turbinates, obliterated sinuses, and deviated septum may develop secondary to maxillary involvement. The alveolar ridges tend to remain symmetric but become grossly enlarged. If the patient is dentulous, the enlargement causes spacing of the teeth. Edentulous patients may complain that their dentures no longer fit because of the increased alveolar size.

Radiographically

The early stages of Paget's disease reveal a decreased radiodensity of the bone and alteration of the trabecular pattern. Particularly in the skull, large circumscribed area s of radiolucency may be present (osteoporosis circum scrtpta). During the osteoblastic phase of the disease, patchy areas of sclerotic bone are formed, which tend to become confluent. The patchy sclerotic areas often are described as having a "cotton wool" appearance. On radiographic examination, the teeth often demonstrate extensive hypercementosis. On initial discovery of Paget's disease, bone scintigraphy should be performed to evaluate fully the extent of involvement. When the mandible is affected, the bones can may demonstrate marked uptake throughout the entire mandible from condyle to condyle, a feature that has been termed black beard or Lincoln's Sign. Radiographic findings of Paget's disease may resemble those of cemento-osseous dysplasia. Patients with presumed cementa-osseous dysplasia who demonstrate clinical expansion of the jaws should be evaluated further to rule out Paget's disease.

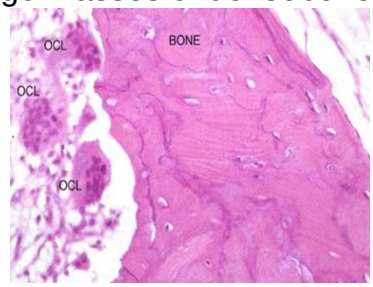




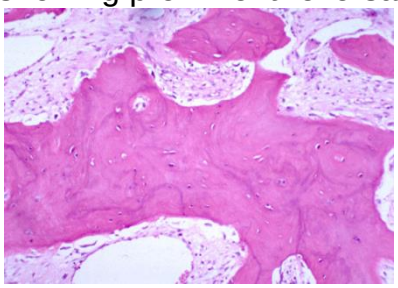
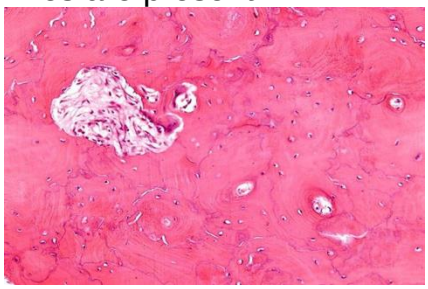


Histopathologic Features

Microscopic examination shows an apparent uncontrolled alternating resorption and formation of bone in the active resorptive stages, numerous osteoclasts surround bone trabeculae and show evidence of resorptive activity. Simultaneously, osteoblastic activity is seen with formation of osteoid rims around bone trabeculae. A highly vascular fibrous connective tissue replaces the marrow. A characteristic microscopic feature is the presence of basophilic reversal lines in the bone. These lines indicate the junction between alternating resorptive and formative phases of the

bone and result in a "jig saw puzzle." or "mosaic." appearance of the bone. In the less active phases, large masses of densebone showing prominent reversal lines are present.



Diagnosis: Patients with Paget's disease show:

1-high elevations in serum alkaline phosphatase levels but usually have normal blood calcium and phosphorus levels.

2-Urinary hydroxyl proline levels also may be elevated markedly.

3-Newer and more sensitive markers of bone resorption are N-telopeptides and pyridinoline cross-link assays. The clinical and radiographic features, combined with supportive laboratory findings, are typically sufficient for diagnosis. Histopathologic examination can be confirmatory but often is unnecessary for a strong presumptive diagnosis

Treatment and Prognosis:

Although Paget's disease is chronic and slowly progressive, it is seldom the cause of death. In patients with more limited involvement and no symptoms. treatment often is not required.

1-In asymptomatic patients, systemic therapy is usually not initiated unless the alkaline phosphatase is more than 25% to 50% above normal.

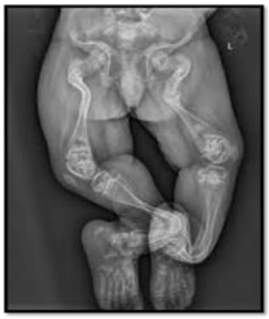
2-Use of parathyroid hormone antagonists, such as calcitonin and biphosphonates, can reduce bone turnover and improve the biochemical abnormalities.

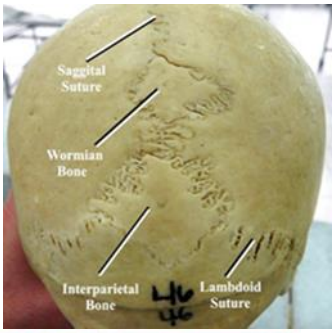
3-Edentulous patients may require new and larger dentures periodically to compensate for progressive enlargement of the alveolar processes. 4-Dental complications include difficulties in extraction of teeth exhibiting significant hypercementosis.

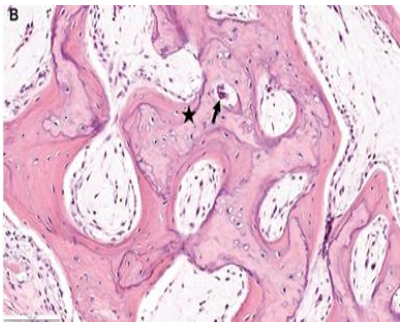
5-Development of a malignant bone tumor, usually an osteosarcoma, is a recognized complication of Paget's disease. Osteosarcoma in adults over the age of 40 is quite uncommon in individuals who do not have Paget's disease.

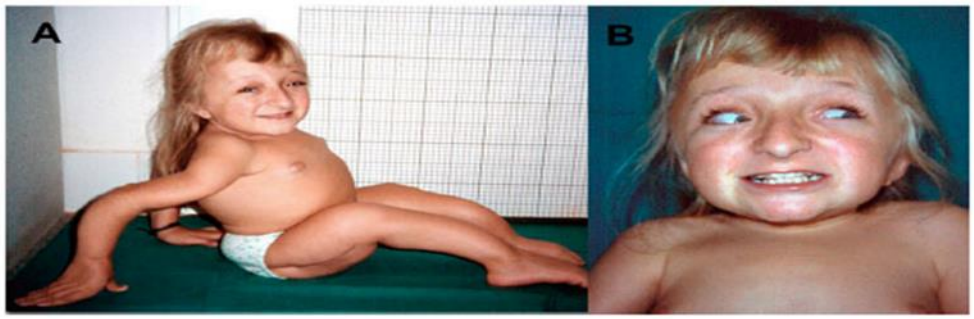
6-Benign and malignant giant cell tumors also may develop in bones affected by Paget's disease. Most of these occur in the craniofacial skeleton.

Lab.8 Metabolic and genetic disease

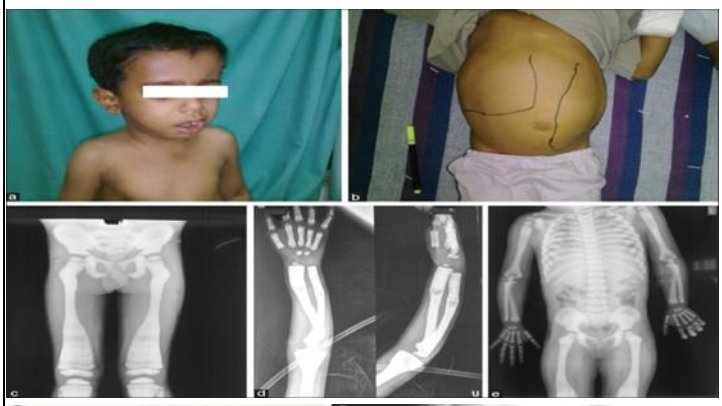




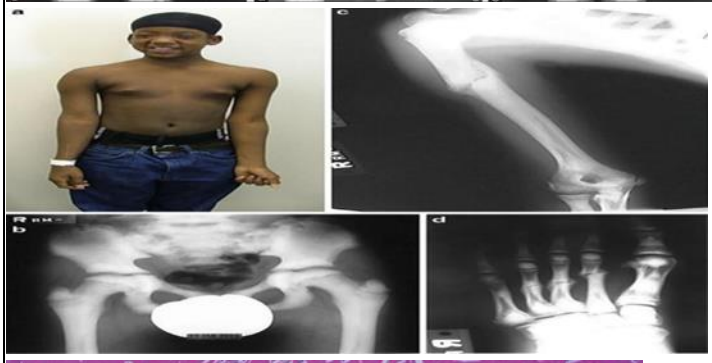




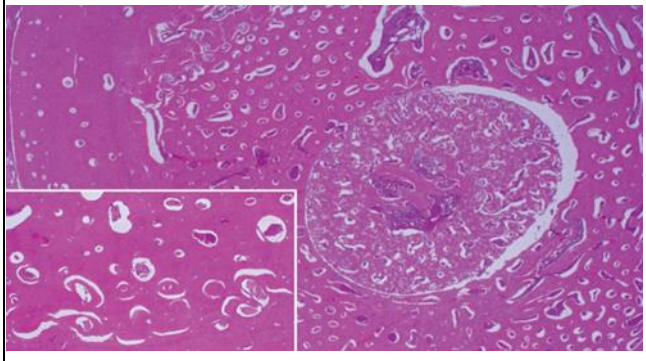
Osteogenesis imperfect



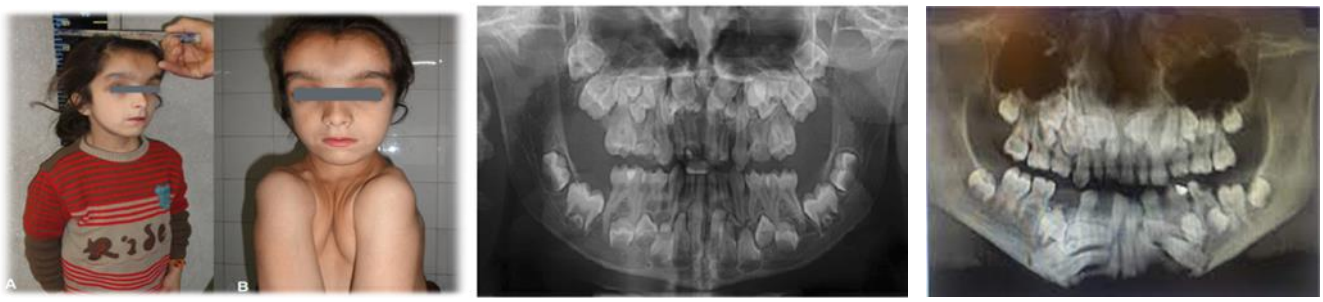
Infantile osteopetrosis



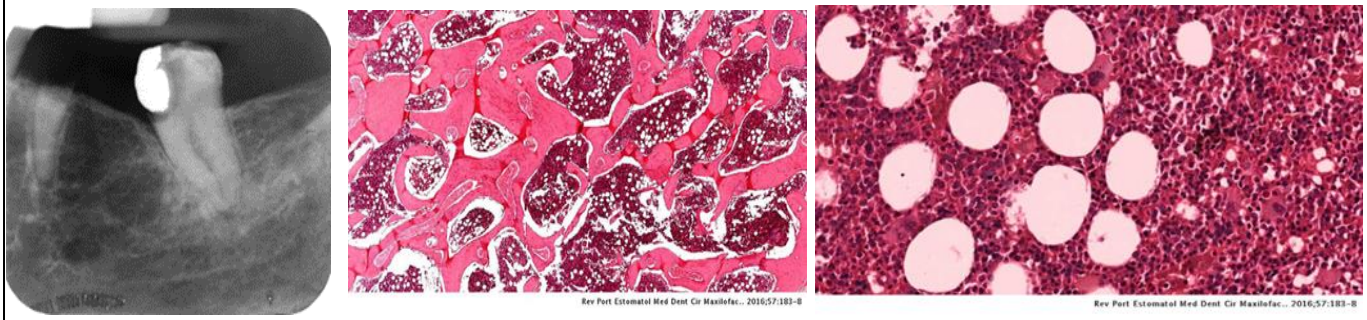
Adult osteopetrosis



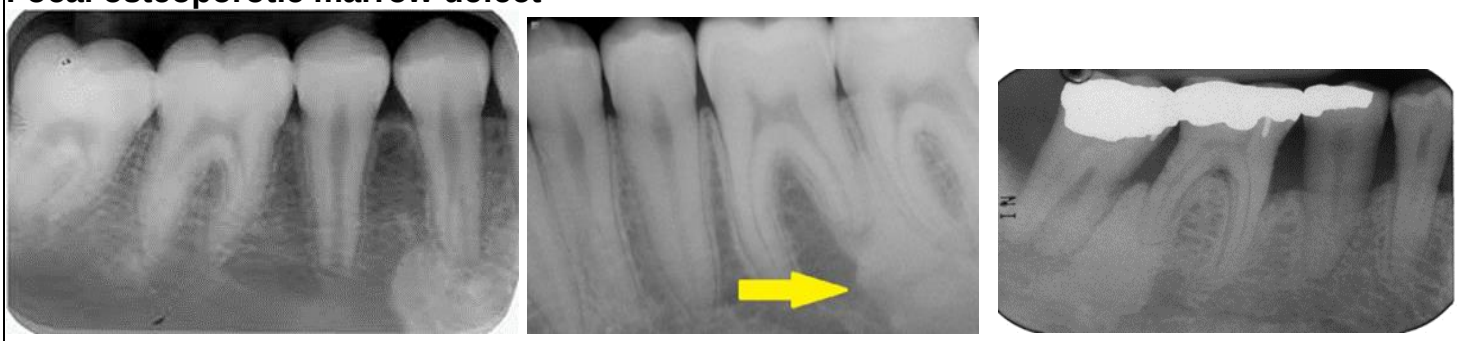
Osteopertosis



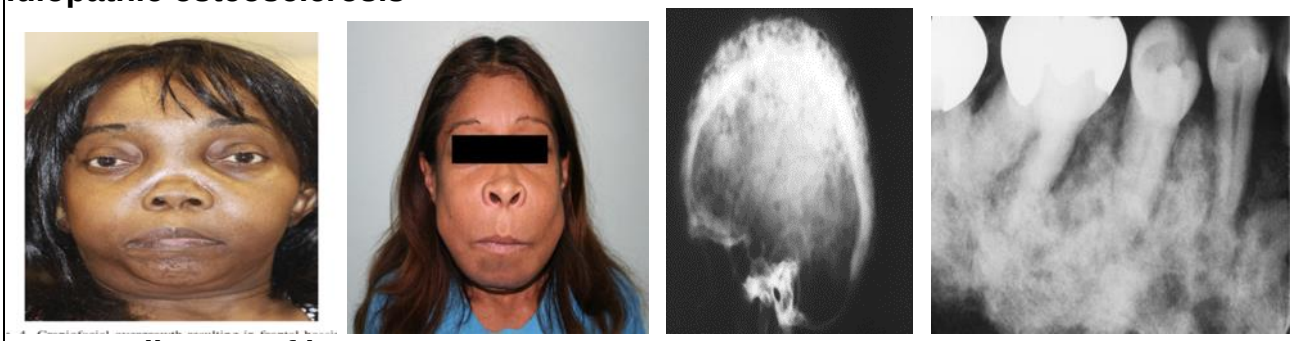
Cleidocranial dysplasia



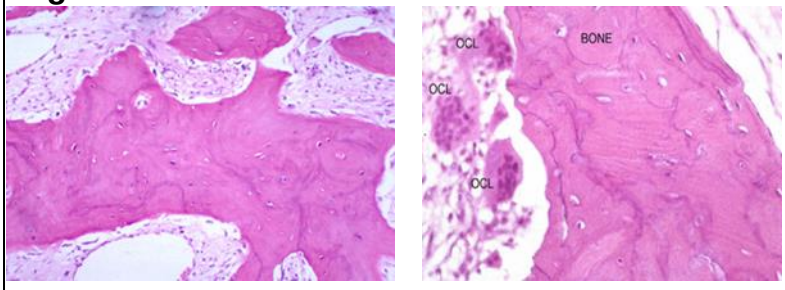
Focal osteoporotic marrow defect



Idiopathic osteosclerosis



Paget's disease of bone



Paget's disease

Oral Pathology

Lec. 12+13

Odontogenic tumor

Odontogenic tumors are derived from the epithelial and/or mesenchymal remnants of the tooth forming apparatus. Therefore, they are found exclusively in the mandible and maxilla (and occasionally in the gingiva). The origin and pathogenesis of this group of lesions are unknown. Clinically, odontogenic tumors are typically asymptomatic, although they may cause jaw expansion, movement of teeth, root resorption, and bone loss. Odontogenic tumors tend to mimic microscopically the cell or tissue of origin. Histologically, they may resemble soft tissue components of the enamel organ or dental pulp, or they may contain hard tissue elements of enamel, dentin, and/or cementum. Biologically, lesions in this group range from hamartomatous proliferations to malignant neoplasms with metastatic capabilities. Several classification schemes based on histologic patterns have been devised for this complex group of lesions. Common to all is the division of tumors into those composed of odontogenic epithelial elements, those composed of odontogenic mesenchyme, and those that are proliferations of both epithelium and mesenchyme (ectomesenchyme). As classified on the basis of biological behavior, they range from clinically trivial (i.e., benign, no recurrence potential) to malignant.

Biological classification of odontogenic tumors

BENIGN, NO RECURRENCE POTENTIAL

Adenomatoid odontogenic tumor
Squamous odontogenic tumor
Cementoblastoma
Odontoma

BENIGN, SOME RECURRENCE POTENTIAL

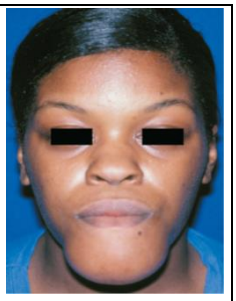
Cystic ameloblastoma
Calcifying epithelial odontogenic tumor
Central odontogenic fibroma
Ameloblastic fibroma and fibro-odontoma

BENIGN AGGRESSIVE

Ameloblastoma
Clear cell odontogenic tumor
Odontogenic ghost cell tumor
Odontogenic myxoma
Odontoameloblastoma

MALIGNANT

Malignant ameloblastoma
Ameloblastic carcinoma
Primary intraosseous carcinoma
Odontogenic ghost cell carcinoma
Ameloblastic fibrosarcoma.



Tumors of Odontogenic Epithelia

- **AMELOBLASTOMA**

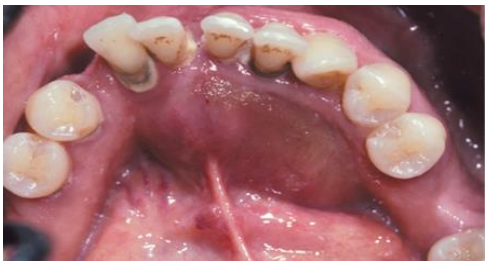
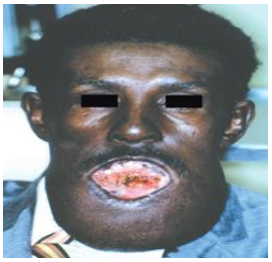
The ameloblastoma is the most common clinically significant odontogenic tumor.

Ameloblastomas are tumors of odontogenic epithelial origin. Theoretically they may arise from rests of dental lamina from a developing enamel organ, from the epithelial lining of an odontogenic cyst, or from the basal cells of the oral mucosa. Ameloblastom as are slow-growing locally invasive tumors that run a benign course in most cases. They occur in three different clinicoradiographic situations which deserve separate consideration because of differing therapeutic considerations and prognosis.

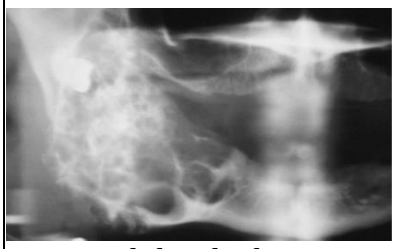
❖ Conventional solid or multicystic intraosseous ameloblastoma

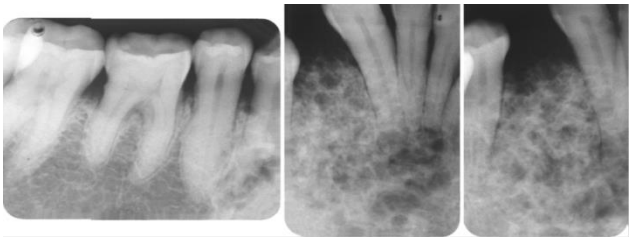
Clinical and Radiographic Features

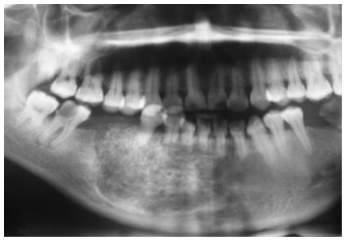
Conventional solid or multicystic intraosscous ameloblastoma is encountered in patients over a wide age range. It is rare in children younger than age 10 and relatively uncommon in the 10-to 19-year-old group. The tumor shows an approximately equal prevalence in the third to seventh decades of life. There is no significant gender predilection. About 85% of conventional ameloblastomas occur in the mandible, most often in the molar-ascending ramus area. About 15% of ameloblastomas occur in the maxilla, usually in the posterior regions. The tumor is often asymptomatic, and smaller lesions are detected only during a radiographic examination. A painless swelling or expansion of the jaw is the usual clinical presentation. If untreated. The lesion may grow slowly to massive tumor. Pain and paresthesia are uncommon, even with large tumors.


The most typical radiographic feature is that of a multilocular radiolucent lesion. The lesion is often described as having a "soap bubble" appearance when the radiolucent loculations are large and as being "honey combed" when the loculations are small. Buccal and lingual cortical expansion is frequently present. Resorption of the roots of teeth adjacent to the tumor is common. In many cases, an unerupted tooth, most often a mandibular third molar is associated with the radiolucent defect. Solid ameloblastomas may radiographically appear as unilocular radiolucent defects which may resemble almost any type of cystic lesion. The desmoplastic ameloblastoma has a marked predilection to occur in the anterior regions of the jaws particularly the maxilla. Radiographically, this type seldom suggests the diagnosis of ameloblastoma and usually resembles a fibro-osseous lesion because of its mixed radiolucent and radiopaque appearance.


Large multilocular lesion

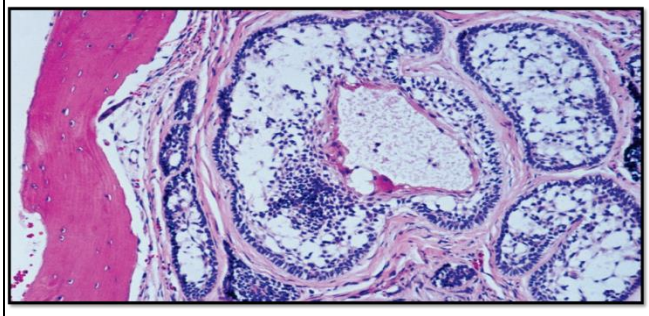
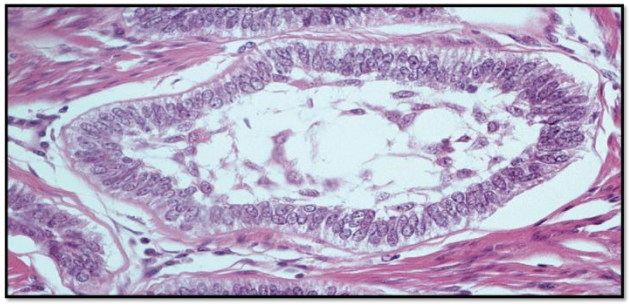

Small multiocular lesion


Desmoplastic Ameloblastoma

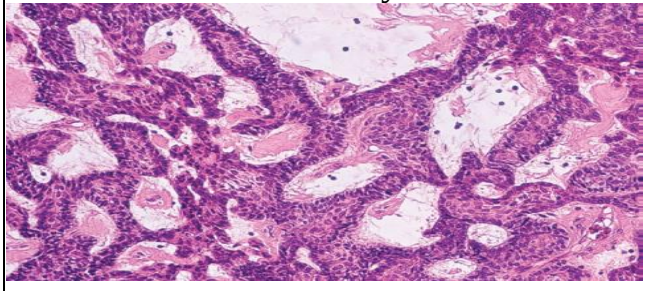
Histopathologic Features (Conventional solid or multicystic intraosscous ameloblastomas)

Shows a remarkable tendency to undergo cystic change; grossly most tumors have varying combinations of cystic and solid features. The cysts may be seen only at the microscopic level or may be present as multiple large cysts that include most of the tumor. Several microscopic subtypes of conventional ameloblastoma are recognized, but these microscopic patterns generally have little significance on the behavior of the tumor. Large tumors often show a combination of microscopic patterns. The follicular and plexiform patterns are the most common. Less common histopathologic patterns include the acanthomatous, granular cell, desmoplastic, and basal cell types.

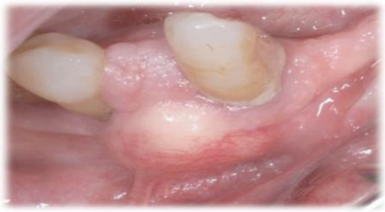
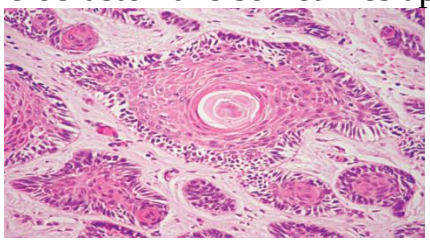
***Follicular pattern*.** The follicular histopathologic pattern is the most common and recognizable. Islands of epithelium resemble enamel organ epithelium in a mature fibrous connective tissue stroma. The epithelial nests consist of a core of loosely arranged angular cells resembling the stellate reticulum of an enamel organ. A single layer of tall columnar ameloblast-like cells surrounds this central core. The nuclei of these cells are located at the opposite pole to the basement membrane (reversed polarity). In other areas the peripheral cells may be more cuboidal and resemble basal cells. Cyst formation is common and may vary from microcysts. Which form within the epithelial islands, to large macroscopic cysts, which may be several centimeters in diameter.

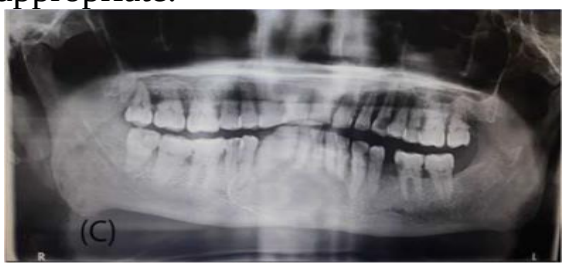
Plexiform pattern. The plexiform type of ameloblastoma consists of long, anastomosing cords or larger sheets of odontogenic epithelium. The cords or sheets of epithelium are bounded by columnar or cuboidal ameloblast-like cells surrounding more loosely arranged epithelial cells. The supporting stroma tends to be loosely arranged and vascular. Cyst formation is relatively uncomm on in this variety.

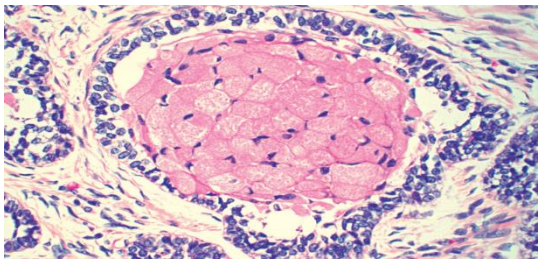


***Acanthomatous pattern"*.** when extensive squamous metaplasia often associated with keratin formation occurs in the central portions of the epithelial islands of a follicular ameloblastoma. The term acanthomatous ameloblastoma is sometimes applied.

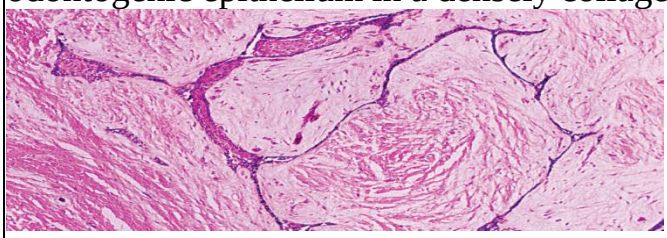



***Granular cell pattern"*.** Ameloblastomas may sometimes show transformation of groups of lesional epithelial cells to granular cells. These cells have abundant cytoplasm filled with eosinophilic granules that resemble Iysosomes ultrastructurally and histochemically. Although originally considered to represent an aging or degenerative change in long-standing lesions, this variant has been seen in young patients and in clinically aggressive tumors. When this granular cell change is extensive in an ameloblastoma the designation of granular cell ameloblastoma is appropriate.

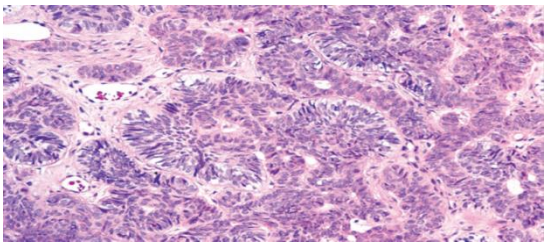




Desmoplastic pattern. This type of ameloblastoma contains small islands and cords of odontogenic epithelium in a densely collagenized stroma.

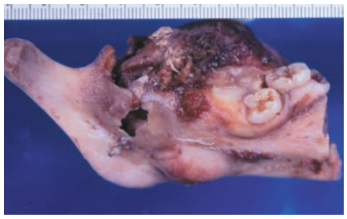


***Basal cell pattern*.** The basal cell variant of ameloblastoma is the least common type. These lesions are composed of nests of uniform basaloid cells and they histopathologically are very similar to basal cell carcinoma of the skin. No stellate reticulum is present in the central portions of the nests. The peripheral cells about the nests tend to be cuboidal rather than columnar.

***Treatment and Prognosis*.** Patients with conventional solid or multicystic intraosseous ameloblastomas have been treated by a variety of means. These range from simple enucleation and curettage to *enbloc* resection. Attempts to remove the tumor by curettage often leave small islands of tumor within the bone, which later manifest as recurrences. Recurrence rates

of 50% to 90% have been reported in various studies after curettage. Marginal resection is the most widely used treatment, but recurrence rates of up to 15% have been reported after marginal or block resection. Ameloblastomas of the posterior maxilla are particularly dangerous because of the difficulty of obtaining an adequate surgical margin around the tumor.

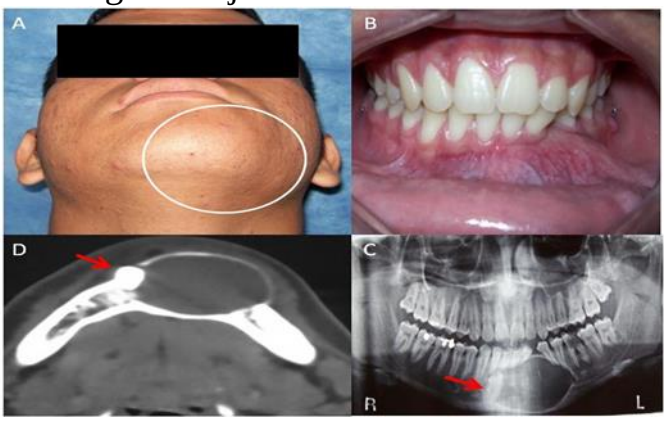


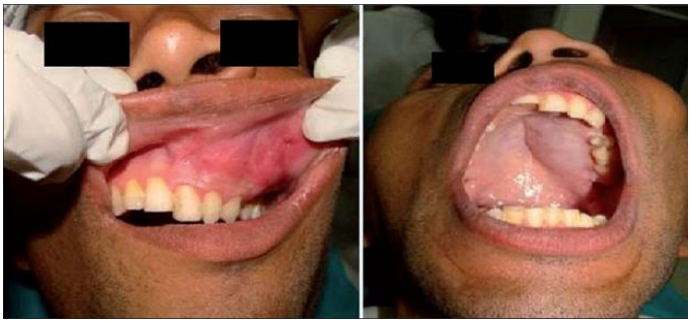
Unicystic ameloblastoma

The unicystic ameloblastoma deserves separate consideration based on its clinical, radiographic, and pathologic features and its response to treatment. Unicystic ameloblastomas account for 10% to 15% of all intraosseous ameloblastomas in various studies. Whether the unicystic ameloblastoma originates *de novo* as a neoplasm or whether it is the result of neoplastic transformation of non-neoplastic cyst epithelium has been long debated. Both mechanisms probably occur, but proof of which is involved in an individual patient is virtually impossible to obtain.

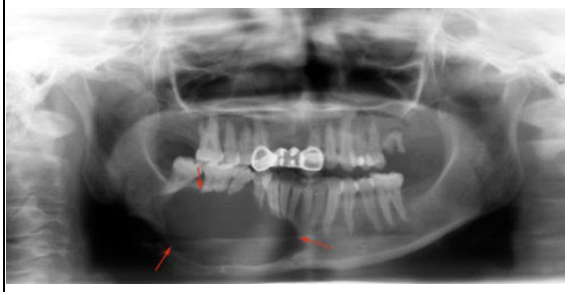
Clinical and Radiographic Features

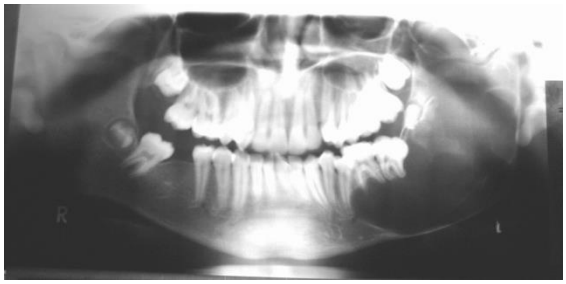
Unicystic ameloblastomas are most often seen in younger patients, with about 50% of all such tumors diagnosed during the second decade of life. The average age in on large series was 23 years. More than 90% of unicystic ameloblastomas are found in the mandible, usually in the posterior regions. The lesion is often a symptomatic, although large lesions may cause a painless swelling of the jaws.





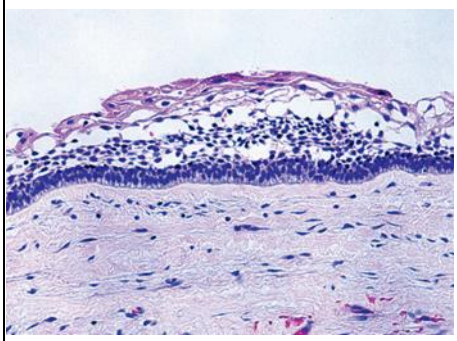
In many patients, this lesion typically appears as a circumscribed radiolucency that surrounds the crown of an unerupted mandibular third molar, clinically resembling a dentigerous cyst. Other tumors simply appear as sharply defined radiolucent areas and are usually considered to be a primordial radicular, or residual cyst, depending on the relationship of the lesion to teeth in the area. In some instances, the radiolucent area may have scalloped margins but is still a unicystic ameloblastoma.



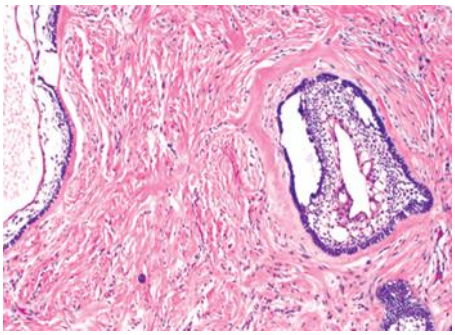


Histopathologic Features (unicystic ameloblastoma)

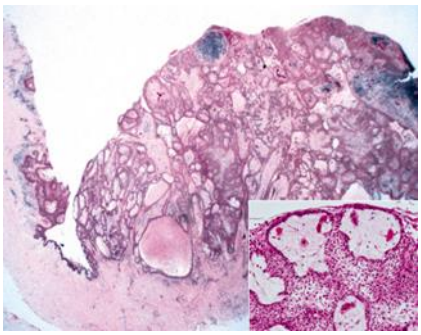
Three histopathologic variants of unicystic ameloblastoma have been described. In the first type **(luminal unicystic ameloblastoma)** the tumor is confined to the luminal surface of the cyst. The lesion consists of a fibrous cyst wall with a lining that consists totally or partially of ameloblastic epithelium. This demonstrates a basal layer of columnar or cuboidal cells with hyper chromatic nuclei that show reverse polarity and basilar cytoplasmic vacuolization. The overlying epithelial cells are loosely cohesive and resemble stellate reticulum. This finding does not seem to be related to inflammatory edema, in the second microscopic variant, one or more nodules of ameloblastoma project from the cystic lining into the lumen of the cyst. This type is called an **intraluminal unicystic ameloblastoma**. These nodules may be relatively small or largely fill the cystic lumen. In some cases, the nodule of tumor that projects into the lumen demonstrates an edematous plexiform pattern that resembles the plexiform pattern seen in conventional amloblastomas. These lesions are sometimes referred to as plexiform unicystic ameloblastomas. The intraluminal cellular proliferation does not always meet the strict histopathologic criteria for ameloblastoma and this may be secondary to inflammation that nearly always accompanies this pattern. Typical ameloblastoma, however, may be found in other less inflamed parts of the specimen in the third variant known as **mural unicystic ameloblastoma** the fibrous wall of the cyst is infiltrated by typical follicular or plexiform ameloblastoma. The extent and depth of the ameloblastic infiltration may vary considerably. With any presumed unicystic ameloblastoma multiple sections through many levels of the specimen are necessary to rule out the possibility *of* mural invasion of tumor cells.



LuminalUA



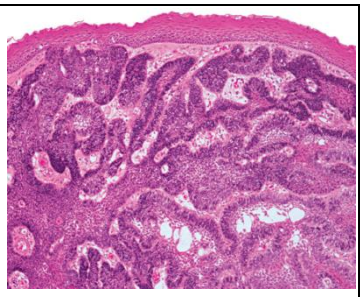
Intraluminal UA



Mural UA

Treatment

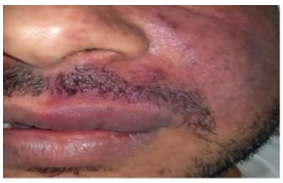
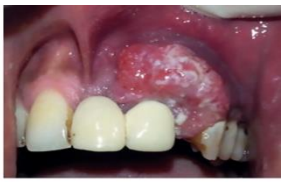
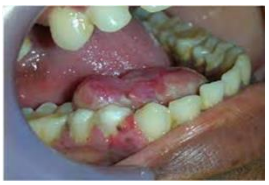
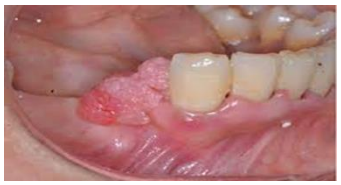
Cystic ameloblastomas may be treated less aggressively, but with the knowledge that recurrences are often associated with simple curettage. For cystic ameloblastoma, treatment options can range from enucleation to resection, although recurrences are more likely if enucleated.



❖ Peripheral (extraosseous) ameloblastoma

The peripheral ameloblastoma is uncommon and accounts for about 1 % of all ameloblastomas. This tumor probably arises from rests of dental lamina beneath the oral mucosa or from the basal epithelial cells of the surface epithelium. Histopathologicall y, these lesions have the same features as the intraosseous form of the tumor.

Clinical Features The peripheral ameloblastoma is usually a painless, non-ulcerated sessile or pedunculated gingival or alveolar mucosal lesion. The clinical features are non-specific and most lesions are clinically considered to represent a fibroma or pyogenic granuloma. Most examples are smaller than 1.5 cm but larger lesions have been reported. The tumor has been found in patients over a wide age range, but most are seen in middle-aged persons with an average reported age of 52 years. Peripheral ameloblastomas are most commonly found on the posterior gingival and alveolar mucosa and they are somewhat more common in mandibular than in maxillary areas. In some cases, the superficial alveolar bone becomes slightly eroded but significant bone involvement does not occur. A few examples of a microscopically identical lesion have been reported in the buccal mucosa at some distance from the alveolar or gingival soft tissues.

Hislopathologic Features: Peripheral ameloblastomas have islands of ameloblastic epithelium that occupy the lamina propria underneath the surface epithelium. The proliferating epithelium may show any of the features described for the intraosseous ameloblastoma; plexiform or follicular patterns are the most common. Connection of the tumor with the basal layer of the surface epithelium is seen in about 50% of cases.

Treatment of peripheral ameloblastoma: Peripheral ameloblastomas should be treated in a more conservative fashion.

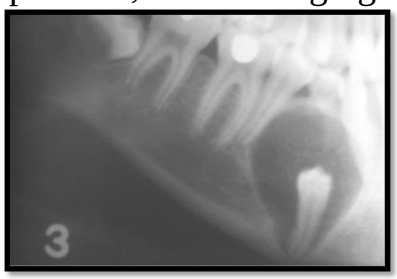
Adenomatoid odontogenic tumor

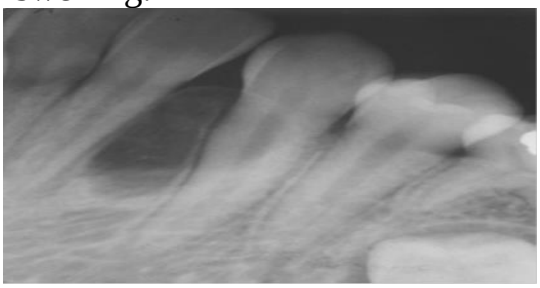
Adenomatoid odontogenic tumor (AOT) was formerly termed *adenoameloblastoma* because it was believed to be a subtype of ameloblastoma that contains duct like or gland like structures. Clinically, microscopically, and behaviorally, it is clearly different from ameloblastoma, and the term *adenoameloblastoma* is not used.

Clinical Features. AOTs are seen in a rather narrow age range—between 5 and 30 years—with most cases appearing in the second decade. Females are more commonly affected than males. Lesions often appear in the anterior portion of the jaws, more often in the anterior maxilla, generally in association with the crowns of impacted teeth. Three variants of this tumor have been identified: follicular (73% of cases),extrafollicular (24%), and peripheral (3%).

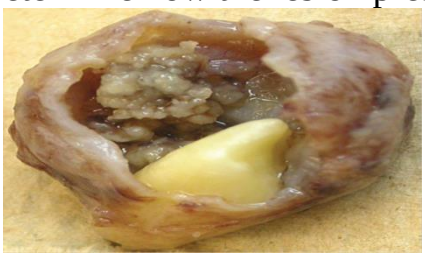
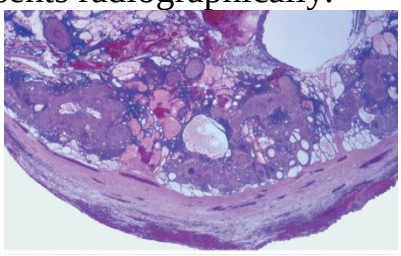
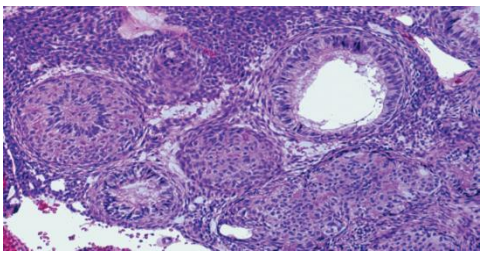
Radiographically, the follicular AOT is a well-circumscribed unilocular lesion that usually appears around the crown of an impacted tooth; the extrafollicular type usually presents as a

well-defined unilocular radiolucency above, between, or superimposed over the roots of an unerupted tooth. Lesions typically are radiolucent but may have small opaque foci distributed throughout, reflecting the presence of calcifications in the tumor tissue. When they are located between anterior teeth, divergence of roots may be seen. The peripheral type is characterized by a painless, nontender gingival swelling.





***Histopathology*.** An intracystic epithelial proliferation is composed of polyhedral to spindle cells. The pattern typically is lobular, although some areas may show a syncytial arrangement of cells. Rosettes and duct like structures of columnar epithelial cells give the lesion its characteristic microscopic features. The number, size, and degree of calcification of these foci determine how the lesion presents radiographically.

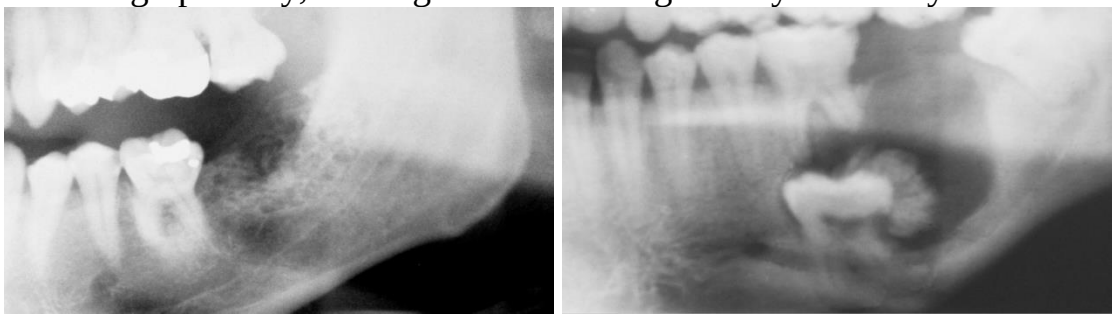
Treatment. Conservative treatment (enucleation) is all that is required. AOTs are benign, encapsulated lesions that do not recur.

Calcifying epithelial odontogenic tumor (pindborg tumor)

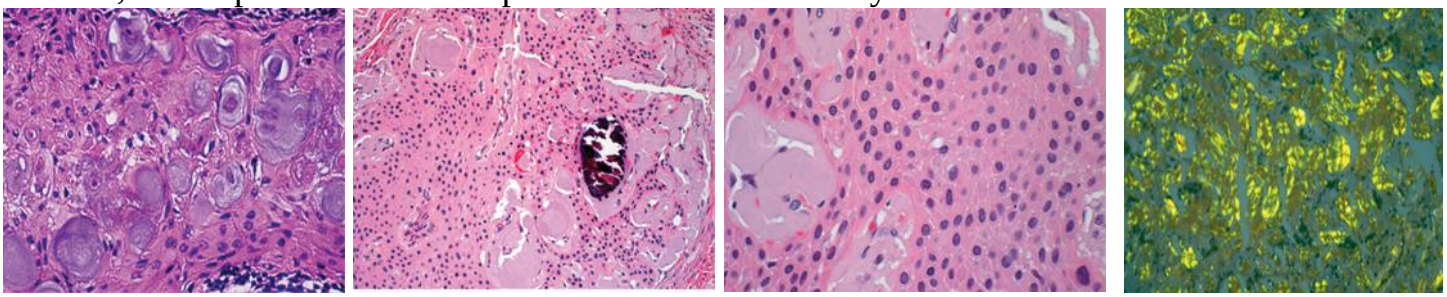
Calcifying epithelial odontogenic tumor (CEOT), also known as *Pindborg tumor* after the oral pathologist who first described the entity, is a benign tumor of odontogenic origin that shares many clinical features with ameloblastoma. Microscopically, however, there is no resemblance to ameloblastoma, and radiographically distinct differences will often be noted. The cells from which these tumors are derived are unknown, although dental lamina remnants and the stratum intermedium of the enamel organ have been suggested.

***Clinical Features*.** CEOTs are seen in patients ranging in age from the second to the tenth decade, with a mean age of about 40 years. There is no gender predilection. The mandible is affected twice as often as the maxilla, and a predilection for the molarramus region has been noted, although any site may be affected. Peripheral lesions, usually in the anterior gingiva, account for less than 5% of cases. Jaw expansion or incidental observation on a routine radiographic survey is the usual way in which these lesions are discovered. Radiographically, the lesions are often associated with impacted teeth. The lesions may be unilocular or multilocular. Small loculations in some lesions have prompted use of the term *honeycomb* to describe this lucent pattern. A CEOT may be completely radiolucent, or it may contain opaque foci—a

reflection of the calcified amyloid seen microscopically. The lesions are usually well circumscribed radiographically, although sclerotic margins may not always be evident.



***Histopathology*.** The CEOT has a unique and sometimes bizarre microscopic pattern. Large polygonal epithelial cells, arranged in sheets or islands, contain nuclei that show considerable variation in size and shape. Mitotic figures are rare. The cytoplasm is abundant and eosinophilic. Focal zones of clear cells occasionally can be seen in a socalled clear cell variant. Extracellular amyloid of epithelial origin is also typical of these tumors. This homogeneous, pale-staining eosinophilic material can be stained with Congo red or thioflavine T. Concentric calcific deposits with a characteristic annular staining pattern (Liesegang rings), seen in the amyloid material, are responsible for radiopacities when sufficiently dense.



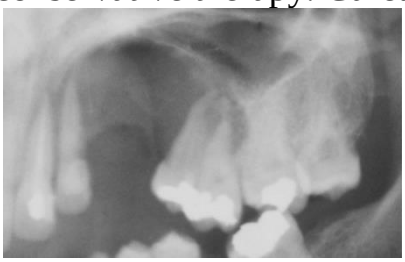
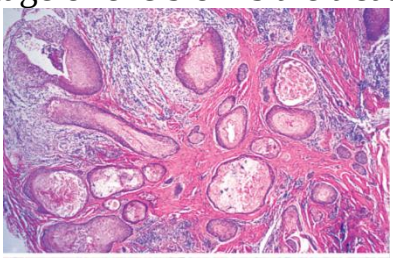
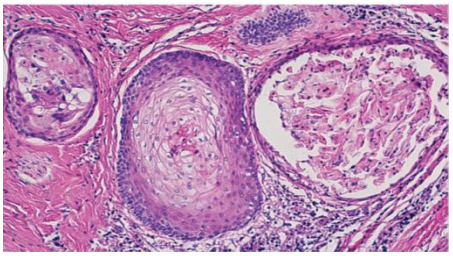
***Treatment*.** This tumor has a locally infiltrative potential but apparently not to the same extent as ameloblastoma. It is slow-growing and causes morbidity through direct tumor extension. Various forms of surgery, ranging from enucleation to resection, have been used to treat CEOTs. The overall recurrence rate has been less than 20%, indicating that aggressive surgery is not indicated for the management of most of these benign neoplasms. very rare examples of malignant transformation of this tumor have been reported.

Squamous Odontogenic Tumor

Squamous odontogenic tumor is one of the rarest odontogenic tumor and account 4% of all odontogenic tumor, because squamous odontogenic tumor involves the alveolar process, the lesion is believed to be derived from neoplastic transformation of the rests of Malassez. It occurs in the mandible and the maxilla with equal frequency, favoring the anterior region of the maxilla and the posterior region of the mandible. Multiple lesions have been described in about 20% of affected patients, as have familial multicentric lesions.

The age range for this tumor extends from the second through seventh decades, with a mean age of 40 years. There is no gender predilection. Patients usually experience no symptoms, although tenderness and tooth mobility have been reported.

Radiographically: this lesion typically is a well-circumscribed, often semilunar lesion associated with the cervical region of roots of teeth. Microscopically, it has some similarity to ameloblastoma, although it lacks the columnar peripherally palisaded layer of epithelial cells. Squamous odontogenic tumors have some invasive capacity and infrequently recur after conservative therapy. Curettage or excision is the treatment of choice.

Mixed OdontogenicTumors :

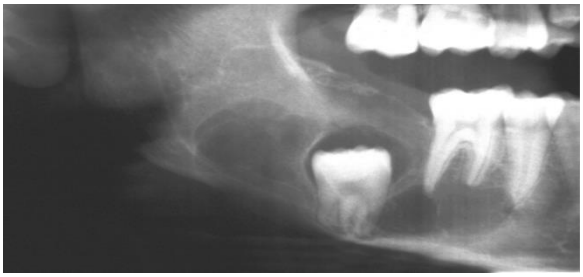
The group of mixed odontogenic tumors, composed of proliferating odontogenic epithelium in a cellular ectomesenchyme resembling the dental papilla, poses problems in classification. Some of these lesions show varying degrees of inductive effect by the epithelium on the mesenchyme, leading to the formation of varying amounts of enamel and dentin. Some of these lesions (the common odontomas) are clearly nonneoplastic developmental anomalies; others appear to be true neoplasms. The nature of others is uncertain. In some instances, the histopathologic findings alone cannot distinguish between the neoplastic lesions and the developmental anomalies. Clinical and radiographic features often are of considerable assistance in making this distinction.

Ameloblastic Fibroma and Ameloblastic Fibro-odontoma

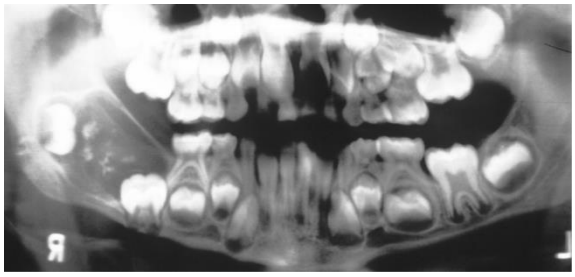
Ameloblastic fibroma and ameloblastic fibro-odontoma are considered together because they appear to be slight variations of the same benign neoplastic process. Except for the presence of an odontoma, people afflicted with either of these two lesions share similar features of age, gender, and location. The biological behaviors of these lesions are also similar. Both are benign mixed odontogenic tumors composed of neoplastic epithelium and mesenchyme with microscopically identical soft tissue components.

Clinical Features. These neoplasms occur predominantly in children and young adults. The mean age is about 12 years, and the upper age limit is around 40 years. The mandibular molar-ramus area is the favored location for these lesions, although they may appear in any region. There is no gender predilection.

Radiographically, these lesions are well circumscribed and usually are surrounded by a sclerotic margin. They may be unilocular or multilocular and may be associated with the crown of an impacted tooth. An opaque focus that appears within the ameloblastic fibro-odontoma is due to the presence of an odontoma. This lesion therefore appears as a combined lucent-opaque lesion; the ameloblastic fibroma is completely lucent radiographically.

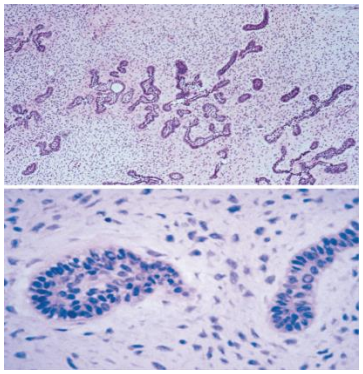


Ameloblastic Fibroma

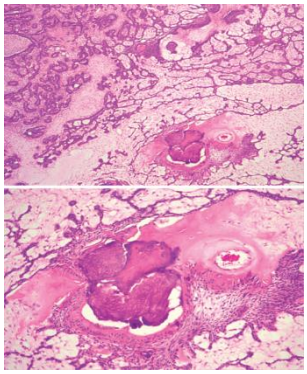


Ameloblastic Fibro-Odontoma

Histopathology. These lesions are lobulated in general configuration and usually are surrounded by a fibrous capsule. The tumor mass is composed predominantly of primitive-appearing myxoid connective tissue. The general absence of collagen gives this component a resemblance to dental pulp. Evenly distributed throughout the tumor mesenchyme are ribbons or strands of odontogenic epithelium that typically are two cells wide. Rarely, the epithelium may be more follicular in appearance, resembling ameloblastoma. The epithelial component has been compared microscopically to the dental lamina that proliferates from oral epithelium in the early stages of tooth development. In ameloblastic fibro-odontoma, one or more foci contain enamel and dentin. This may be seen in the form of a compound or complex odontoma, the presence of which does not alter treatment or prognosis.



Ameloblastic Fibroma



Ameloblastic Fibro-Odontoma

Treatment. Because of tumor encapsulation and the general lack of invasive capacity, this lesion is treated through a conservative surgical procedure such as curettage or excision. Recurrences have been documented, but they are uncommon. A rare malignant counterpart known as *ameloblastic fibrosarcoma* has been documented as arising in the jaws de novo or from preexisting or recurrent ameloblastic fibroma. In this lesion, the mesenchymal component has the appearance of a fibrosarcoma, and the epithelial component appears as it does in the benign lesion. Clinically, ameloblastic fibrosarcoma occurs at about 30 years of age and more often in the mandible than in the maxilla. Symptoms of pain and paresthesia may be present. This locally aggressive lesion has metastatic potential. Resection is therefore the treatment of choice.

❖ Odontoameloblastoma

The odontoameloblastoma is an extremely rare odontogenic tumor that contains an ameloblastomatous component and odontoma-like elements. Because of the rarity of odontoameloblastomas little reliable information is available. The lesion appears to occur more often in the mandible of younger patients, Pain, delayed eruption of teeth . and expansion of the

affected bone may be noted. Radiographically. the tumor shows a radiolucent destructive process that contains calcified structures. These have the radiodensity of tooth structure and may resemble miniature teeth or occur as larger masses of calcified material similar to a complex odontoma.

Histopathologic Features

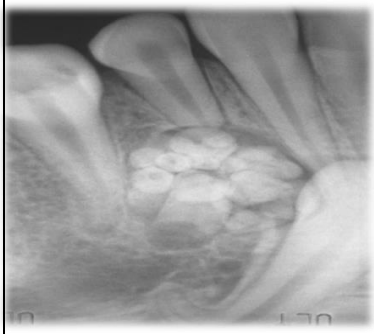
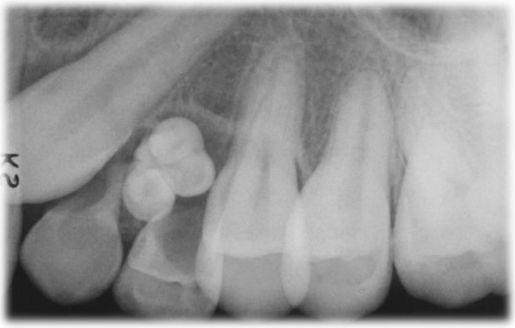
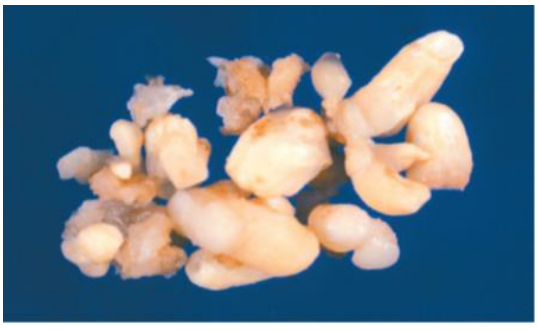
The histopathologic features of the odontoarneloblastoma are complex. The proliferating epithelial portion of the tumor has features of an ameloblastoma. Most often of the plexiform or follicular pattern which is intermingled with immature or *more* mature dental tissue in the form of developing rudimentary teeth which is similar to the appearance of a compound or complex odontoma.

Treatment and Prognosis As ameloblastoma

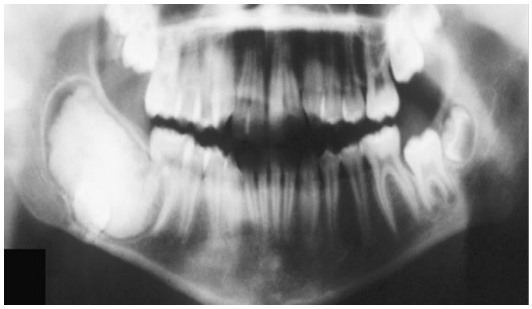
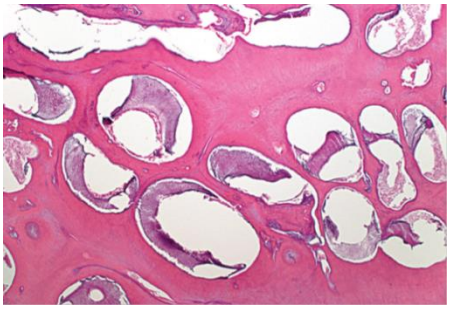
❖ ODONTOMA

Odontomas are *mixed odontogenic tumors,* in that they are composed of both epithelial and mesenchymal dental hard tissues. These fully differentiated tissues are a composite of enamel and dentin. Biologically, odontomas can be regarded as hamartomas rather than neoplasmsThese calcified lesions take one of two general configurations. They may appear as numerous miniature or rudimentary teeth, in which case they are known as *compound odontomas,* or they may appear as amorphous conglomerations of hard tissue, in which case they are known as *complex odontomas.* They are the most common odontogenic tumors.

***Clinical Features*.** Odontomas are lesions of children and young adults; most are discovered in the second decade of life. The range does, however, extend into later adulthood. The maxilla is affected slightly more often than the mandible. There is also a tendency for compound odontomas to occur in the anterior jaws, and for complex odontomas to occur in the posterior jaws. There does not appear to be a significant gender predilection. Clinical signs suggestive of an odontoma include a retained deciduous tooth, an impacted tooth, and alveolar swelling. These lesions generally produce no symptoms. **Radiographically:** compound odontomas typically appear as numerous tiny teeth in a single focus. This focus is typically found in a tooth-bearing area, between roots or over the crown of an impacted tooth.

Complex odontomas appear in the same regions, but as amorphous, opaque masses. Lesions discovered during early stages of tumor development are primarily radiolucent, with focal areas of opacity representing early calcification of dentin and enamel.

Histopathology. Normal-appearing enamel, dentin, cementum, and pulp may be seen in these lesions. A prominent enamel matrix and the associated enamel organ are often seen before final maturation of hard tissues. So called ghost cell keratinization is seen occasionally in the enamel-forming cells of some odontomas. This microscopic feature has no significance other than to indicate the potential of these epithelial cells to keratinize.

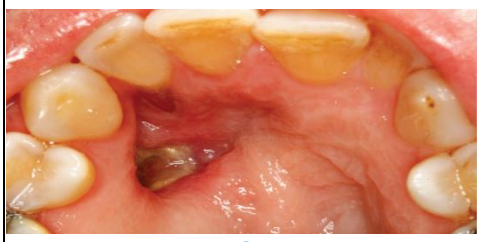
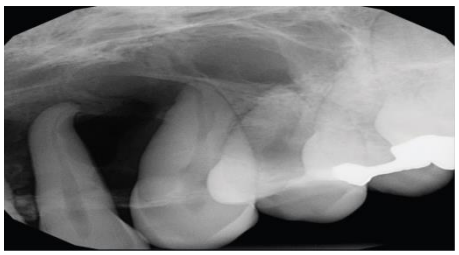
***Treatment*.** Odontomas have very limited growth potential, although an occasional complex odontoma may achieve considerable mass. Enucleation is curative, and recurrence is not a problem.

Tumors of Odontogenic Ectomesenchyme

Central Odontogenic Fibroma

The central odontogenic fibroma is a relatively uncommon odontogenic that is described in the WHO classification of odontogenic tumors. Before that time the lesions with the specific features ascribed to this tumor were likely diagnosed as either a typical form of CEOT.

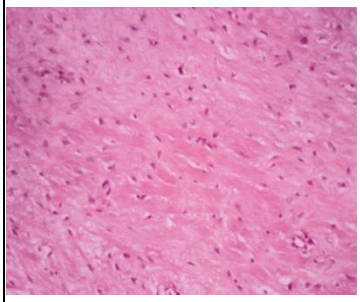
Clinical features: Lesions are usually asymptomatic, painless swelling commonly located in the mandible

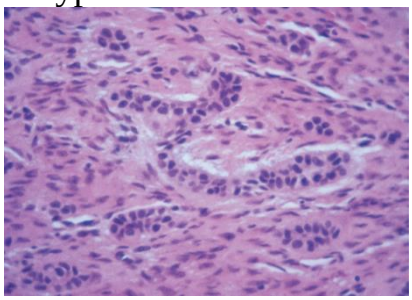
Radiographic features The radiographic appearance is that a non-specific radiolucency that is unilocular and well circumscribed in some and multilocular in others, some faint radiopaque flecks is sometimes observed.

Histopathology The central odontogenic fibroma is composed of a cellular connective tissue that contains widely scattered thin strands of odontogenic epithelium. The epithelial component closely resembles dental lamina and often contains with clear cytoplasm. Some lesions will contain varying amounts of spherical and diffuse calcifications that are usually associated with the odontogenic epithelial strands. Recently there have been several cases in which the central odontogenic fibroma contained histologic components of central giant cell lesions. The significance of this findings in not known. In the complex (World Health Organization [WHO]) type, mature connective tissue contains an abundant odontogenic epithelial component in the form of rests, along with calcified deposits of what is regarded as dentin or cementum. This

microscopic differentiation may be academic, in that there appears to be no difference in clinical behavior between the two subtypes.



Simple Type



World Health Organization type

Treatment Most cases have responded to conservative treatment such as curettage, and reports indicate that lesions separate from the surrounding bone with ease. There have been some recurrences after several years.

PERIPHERALODONTOGENIC FIBROMA

The relatively uncommon peripheral odontogenic fibroma is considered to represent the soft tissue counterpart of the central (lntraosscous) odontogenic fibroma.

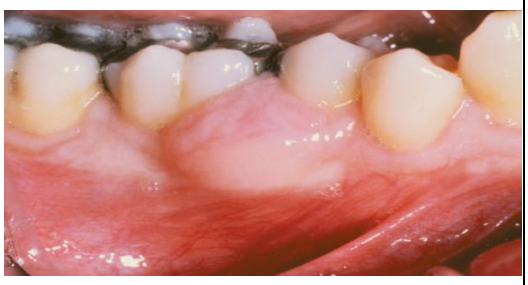
Clinical and Radiographic Features:

The peripheral odontogenic fibroma appears as a firm, slow-growing, and usually sessile gingival mass covered by normal-appearing mucosa. Rarely, multifocal or diffuse lesions have been described. Clinically, the peripheral odontogenic fibroma cannot be distinguished from the much more common fibrous gingival lesions. The lesion is most often encountered on the facial gingiva of the mandible. Most lesions are between 0.5 and 1.5 cm in diameter and they infrequently cause displacement of the teeth. Peripheral odontogenic fibrom as have been recorded in patients over a wide age range, with most identified from the second to the seventh decades of life.

Radiographic studies demonstrate a soft tissue mass, which in some cases has shown areas of calcification. The lesion, however, does not involve the underlying bone.

Histopathologic Features

The peripheral odontogenic fibroma shows similar histopathologic features to the central odontogenic fibroma (WHO type). The tumor consists of interwoven fascicles of cellular fibrous connective tissue, which may be interspersed with areas of less cellular, myxoid connective tissue. A granular cell change has been rarely identified in the connective tissue component. Islands or strands of odontogenic epithelium are scattered throughout the connective tissue. These may be prominent or scarce. The epithelial cells may show vacuolization. Dysplastic dentin, amorphous ovoid cementum-like calcifications, and trabeculae of osteoid may also be present.



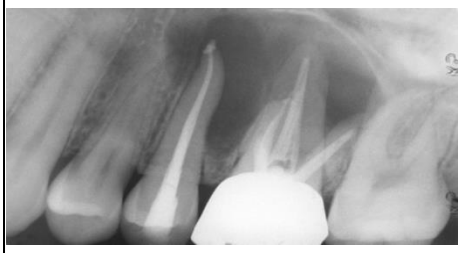
Treatment and Prognosis

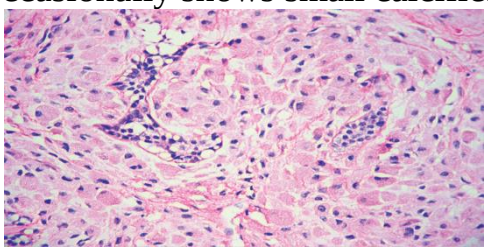
The peripheral odontogenic fibroma is treated by local surgical excision, and the prognosis is excellent. Recurrence of this lesion has been documented. However, so the patient and clinician should be aware of this possibility.

Granular cell odontogenic tumor (granular cell odontogenic fibroma)

The rare granular cell odontogenic tumor was initially reported as "granular cell ameloblastic fibroma." Subsequently, it was designated as granular cell odontogenic fibroma, but the noncommittal term granular cell odontogenic tumor is probably more appropriate, given the controversial nature of the lesion. Approximately 20 cases of this unusual tumor have been reported.

Clinical and Radiographic Features Patients with granular cell odontogenic tumors have all been adults at the time of diagnosis, with over half being older than 40 years of age. The tumor occurs primarily in the mandible and most often in the premolar and molar region. Some lesions are completely asymptomatic; others present as a painless, localized expansion of the affected area. Radiographically, the lesion appears as a well demarcated radiolucency, which may be unilocular or multilocular and occasionally shows small calcifications.





Histopathologic Features

The granular cell odontogenic tumor is composed of large eosinophilic granular cells resembling the granular cells seen in the granular cell variant of the ameloblastoma. which Narrow cords or small islands of odontogenic epithelium are scattered among the granular cells. Small cementum-like or dystrophic calcifications associated with the granular cells have been seen in some lesions. The nature of thegranular cells is controversial. Ultrastructural studies reveal the features of mesenchymal cells,

Treatment and Prognosis

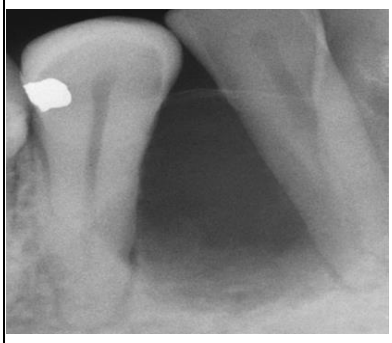
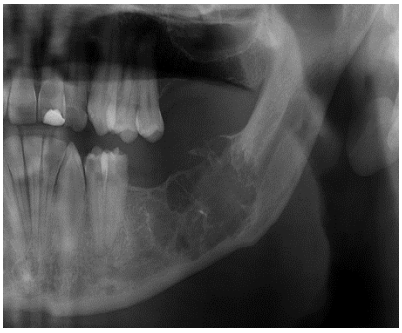
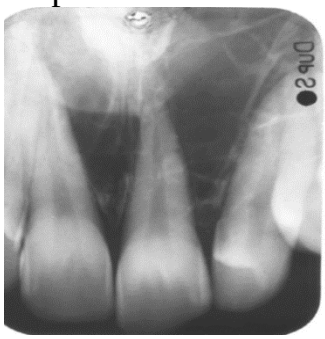
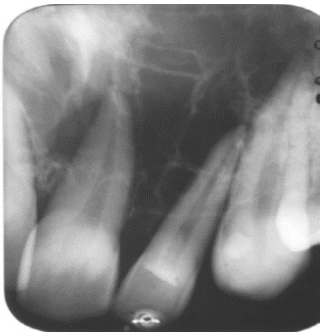
The granular cell odontogenic fibroma appears to be completely benign and responds well to curettage. No recurrences have been reported.

Odontogenic Myxoma

Odontogenic myxoma is a benign mesenchymal lesion that mimics microscopically the dental pulp or follicular connective tissue. It is a relatively common odontogenic tumor, representing 1% to 17% of all tumor types. Although myxomas are noted at various sites of the body, including the dermis, heart (left atrium), and other head and neck sites, only odontogenic myxoma of the jaws is derived from odontogenic ectomesenchyme. This benign neoplasm is infiltrative and may recur after inadequate treatment

Clinical Features. The age range in which this lesion appears extends from 10 to 50 years, with a mean of about 30 years. There is no gender predilection, and the lesions are seen anywhere in the mandible and maxilla with about equal frequency. Radiographically, this lesion is always

lucent, although the pattern may be quite variable. It may appear as a well-circumscribed or diffuse lesion. It is often multilocular with a honeycomb pattern.

CEMENTOBLASTOMA (TRUE CEMENTOMA)

Cementoblastoma is an odontogenic neoplasm of cementoblasts, and many authorities believe this neoplasm represents the only true neoplasm of cementum.

Clinical and Radiographic Features

Cementoblastomas are rare neoplasms, representing less than 1% of all odontogenic tumors. Greater than 75% arise in the mandible. with 90% arising in the molar and premolar region. Almost 50% involve the first permanent molar. Cementoblastomas rarely affect deciduous teeth. There is no significant sex predilection. The neoplasm occurs predominantly in children and young adults, with about 50% arising under the age of 20 and 75% occurring before 30 years of age. Pain and swelling are present in approximately two thirds of reported patients. Radiographically, the tumor appears as a radiopaque mass that is fused to one or more tooth roots and is surrounded by a thin radiolucent rim. The outline of the root or roots of the involved tooth is usually obscured as a result of root resorption and fusion of the tumor with the tooth.

Histopathologic Features

The histopathologic presentation of cementoblastoma closely resembles that of osteoblastoma, with the primary distinguishing feature being tumor fusion with the involved tooth. The majority of the tumor consists of sheets and thick trabeculae of mineralized material with irregularly placed lacunae and prominent basophilic reversal lines. Cellular fibrovascular tissue is present between the mineralized trabeculae. Multinucleated giant cells often are present. and the mineralized trabeculae are frequently lined by prominent blast like cells. The periphery of the lesion, corresponding to the radiolucent zone seen on the radiograph, is composed of uncalcified matrix. which often is arranged in radiating columns.

Treatment and Prognosis Treatment of a cementoblastoma usually consists of surgical extraction of the tooth together with the attached calcified mass. Surgical excision of the mass with root amputation and endodontic treatment of the involved tooth may be considered. The prognosis is excellent and the tumor does not recur after total removal.

Malignant odontogenic tumors

1- Malignant ameloblastoma
2- Ameloblastic carcinoma
3- Metastasizing ameloblastoma
4- Ameloblastic fibrosarcoma

5- Clear cell odontogenic carcinoma

These are rare malignant tumors of odontogenic origin. Some of epithelial origin like malignant ameloblastoma and ameloblastic carcinoma. Others are mixed epithelial and mesenchymal (ameloblastic fibrosarcoma). Mostlly presented clinically as rapidly growing tumors, with losing of the teeth and bone destruction, requiring radical. Surgical treatment, with high recurrence rate.

Malignant ameloblastoma: ameloblastoma with histological features of malignancy (atypia, mitoses and hyperchromasia)

Ameloblastic carcinoma: ameloblastoma with features of epithelial squamous cell carcinoma.

Metastasizing ameloblastoma: histologically benign ameloblastoma with metastasizing tumor nodules and also benign looking tissue in the lymph nodes or lung

Ameloblastic fibrosarcoma: Here the malignant portion is the mesenchymal components not the epithelium part.

Clear cell odontogenic carcinoma (clear cell odontogenic tumor)

HISTOGENESIS

— Unknown; probably odontogenic

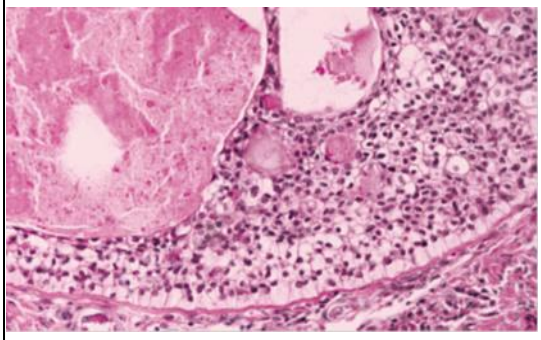
HISTOPATHOLOGY

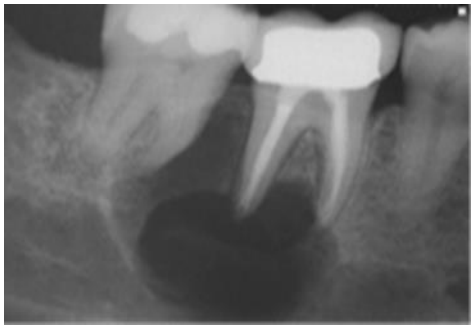
— Nests/cords of clear cells, some palisades

— Some glycogen; mucin negative

BEHAVIOR

— Recurrence and metastasis (neck nodes/lung)





Oral pathology

Bone Neoplasms

Primary tumors of bone are uncommon lesions in the jaws. They may arise from any of the number of different cells and tissues present in bone including cells (osteoblasts), cartilage, marrow, vascular and fibrous tissues.

No.	Tumor origin	Benign	Malignant
1.	**Primary bone tumors**		
	a- Bone origin	Osteoma Osteoid osteoma	Osteosarcoma
	b- Chondroid origin	Chondroma	Chondrosarcoma
	c- Marrow origin		Ewings sarcoma Lymphoma Multiple myeloma Leukemia
	d- Fibrous tissue origin(fibroblastic)	Desmoblastic Fibroma	
	e- others of vascular origin	Haemangioma	
2.	**Metastatic tumor**		Lung, adenocarcinoma, ovary, prostate and renal

Benign tumors

Osteoma

Osteomas are benign tumors composed of mature compact or cancellous bone. They are essentially restricted to the craniofacial skeleton and rarely if ever, are diagnosed in other bones. The lesion is benign and probably not a true neoplasm. Some cases may represent end stage of other conditions, e.g. fibrous dysplasia or related fibro-osseous lesions. The common palatal and mandibular tori are not considered to represent osteomas, although they are histopathologically identical.

Clinical and Radiographic Features

Osteomas are most frequently diagnosed in 2nd to 4th decades of life, being uncommon in the 1st decade. Average patient age is from 25 to 35 years. The lesion may arise on the surface of the bone, as a polypoid or sessile mass "periosteal osteoma", or may be located in the medullary bone "endosteal osteoma". The majority of cases are seen in young adults. It is generally asymptomatic, solitary lesions, or it could be an incidental finding in radiographic evaluation of the jaw for other problems. In the head and neck region, the most common sites of origin are the paranasal sinuses, inner and outer tables of the cranial bones and the jaw bones. Extra skeletal osteomas occur in the buccal mucosa, tongue and nasal cavity; however, these are not true neoplasms and are termed "choristomas."

In the gnathic region, the most common locations are the body of the mandible and the condyle. When it is located in the body, it occurs mostly to the premolars on the lingual surface.

Periosteal osteomas appear as slowly growing masses on the surface of the mandible or maxilla. Some types may reach a large size, resulting in facial deformity. Small endostealosteomas are asymptomatic, but large lesions cause a slowly progressive enlargement of the affected area. An osteoma involving mandibular condyle may cause a slowly progressing shift in the patient's occlusion, with deviation of the midline of the chin toward the unaffected side. Other signs and symptoms include facial swelling, pain, and limited mouth opening.

Symptoms of osteomas in the head and neck region may be quite variable depending on the lesion's location and include, chronic sinusitis, local pain, headache, nasal obstructio, exophthalmus, focal facial asymmetry, difficulty in mouth opening.

Radiographically

Osteoma typically appears as a dense, opaque, sharply demarcated mass that is usually broad based and ranges from 1 cm. to 8.5 cm. in diameter. Periosteal osteomas may show a uniform sclerotic pattern or may demonstrate a sclerotic periphery with a central trabecular pattern. Small endosteal osteomas are almost impossible to be differentiated from foci of sclerotic bone representing the end stage of an inflammatory process.

Histopathologic Features

Histologically, most osteomas are composed of hard, dense, compact lamellar bone, similar to cortical bone, in which haversian systems are present. These so-called ivory or compact osteomas have little stroma, and that which is present consists of bland fibrous tissue.

Osteomas may also be composed predominantly of mature lamellar trabecular bone between which fat and marrow elements are found.

Treatment and Prognosis

Osteomas found incidentally in asymptomatic patients do not need removal, as follow up studies frequently have shown no increase in size over several years duration. For symptomatic lesions, local excision is curative in almost all cases. Recurrence is quite unusual.

Gardner Syndrome

Gardner syndrome is a rare disorder that is inherited as an autosomal dominant trait. The condition represents spectrum of diseases characterized by adenomatous polyps of the large bowel associated with multiple osteomas of the skull and mandible, multiple keratinous cysts of the skin and soft tissue neoplasms especially fibromatosis. Most of the fibromatoses are intra-abdominal and develop following surgical intervention.

These show coexistence of somatic and germline mutations of the APC gene (adenomatous polyposis coli gene) on chromosome 5q21, suggesting that inactivation of both alleles of this gene is involved in their development. In this association, the osteomas tend to be multiple and most frequently arise in the mandible, especially in the mandibular angle, and the maxilla. Osteomas may be the 1st manifestation of these syndromes and occur up to 10 years prior to the discovery of the intestinal polyps that ultimately transform into **adenocarcinoma.**

Clinical Features

The colonic polyps typically develop during the second decade. In addition, detection of extracolonic polyps is not rare in small intestine or stomach. About 90% of patients demonstrate skeletal abnormalities, the most common of which are osteomas. Although any part of the skeleton may be affected, the most common sites are the skull, paranasal sinuses, and the mandible, mostly at the mandibular angle, with prominent facial deformity. The osteomas are usually seen during puberty and precede the development of, or any symptoms from, the bowel polyps. Most patients demonstrate between 3-6 osseous lesions. Dental abnormalities an increased prevalence of odontomas, supernumerary teeth, and impacted teeth. Most patients show one or several epidermoid cysts of the skin. To a lesser extent, an increased risk for thyroid carcinoma.

Histopathology

The same as osteoma.

Treatment and Prognosis

The major problem is the high rate of malignant transformation of bowel polyps into invasive adenocarcinoma. Prophylactic colectomy is usually recommended.

Osteoid osteoma and Osteoblastoma

Osteoid osteoma is a benign bone neoplasm that is found more frequently in patients between 10 and 30 years of age, and exhibit 2:1 male female ratio. Intense pain is the most

prominent symptom, this is often sharply localized . Osteoid osteoma has been reported in every bone but occurs more frequently in femur, tibia, humerus, bones of the hands and feet, vertebrae, and fibula. The tumor is very rare in the jaw bone. In the head and neck area, the cervical spine is the most common site.

Radiographically

The typical finding is a radiolucent central nidus that is seldom less than 1.5 cm. and that may, or may not, contain a dense center. This nidus is surrounded by a peripheral sclerotic reaction that may extend for several centimeters

Microscopically

The sharply delineated central nidus is composed of more or less calcified osteoid lined by plump osteoblasts and growing within highly vascularized connective tissue, without evidence of inflammation. Loose fibrous stroma includes dilated vessels and occasional hemorrhage.The vascularity tends to be more prominent in osteoblastoma than osteoid osteoma . Surrounding the nidus, there is a variably thick layer of dense bone.

The pain associated with this tumor is characteristically more intense at night, relieved by nonsteroidal anti-inflammatory drugs such as aspirin, and eliminated by excision of the lesion. The pain has been attributed to be the effect on nerves and vessels of osteoblast-produced prostaglandin E2, which is typically present in large amounts in those lesions. Another suggestion is that pain is due to the presence of entrapped and proliferating nerves within and particularly around the nidus.

Osteoblasoma "Giant osteoid Osteoma" is a tumor closely related to osteoid osteoma both microscopically and ultrastructurally. It is distinguished from the osteoid osteoma by the larger size of the nidus, the absence or inconspicuousness of a surrounding area of reactive bone formation. Most cases arise in the medulla of the spine or major bones of the lower extremity, although cortical and subperiosteal forms also occur. Because of the significant similarities between oseoblastoma and cementoblastoma some consider them to be identical, with one primary difference, which is fusion of the lesion to a tooth or not.

Clinically

Rarely affect the jaw bone, with slight mandibular predilection, mostly in the posterior regions. A slight male predominance is noted, and about 85 % occur before age 30. Most of the lesions are between 2 to 4 cm. but may be as large as 10 cm. Pain is a common presenting feature. Unlike osteoid osteoma, the pain is not relieved with aspirin. In some cases it is difficult to distinguish between aggressive osteoblastoma and low grade osteosarcoma.

Radiograph

Radiographically, the osteoblastoma typically appears as a well- or ill-defined, round to oval radiolucency with patchy areas of mineralization

Treatment

Complete enblock resection, is curative if not possible marginal resection, or curettage must be used with 10-20% recurrence rate.

Prognosis is good. The lesion rarely recurs or transform into osteosarcoma.

Chondroma

Chondroma are benign tumors of mature hyaline cartilage.They comprise about 16% of benign bone tumors and most often arise in the small bones of the hands and feet. However, a diagnosis of chondroma in the craniofacial bones should be viewed with great skepticism because many purported cases have recurred and exhibited malignant behavior. There are only a few individual reports and small series of gnathic chondromas, with most examples thought to arise from cartilage or cartilaginous rests in the condyle, anterior maxilla, mandibular symphysis, and coronoid process.

Clinical Features

Approximately 50% of chondromas are diagnosed in the second, third, and fourth decades of life, and there is a female predilection. Most gnathic examples occur in the condyle or anterior maxilla of adult patients. Usually, the lesions are painless and grow slowly. However, condylar tumors may cause pain, limited mouth opening, and deviation of the mandible from the midline. Lesions arising adjacent to teeth may cause tooth mobility and root resorption.

Radiographically

The chondroma typically appears as a well-defined radiolucency with central opacification. Most cases arise within medullary bone (enchondromas), but some
may arise just beneath the periosteum (periosteal chondromas). Most chondromas are solitary, although multiple lesions may develop in Ollier disease (sporadic chondromatosis with a unilateral tendency) or (Maffucci syndrome sporadic chondromatosis with soft tissue angiomas).

Histopathological Features

Histopathologically, a chondroma appears as a well circumscribed, lobular mass of mature hyaline cartilage. The cartilage typically demonstrates well-formed lacunae containing small chondrocytes with pale cytoplasm and small, round nuclei. Microscopic distinction between a chondroma and a low-grade chondrosarcoma of the jaws may be difficult .

Treatment and Prognosis

It is wise to consider any jaw lesion diagnosed as a chondroma to represent a potential chondrosarcoma. Treatment typically consists of complete surgical removal.

Desmoplastic Fibroma

Desmoplastic fibroma is a benign, locally aggressive lesion of bone that can be considered the bony counterpart of fibromatosis. The tumor appears usually in long bones and the pelvis but may occasionally affect the jaws. The cause of desmoplastic fibroma is unknown. The lesion usually exhibits locally aggressive clinical behavior, suggesting a neoplastic process. The potential role of genetic, endocrine, and traumatic factors in the pathogenesis of the lesion has led to speculation that it might represent an exuberant reactive proliferation.

Clinical Features

Most cases of desmoplastic fibroma of the jaws have occurred in patients under the age of 30 years, with a mean age of 14 years. There appears to be no gender predilection. The

mandible, usually the body ramus region, is affected more often than the maxilla. The lesions are slowly progressive and asymptomatic, eventually causing swelling of the jaw.

Radiographically

Desmoplastic fibroma may be unilocular or multilocular. The radiographic margins may be either well demarcated or poorly defined. Cortical perforation and root resorption may be seen.

Histopathology

The lesion consists of interlacing bundles and whorled aggregates of densely collagenous tissue that contains uniform spindled and elongated fibroblasts. Some areas may exhibit hypercellularity with plumper fibroblast nuclei. However, cytologic atypia and mitotic figures are not found. Bone is not produced by lesional tissue.

Differential Diagnosis

Differential radiographic diagnostic considerations include odontogenic cysts, odontogenic tumors, and nonodontogenic lesions that typically occur in this age group. The presence of aggressive features, such as cortical perforation, or local symptoms might suggest the possibility of a malignancy. In some cases histopathologic distinction between desmoplastic fibroma and well-differentiated fibrosarcoma may be difficult. The latter would exhibit greater cellularity, mitotic figures, and nuclear pleomorphism. Some similarities are noted histologically with central odontogenic fibroma, a nonaggressive lesion that contains odontogenic rests.

Treatment

Surgical resection of the lesion is generally reported as the treatment of choice. Curettage alone has been associated with a significant recurrence rate.

Hemangioma of Bone

Hemangiomas of bone are rare intraosseous vascular malformations that, when seen in the jaws, can mimic both odontogenic and nonodontogenic lesions. Difficult to control hemorrhage is a notable complication of surgical intervention.

Clinical Features More than half of the central hemangiomas of the jaws occur in the mandible, especially the posterior region. The lesion occurs approximately twice as often in females as in males. The peak age of discovery is the second decade of life. A firm, slow-growing, asymmetric expansion of the mandible or maxilla is the most common patient complaint. Spontaneous gingival bleeding around teeth in the area of the hemangioma may also be noted. Paresthesia or pain, as well as vertical mobility of involved teeth, is occasionally evident. Bruits or pulsation of large lesions may be detected with careful auscultation or palpation of the thinned cortical plates. Trophic effects of the hemangioma on adjacent hard and soft tissues are also common. Significantly, hemangiomas may be present without any signs or symptoms.

Radiographic findings: more than half of jaw hemangiomas occur as multilocular radiolucencies that have a characteristic soap bubble appearance. A second form of these lesions consists of a rounded, radiolucent lesion in which bony trabeculae radiate from the center of the lesion, producing angular loculations. Less commonly, hemangiomas appear as cyst-like radiolucencies. The lesions may produce resorption of the roots of teeth in the area.

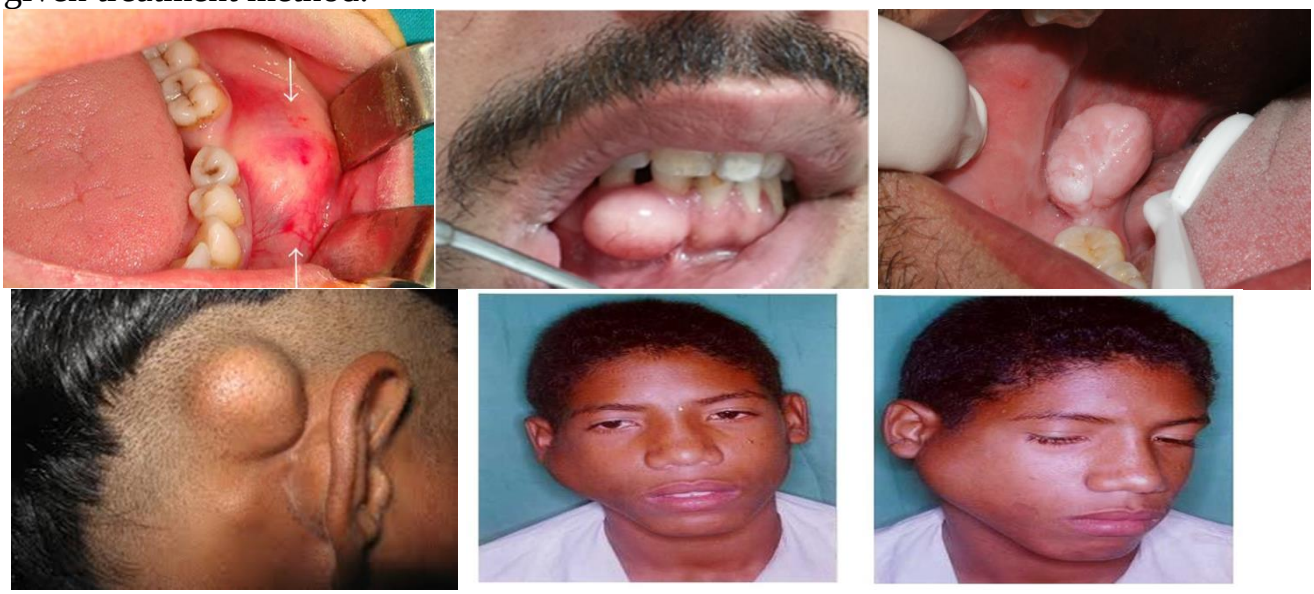
Histopathology

Hemangiomas of bone represent a proliferation of blood vessels. Most intrabonyhemangiomas are of the cavernous type (large-caliber vessels); fewer are of the capillary type (smallcaliber vessels). Separation of hemangiomas into one of these two microscopic subtypes is, however, academic, since there is no difference in biologic behavior.

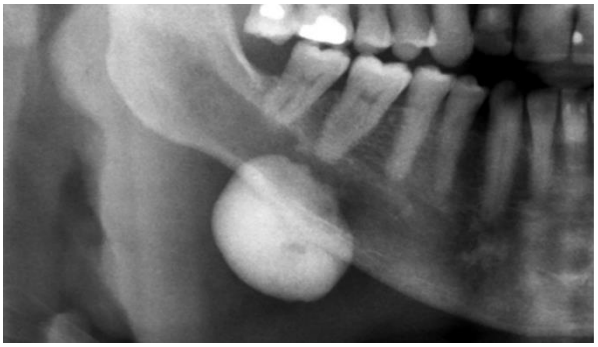
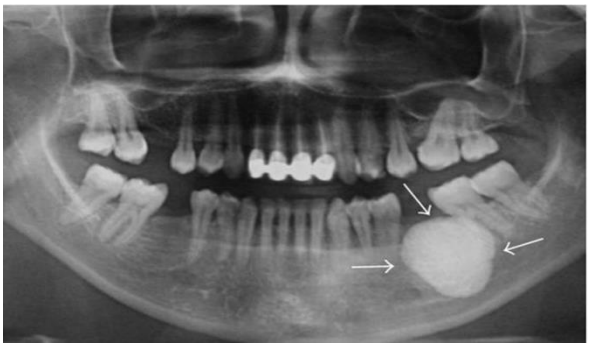
Differential Diagnosis The differential diagnosis of multilocularhemangioma of bone includes ameloblastoma, odontogenicmyxoma, odontogenickeratocyst, CGCG, and aneurysmal bone cyst. A unilocular lesion may be easily confused with other cystic processes that occur within the jaws. Angiography often provides useful information in establishing the diagnosis of hemangioma.

Treatment and Prognosis

The most significant feature of hemangiomas of bone is that these lesions may prove life threatening if improperly managed. Extraction of teeth in an area involved by a central vascular lesion may result in potentially fatal bleeding. It is imperative to perform needle aspiration of any central lesion that may be of vascular origin before performing a biopsy. Methods used in the treatment of hemangioma of bone include surgery, radiation therapy, sclerosing agents, cryotherapy, and presurgical embolization techniques. The vascular supply of a given lesion, as well as its size and location, must be evaluated before the selection of a given treatment method.



Osteoma

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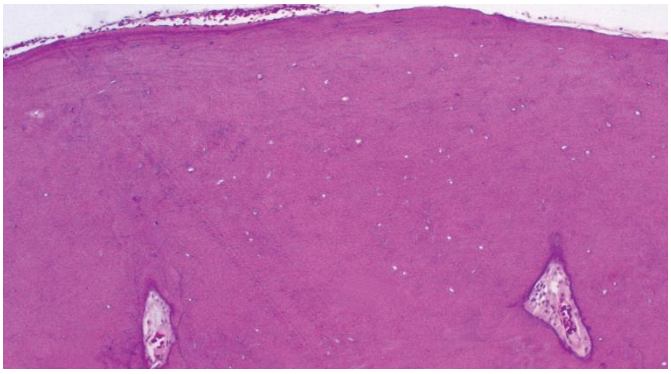
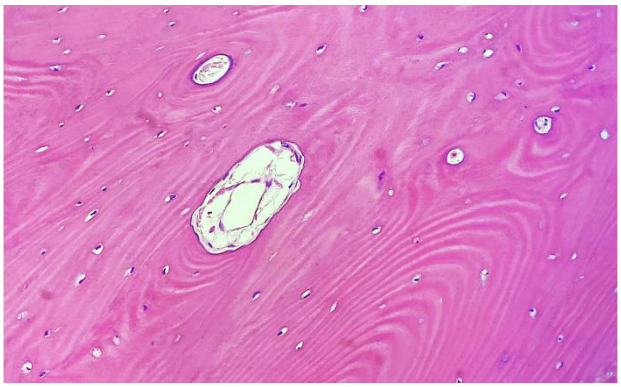

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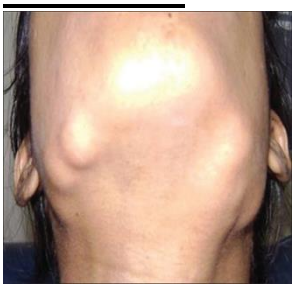
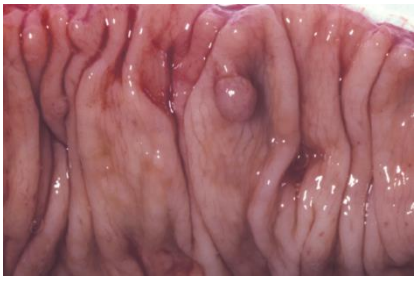
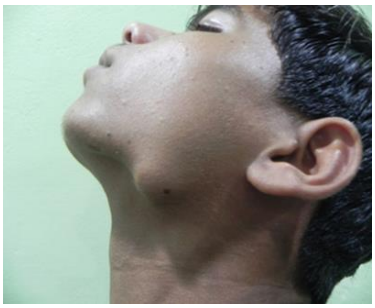
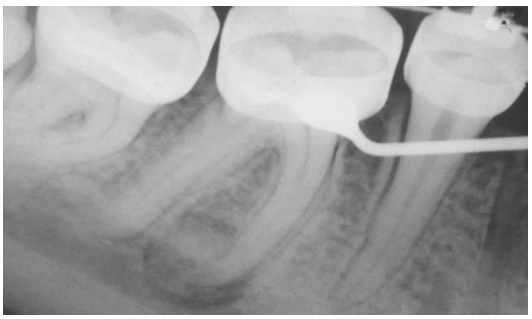
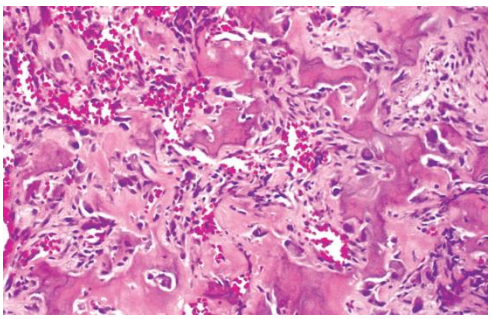
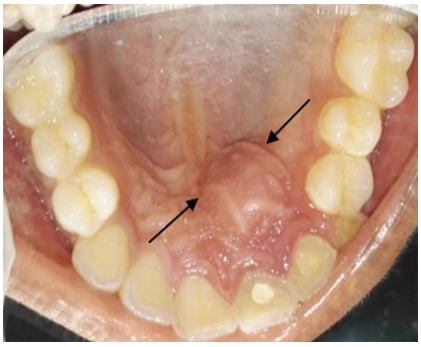
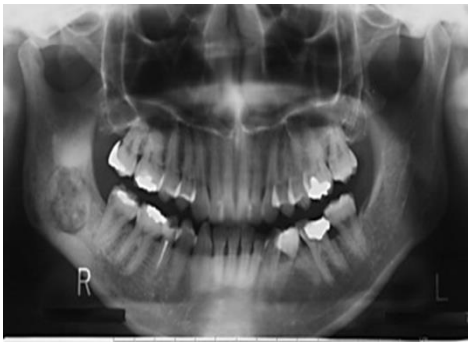
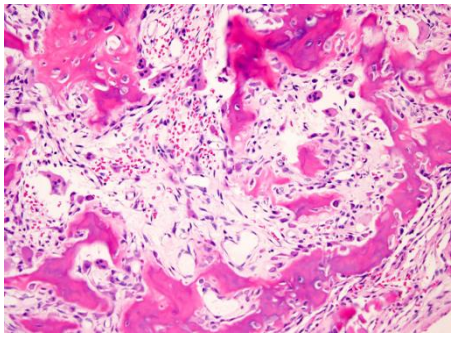




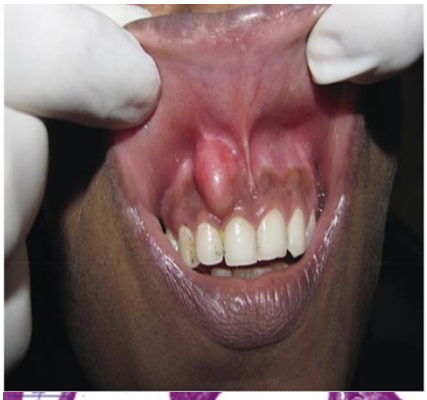
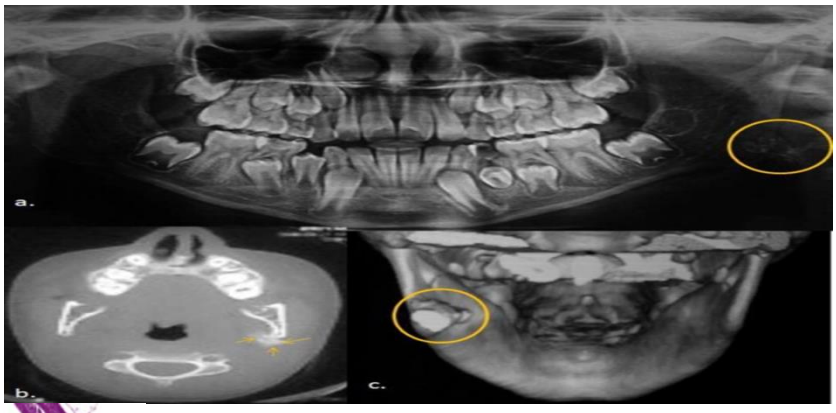
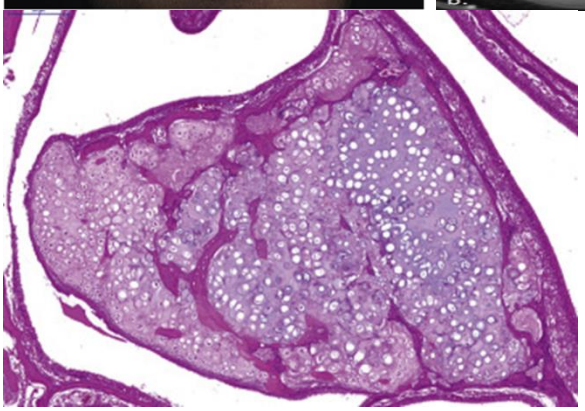
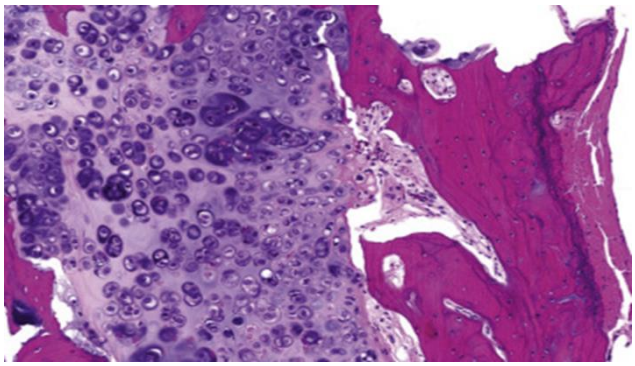
Gardener syndrome

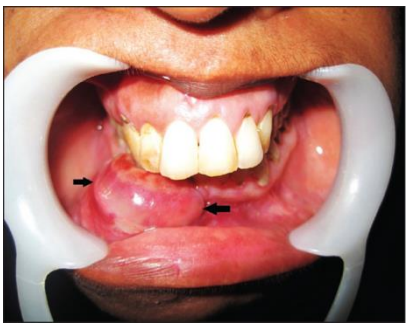
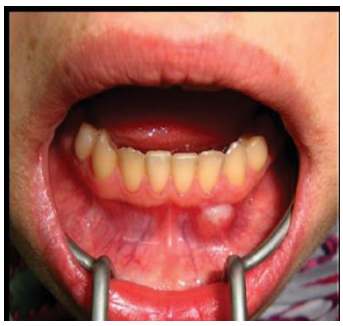
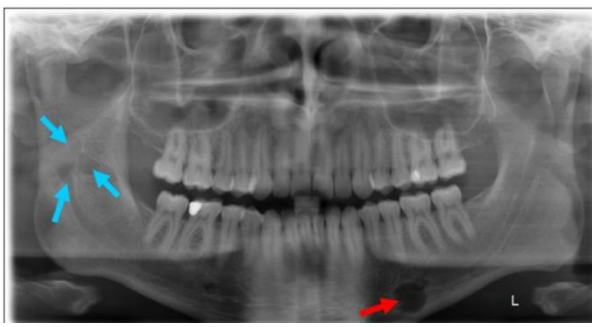
Osteoid osteoma

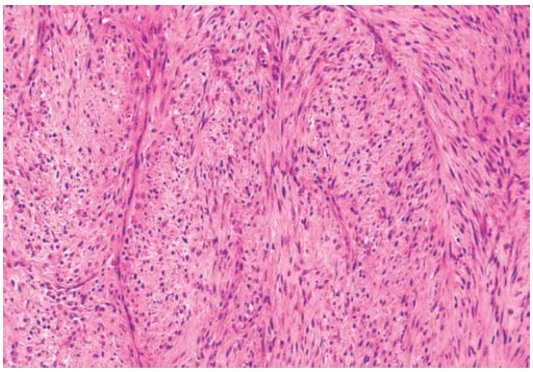
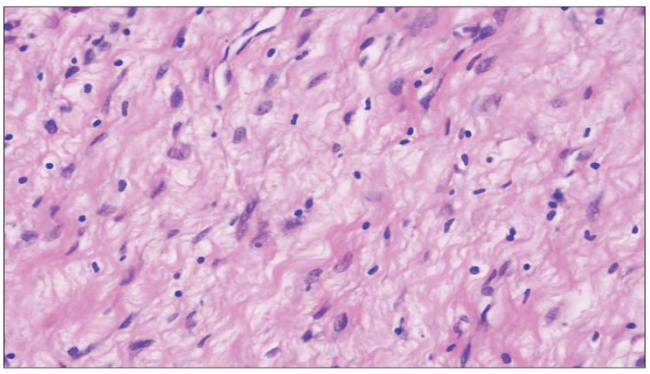




Osteoblastoma

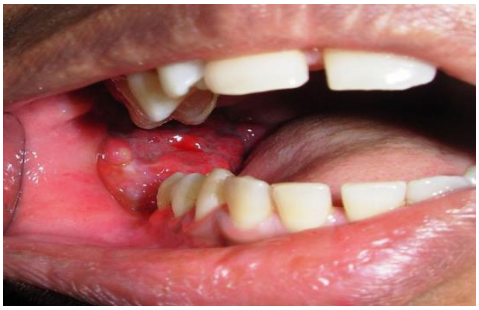
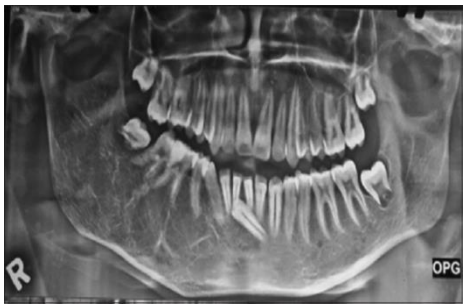





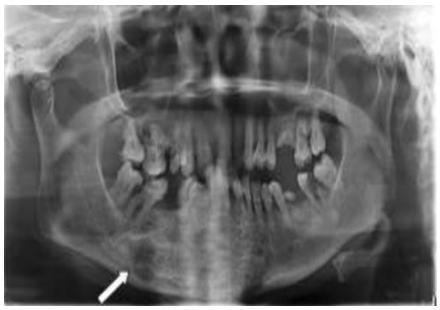
Chondroma

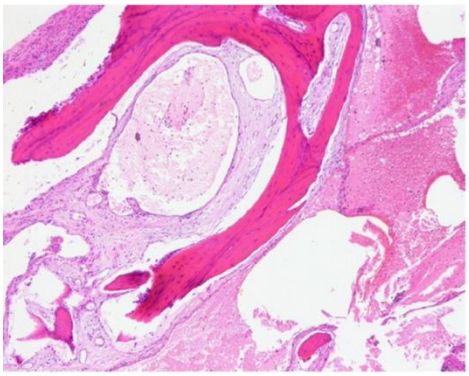
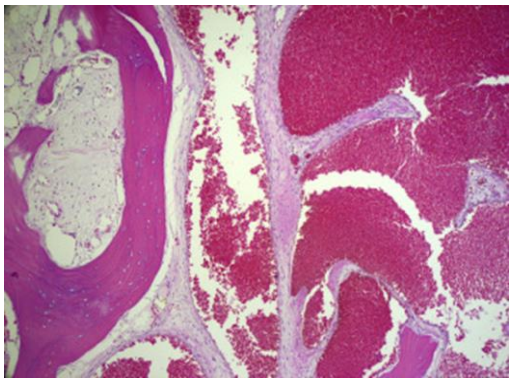
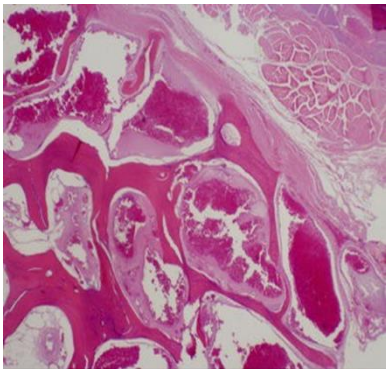




Desmoplastic fibroma



Hemangioma of Bone

Oral pathology

MALIGNANT BONE TUMORS

Osteosarcoma

Osteosarcoma is the most frequent primary bone malignancy, exclusive of hematopoietic malignancies. It usually occurs in patients between 10 to 25 years of age and is exceptionally rare in preschool children. Another peak age incidence occurs after 40, in association with other disorders. Osteosarcomas of the jaws are uncommon and represent 6-8 % of all osteosarcomas. The tumors have been diagnosed in patients ranging from young children to the elderly, but they occur most often in the 3rd to 4th decade of life. The mean age for patients with osteosarcoma of the jaw is about 33 years, which is 10 to 15 years older than the mean age for osteosarcomas of the long bones. As is seen in extragnathic locations, a slight male predominance is noticed.

Predisposing Factors

Most osteosarcomas arise de novo; however, some arise within the context of the following:

1. Paget's disease.
2. Radiation exposure.
3. Chemotherapy.
4. Pre-existing benign bone lesions, e.g. fibrous dysplasia.
5. Foreign bodies, e.g. orthopedic implants.

Location

Most osteosarcomas in the long bone are located in the metaphyseal region particularly the lower end of the femur, upper end of the tibia, and the upper end of the humerus. A few cases arise in the diaphysis and even smaller number in the epiphysis. Less commonly, they are found in flat bones e.g. (craniofacial bones, pelvis, and scapula), spine and short bones.

Jaw Tumor

Clinical Features

The maxilla and mandible are equally affected. The mandibular tumors mostly arise in the posterior body and ramus. Maxillary lesions are discovered more commonly in the inferior portion (alveolar ridge, sinus floor, palate). Swelling and pain are the most common symptoms. Other features include loosening of the teeth, parasthesia, and nasal obstruction.

Radiographically: variable, from dense sclerosis to a mixed sclerotic and radiolucent lesion, to an entirely radiolucent. The border is mostly ill defined, making it difficult to determine the extent of the tumor. Occasionally, there is resorption of the roots of the teeth involved by the tumor. The classical sunburst, or sunray appearance is due to the osteophytic bone production on the surface of the lesion noted in about 25% of jaw osteosarcoma, mostly seen on an occlusal projection. Widening of the periodontal ligament may be seen as an early finding due to tumor infiltration along the PDL.

Gross and Histological Findings The gross appearance of the cut surface of an osteosarcoma varies a great deal, depending on the relative amount of bone, cartilage and cellular stroma, and vessels. The range extends from bony hard to cystic, friable and hemorrhagic. The tumor may spread from the following pathways :

1. Spread along the marrow cavity.
2. Invade the cortex.
3. Elevate or invade the periosteum.
4. Extend into the soft tissue.
5. Metastasize through blood stream to distant sites, particularly to the lung.

Microscopic Findings

Osteosarcoma may destroy the pre-existing bone trabeculae or grow around them in an appositional fashion. The key feature for the diagnosis is the detection, somewhere in the tumor, of osteoid and calcified osteoid produced directly by the tumor cells, without interposition of cartilage. Osteoid is recognized by its eosinophilic-staining quality, its glassy appearance, irregular contours, and the fact that it is surrounded by a rim of osteoblasts. In addition to osteoid, the cells of the tumor may produce chondroid material and fibrous connective tissue. The tumor cells may vary from uniform round or spindleshaped cells to highly pleomorphic cells with bizarre nuclear and cytoplasmic shapes. Depending on the relative amounts of osteoid, cartilage, or collagen fibers produced by the tumor, many pathologists subclassify osteosarcomas into the following types:

1. osteoblastic.
2. chondroblastic.
3. fibroblastic.

These histopathologic subtypes do not have any prognostic significance. Other variants, may include, malignant fibrous histiocytoma-like, small cell, epitheloid, telangiectatic, and giant cell rich.The chondroblastic type constitute the major portion of all osteosarcomas of the jaws.

Treatment and Prognosis

It is believed that osteosarcoma of the jaw is less aggressive than those occurring in the long bones. Most of these tumors are low grade and metastases are seen less frequently. Treatment is by excision with safe margin, i.e. complete surgical removal ± chemotherapy, the prognosis remains serious, with 30-50% survival rates.

Other variants include:

Peripheral "juxtracortical" osteosarcoma:

These tumors grow outward from the surface, and do not involve the medullary bone, this type my include:

Parosteal type: is a lobulated nodule attached to the cortex by a short stalk. There is no elevation of the periosteum and no peripheral periosteal reaction.

Periosteal type: is sessile lesion that arises within the cortex and elevates the overlying periosteum, which provokes the production of peripheral periosteal reaction.

The prognosis of periosteol is poorer than paraosteol type.

Chondrosarcoma

Is a malignant tumor characterized by the formation of cartilage, but not bone, by the tumor cells. Chondrosarcoma comprises about 10% of all primary tumors of the skeleton but are considered to involve the jaws very rarely. Only 1-3 % of all chondrosarcomas arise in the head and neck area.

Clinical Features

It is a disease of adulthood with peak prevalence in the 5th to 7th decade of life. Although chondrosarcoma arise over a wide age range, the majority of affected patients are over 50 years of age. When occurring in the head and neck, chondrosarcoma mostly arise in the maxilla, body of mandible, ramus, nasal septum, and paranasal sinuses. A painless mass is the most common presenting sign. This may be associated with separation or loosening of teeth. In contrast to osteosarcoma, pain is an unusual complaint. Maxillary tumors may cause nasal obstruction, congestion, epistaxis, photophobia, or visual loss.

Radiographically

The tumor shows a radiolucent process with poorly defined borders. The radiolucent area usually contains a variable amount of radio-opaque masses, which is caused by calcification or ossification of cartilage matrix.

Histopathology

The tumor is composed of cartilage showing varying degrees of maturation and cellularity. In most cases, typical lacunae formation within chondroid matrix is visible. Chondrosarcoma may be divided into 3 grades of malignancy, which correlates well with the rate of tumor growth and prognosis, e.g. grade I, closely resemble chondroma, which is composed of chondroid matrix and chondroblast, that show only subtle variation from the appearance of normal cartilage. The tumor should be considered malignant when large-plump chondroblasts and binucleated chondrocytes are present.

Grade II, present with greater number of cells with moderately sized nuclei and increased cellularity.

Grade III is highly cellular, with spindle cells proliferation. Mitoses may be prominent.

Treatment and Prognosis

Treatment is by resection. Prognosis is related to size and location. 5-years survival rate varies from 43%-95%.

MARROW TUMORS

Ewing's Sarcoma/Primitive Neuroectodermal Tumor

This tumor has been traditionally regarded as an undifferentiated type of bone sarcoma of children, now it has been linked with the peripheral or primitive neuroectodermal tumor "PNET", and the term Ewing's sarcoma /PNET "ES/PNET" is currently used. The tumor cells demonstrate a reciprocal translocation between chromosomes 11 and 22.

Clinical Features

ES/PNET of bone is usually seen in patients between the age of 5 and 20 years, with only a minority of the cases presenting in infancy or adulthood. The peak incidence is in the second decade of life, with approximately 80% of patients being younger than 20 years of age at time of diagnosis. The vast majority of affected patients are white, with blacks almost never developing this tumor. The long bones, pelvis, and ribs are affected most frequently, but almost any bone can be affected. Jaw involvement is uncommon, with only 1% to 2% occurring in the gnathic or craniofacial bones. Pain, with swelling, is the most common symptom. It is usually intermittent and varies from dull to severe. Fever, leukocytosis, and an elevated ESR also may be present and this may cause an erroneous diagnosis of osteomyelitis.

The tumor commonly penetrates the cortex, resulting in a soft tissue mass, overlying the affected area of bone. Jaw involvement is more common in the mandible, parasthesia and loosening of teeth are common findings.

Radiographically, there is irregular lytic bone destruction with ill-defined margins. Cortical destruction or expansion may or may not be present.

Histopathologic Features Microscopically, the tumors consist of sold sheets of cells divided into irregular masses by fibrous strands. The cells are small and uniform. The cell outlines are indistinct, resulting in a "syncytial appearance". The nuclei are round, with frequent indentations, small nucleoli, and variable mitotic activity. There is a well-developed vascular network; large areas of hemorrhage and necrosis are commonly present. Some contain foci or may be composed mostly of larger cells, these are designated as Large cell "atypical" Ewing's sarcoma. About 75% of cases contain glycogen granules in the cytoplasm of the tumor cells. This help in the diagnosis, to differentiate it from other round cell tumors. The diagnosis may be very difficult, and should be differentiated from other primitive "small cell tumors" involving bone and soft tissues in young patients particularly, lymphoblastic lymphoma, desmoplastic small cell tumor. And embryonal/alveolar rhabdomyosarcoma. The immunohistochemical and molecular genetic features are very useful for differentiation.

Spread and Metastases

To lung and pleura, other bones particularly the skull, CNS, and rarely to the lymph nodes.

Treatment

The treatment in the past consisted of surgical excision, and radiation therapy resulting in a 5 year survival rate of less than 10%. The combination of high dose radiotherapy and multidrug chemotherapy has dramatically changed the picture and the 5 year survival to 75%.

Malignant Lymphoma

Malignant lymphoma can involve the skeletal system primarily or as a manifestation of systemic disease.

1) Large Cell Lymphoma

Primary of bone is more common in adults than children, 60% of cases occurring in patients over the age of 30 years. Grossly, most cases involve the diaphysis or metaphysis of long bones or the vertebrae producing patchy cortical and medullary destruction. Lymphoma of bone may cause vague pain or discomfort, which might be mistaken for a toothache. The patient may complain of parasthesia, particularly with the mandibular region. Radiographically, ill-defined or ragged radiolucency, although in the early stages, may be non-existent. Gradually the process causes bone expansion, and eventually perforation of the cortical plate producing a soft tissue lesion.

Microscopically

The tumor is composed of sheets of large cells with pleomorphic nuclei, some are indented, multilobulated, or horse-shoe shaped. They usually have prominent nucleoli. The cytoplasmic outlines are well defined. These are distinguishing features from Ewing's sarcoma cells, which are smaller, with fine nucleoli, the cytoplasmic borders are indistinct, with less amount of cytoplasm.

Treatment

According to the stage, and includes radiation and chemotherapy.

2) Burkitt's Lymphoma

Is a malignancy of B-lymphocyte origin that represents an undifferentiated lymphoma and it seems to have a predilection to jaws. This type of lymphoma was originally described in young children from Africa and was termed the African Burkitt's lymphoma or endemic Burkitt's lymphoma. This tumor is thought to be related pathogenetically to Epstein-Bar virus (EBV), because more than 90% of the tumor cells, particularly in the African type, show expression of EBV nuclear Ag. and the affected patients have a high titer to EBV. Tumors with a similar histomorphology, commonly referred to as sporadic or American Burkitt's lymphoma have been observed in other countries where the neoplasm is usually first detected as an abdominal mass.

Clinical and Radiographical Features

50-70% of the cases presented with jaw mass. The malignancy usually affects children (peak prevalence 7 years of age). The posterior segments of the jaws are more commonly affected maxilla more than the mandible. The American type tends to affect patients over a greater age range, with the abdominal region typically affected, although the jaw has been reported to be affected. The tumor may produce facial swelling and proptosis, pain, tenderness, and parasthesia, with marked tooth mobility. Radiographically, radiolucent destruction of the bone with ragged ill-defined margins.

Histopathology

Undifferentiated small, non-cleaved B-lymphocytes. The lesion is composed of sheets of tumor cells that exhibit round nuclei with minimal cytoplasm, prominent nucleoli, and prominent mitoses. The classic starry sky pattern associated with the lesion is caused by the presenc of histiocytes within the tumor tissue, which appear less intensely deeply stained malignant lymphocytes.

Treatment and Prognosis

The tumor is aggressive; death will result in 4-6 months if not treated. Treatment by intensive chemotherapy.

3) Angiocentric T-cell lymphoma

Is a rare condition that characterized clinically by aggressive destruction of the midline structures of the palate and nasal fossa. For many decades the nature of this disease has been controversial, this reflects the variety of terms by which this tumpr has been called (e.g. Midline lethal granuloma, Midline malignant reticulosis, etc.). Based on modern diagnostic cytogenic, immunologic, and molecular methods, this lesion has been classified as T-cell lymphoma. The tumor should be differentiated from other that lead to destruction of the palate e.g. Wegener's granulomatosis, Tertiary syphilis.

Clinical Features

The condition mostly affects adults, which presents initially as nasal stuffiness or epistaxis, pain may be present. Swelling of the soft palate may precede the formation of a deep, necrotic, ulceration that ends with palatal destruction, which typically creates oroantral fistula.

Histopathology

Mixed infiltrates of inflammatory cells, arrange around blood vessels "angiocentric". The lesion destroys tissues, with necrosis. Large angular lymphocytes with an atypical appearance

are usually present. Immunohistochemical evaluation of this infiltrates often shows a monoclonal T-lymphocyte proliferation.

Treatment Untreated tumor will lead to death, which follow progressive and highly destructive malignancy. Localized condition is treated by radiation. Disseminated condition is treated by chemotherapy.

Multiple Myeloma and Plasmacytoma (MM)

MM. is a relatively uncommon malignancy of plasma cell origin within bone. MM. accounts for nearly 50% of all malignancies that involve the bone(most common malignant tumor in bone) . The malignant plasma cells that compose this tumor are monoclonal, which arise from a single malignant precursor that has spread throughout the body. Because the neoplasm develops from a single cell, all the daughter cells have the same genetic makeup and produce the same proteins.

The proteins are the immunoglobulin components, which the plasma cell would normally produce. The effects of tumors results due to abnormal proliferation of the cells and the uncontrolled production of their protein product.

Clinical Features

MM. is a disease of adults, the median age at diagnosis is 60-70 years, and rarely diagnosed before the age of 40. Bone pain, pathologic fractures, fatigue, fever, infection, and bleeding tendency due to abnormal platelet function.

Radiologically

Multiple well-defined, punched out radiolucencies, or ragged radiolucencies may be seen in MM. These may affect the skull, although any bone can be affected. The jaws may be involved in 30% of cases.

Histopathology

Show diffuse, monotonous sheets of neoplastic, variably differentiated, plasmacytoid cells that invade and replace the normal host tissue, with frequent mitoses. Amyloid deposits may be seen in association with neoplastic cells, which appear as a homogenous, eosinophilic acellular material.

Diagnosis

1. Skeletal X-ray ► Radiolucency.
2. Histopathology ► Neoplastic plasma cells.
3. Bone-marrow examination ► at least 10% atypical plasma cells of marrow population.
4. Bence-Jones proteins in urine (30-50%).
5. serum protein electrophoresis ► Myeloma protein (M band), massive overproduction of one abnormal protein “immunoglobulin” by the neoplastic clone of cells.

Treatment

Chemotherapy – with poor prognosis, 5 year survival rate is 25% only.

Metastatic Tumors to the Jaw

Metastatic carcinoma is the most common form of cancer involving bone. Studies show that 2/3 of breast carcinoma. 1/2 of prostate carcinoma, 1/3 of kidney and lung cancer ► bone spread.

Jaw bone metastasis is mainly from breast, lung, kidney, thyroid, prostate ► by hematogenous route.

Clinical Findings

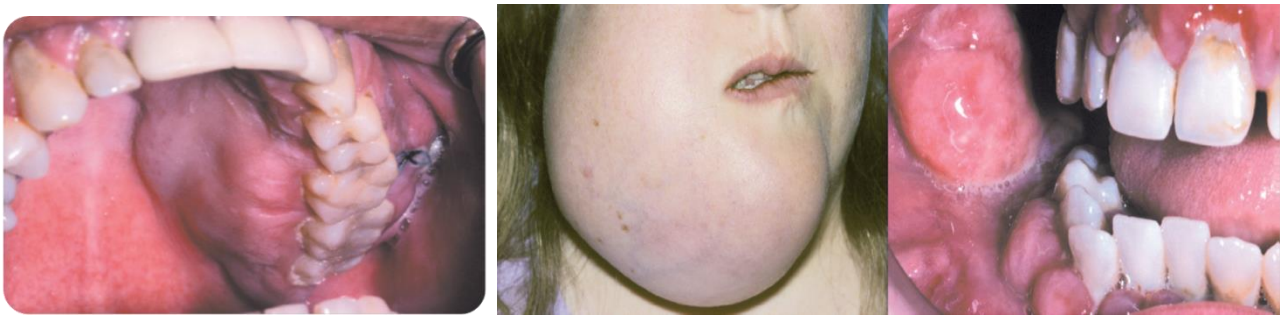
Elderly individuals are mostly affected. The mandible may be involved in about 10% of metastatic extra oral carcinoma. Maxillary metastasis is uncommon. Clinically, the patient may report pain, lump, loosening of teeth, and parasthesia, or the patient may be completely asymptomatic. The jaw lesion may be the 1st indication of the existence of an occult primary tumor.

Radiographic Features May be lytic, resembling a cyst, sometimes causing widening of periodontal ligament. Others may stimulate new bone formation ► radiopaque or mixed lesion e.g. prostate and breast carcinoma.

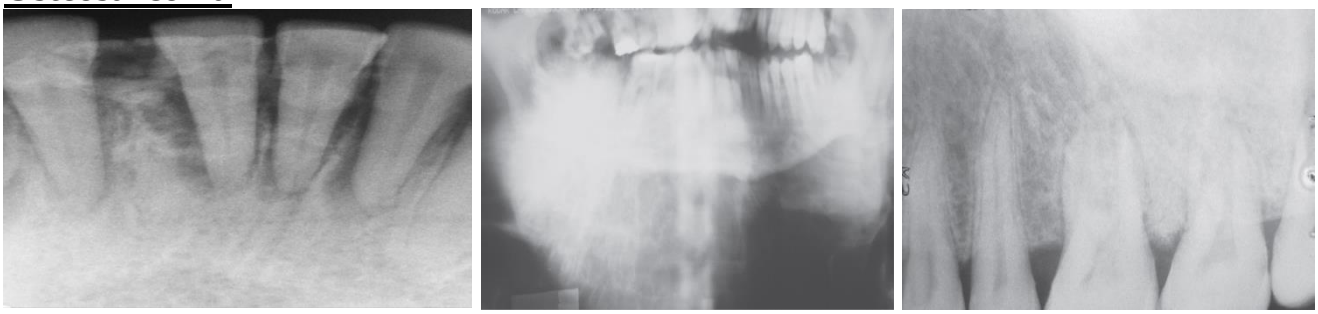
Histopathological Features The microscopic appearance of metastatic carcinoma in bone varies. In some instances, the metastatic tumor is well differentiated and closely resembles a carcinoma of a specific site, such as the kidney, colon, or thyroid. In such instances, the pathologist can say with reasonable certainty that a given metastatic tumor comes from a specific primary site . More often, however, metastatic carcinomas are poorly differentiated and histopathologic study of the metastatic deposit gives little clue as to the primary site of the tumor. Poorly differentiated metastatic carcinoma may be difficult to differentiate from anaplastic small cell sarcomas, malignant lymphomas, and malignant melanoma . Immunohistochemical reactions are usually necessary in such cases to establish the diagnosis. Although the diagnosis of metastatic carcinoma can usually be determined by microscopic examination, the final diagnosis depends mostly on a careful medical history and complete physical examination with appropriate laboratory studies.

Treatment and Prognosis

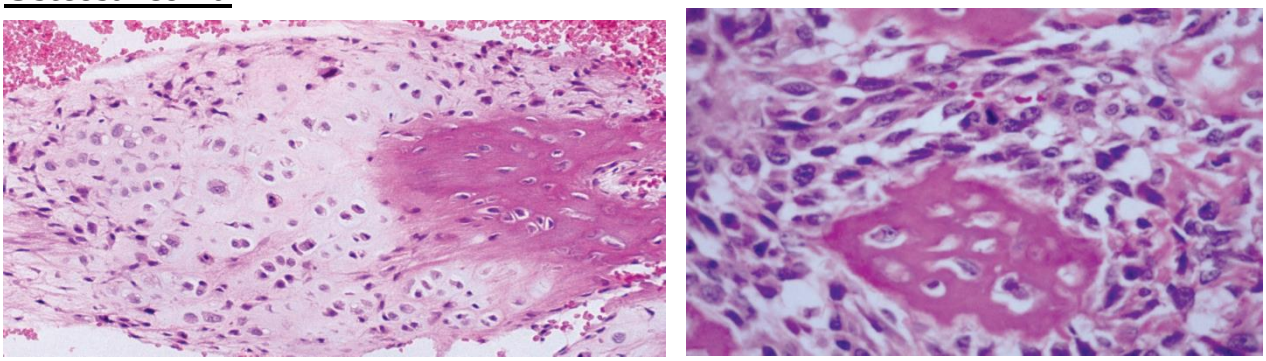
The prognosis for metastatic carcinoma of the jaws is poor because. by definition, osseous metastasis automatically places the patient in Stage IV disease, Although a solitary metastatic focus may be treated by excision or radiation therapy, jaw involvement almost always is associated with widely disseminated disease, Five-year survival after detection of metastatic carcinoma Involving the jaws is exceedingly rare, and most patients do not survive more than 1 year.



Osteosarcoma



Osteosarcoma



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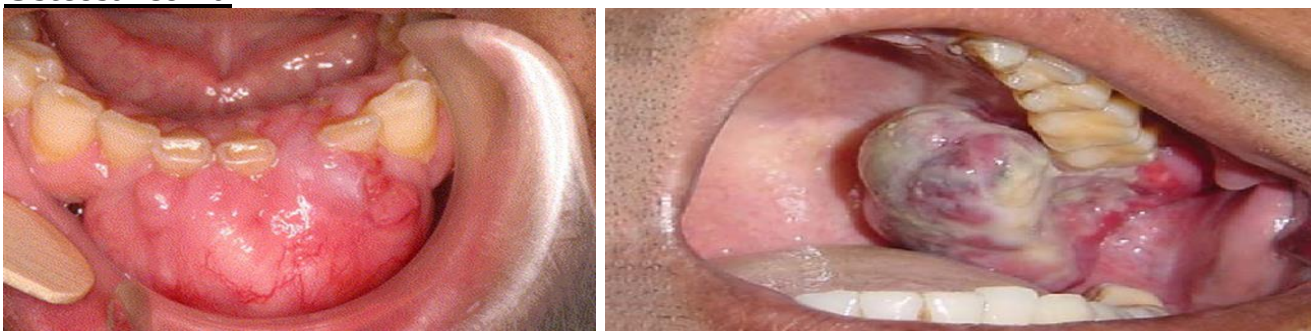
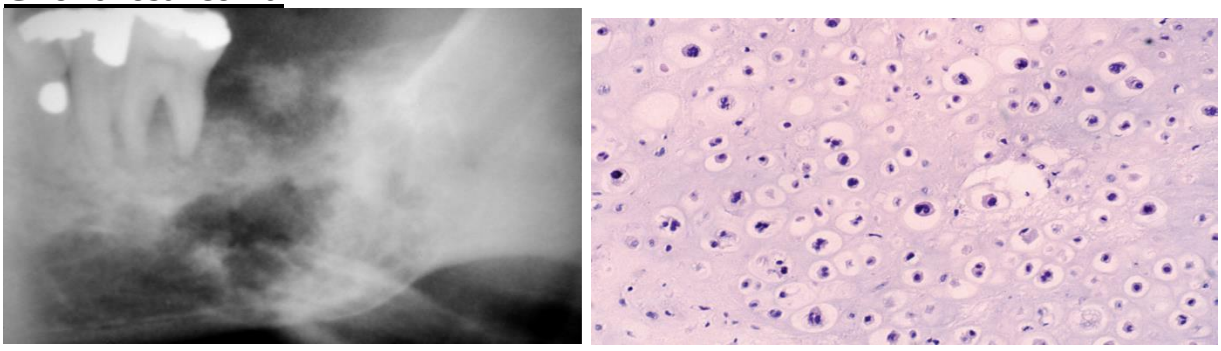
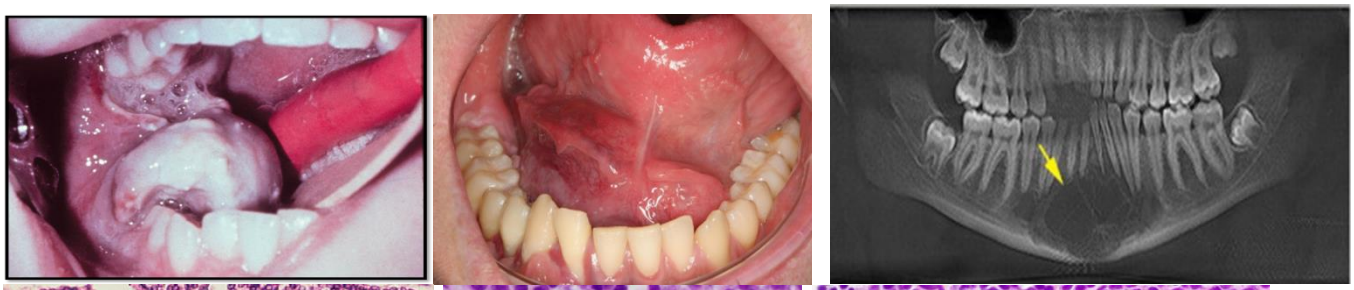


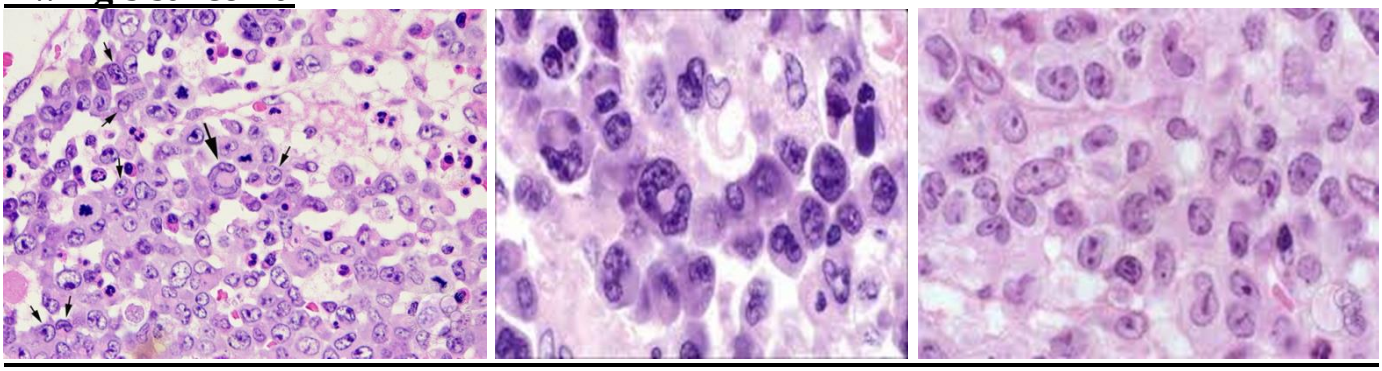
Chondrosarcoma



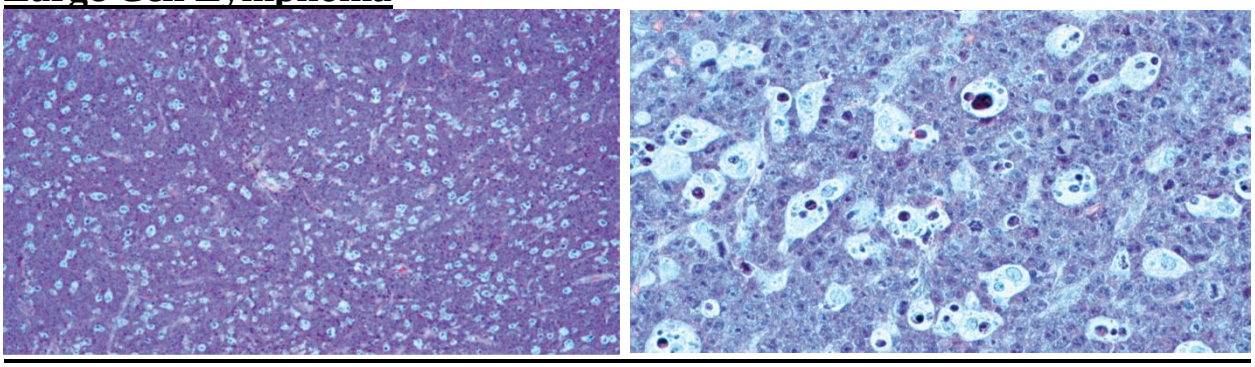
Chondrosarcoma



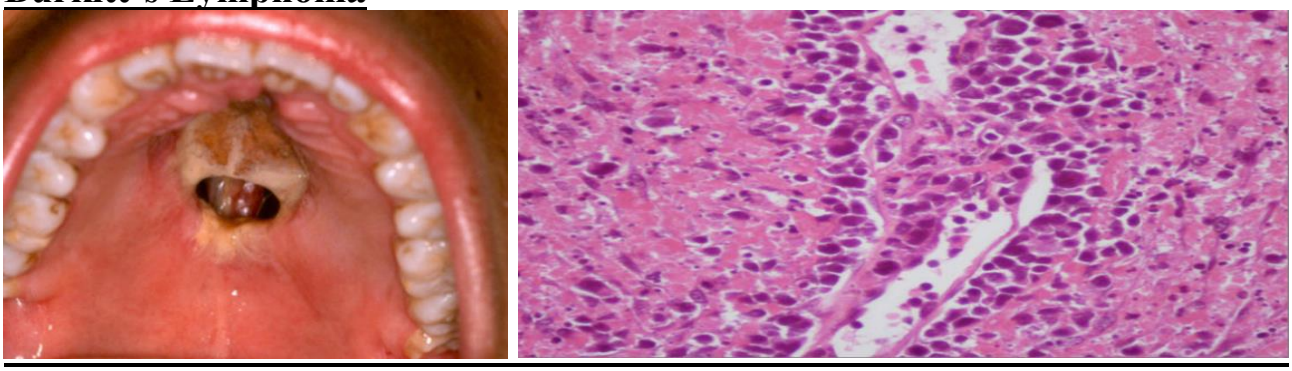
Ewing's sarcoma



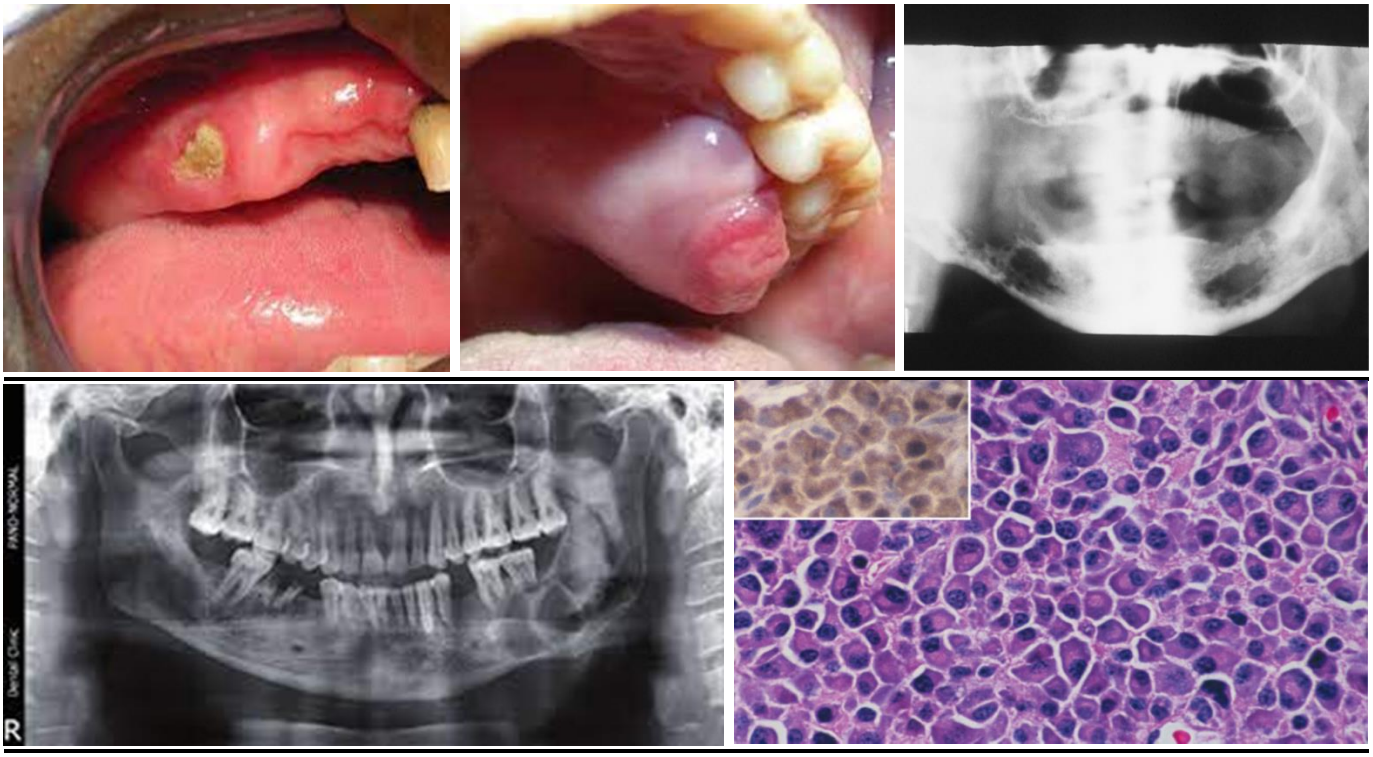
Large Cell Lymphoma



Burkitt's Lymphoma



Angiocentric T-cell lymphoma



Multiple myeloma mm

Oral pathology

Oral mucosal lesions

The oral cavity is lined by a membrane composed of stratified squamous epithelium. This epithelium serves as a cover for the oral soft tissues as a barrier to the entry of external pathogenic factors. Depending on the intraoral site, the stratified squamous epithelium may be non-keratinized, orthokeratinized or parakeratinized. Knowledge of clinical aspects of oral mucosal diseases must be correlated with oral anatomy. E.g. recurrent aphthous stomatitis occurs primarily on the non-keratinized mucosa, whereas recurrent herpes simplex infections occur almost exclusively on the keratinized mucosa.

Keratinized mucosa (functional mucosa) e.g. gingiva and hard palate.

Non –keratinized mucosa (lining mucosa) e.g. floor of the mouth and buccal mucosa.

-Specialized mucosa e.g. dorsal surface of the tongue .

In general, oral mucosal lesions could be divided into:

-Oral infections

- Viral
- Bacterial
- Fungal

-Immune mediated lesions

- Ulcerative conditions
- Vesiculobullous diseases

The clinician should be familiar with the following terms :

Macule: Focal area of color change which is not elevated or depressed in relation to its surroundings.

Papule: Solid, raised lesion which is less than 5 mm in diameter.

Nodule: Solid, raised lesion which is greater than 5 mm in diameter.

Sessile: Describing a tumor or growth whose base is the widest part of the lesion.

***Pedunculated*:** Describing a tumor or growth whose base is narrower than the widest part of the lesion.

Papillary: Describing a tumor or growth exhibiting numerous surface projections.

Verrucous: Describing a tumor or growth exhibiting a rough, warty surface.

Vesicle: Superficial blister, 5 mm or less in diameter, usually filled with clear fluid.

Bulla: Large blister, greater than 5 mm in diameter.

Pustule: Blister filled with purulent exudate.

Ulcer: Lesion characterized by loss of the surface epithelium and frequently some of the underlying connective tissue. It often appears depressed or excavated.

Erosion: Superficial lesion. Often arising secondary to rupture of a vesicle or bulla, that is characterized by partial or total loss of the surface epithelium.

Fissure: Narrow, slit like ulceration or groove.

Plaque: Lesion that is slightly elevated and is flat on its surface.

Petechia: Round, pinpoint area of hemorrhage.

Ecchymosis: Nonelevated area of hemorrhage, larger than a petechia.

Telangiectasia: Vascular lesion caused by dilatation of a small, superficial blood vessel.

Cyst: Pathologic epithelium-lined cavity often filled with liquid or semi-solid contents.

Microscopic changes of oral mucosa:

Epithelial changes:

Hyperkeratosis: refers to an increase in the thickness of stratum cornium , which yields a white appearance of the oral mucosa clinically. This hyperkeratinizations can occur in keratinized area or abnormally in non-keratinized area. When the nuclei are lost from the surface the

conditions is named (hyperorthokeratosis). When remnants of the nuclei persist the condition is named (hyperparakeratosis).

Hyperplasia: an increase in the thickness of the epithelium from surface to basal cell layer.

Acanthosis : An increase in the prickle cell layer is termed .

Epithelial dysplasia (dyskeratosis or epithelial atypia): an abnormal growth pattern of epithelial cells. Generally indicates a premalignant change.

***Acantholysis* :** loss of adhesion between the cells of prickle cell layer (spinous cell layer) the cells appear to fall apart, which lead to vesicle formation, e.g. pemphigus vulgaris.

Connective tissue changes:

-Inflammatory infiltrate are common, as chronic inflammatory cells infiltration, e.g. gingivitis.

-Hyperplasia of connective tissue refers to an increase in the amount of collagen fibers.

-Ductal and glandular distension could be seen in many accessory mucous glands due to pressure and obstruction.

Oral infections

I-Bacterial Infections

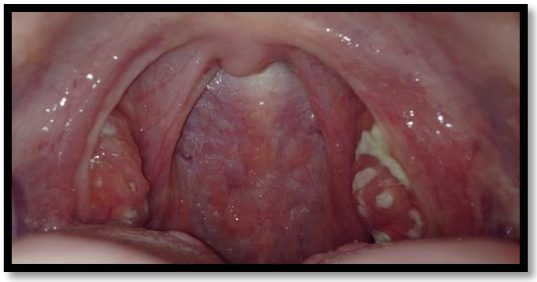
Tonsillitis and Pharyngitis

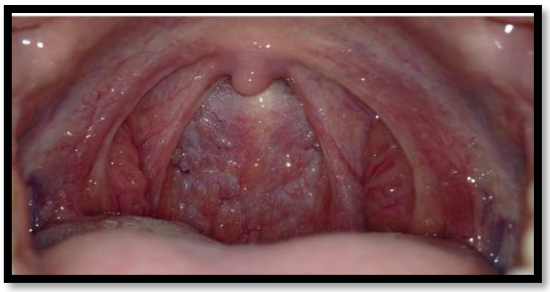
Tonsillitis and Pharyngitis are extremely common and may be caused by many different organisms .Group A streptococci is responsible for 20% to 30% of acute pharyngitis cases in children and 5% to 15% of cases in adults .Spread is typically by person-to-person contact through respiratory droplets or oral secretions, with a short incubation period of 2 to 5 day.

Clinical Features:

Although the infection can occur at any age, the greatest prevalence occurs in children 5 to 15 years old, with most cases in temperate climates arising in the winter or early spring.

The signs and symptoms of tonsillitis and pharyngitis vary from mild to intense. Common findings include sudden onset of sore throat, temperature of 101° to 104° F, dysphagia, tonsillar hyperplasia, redness of the oropharynx and tonsils, palatal petechiae, cervical lymphadenopathy, and a yellowish tonsillar exudate that may be patchy or confluent .Systemic symptoms, such as headache, malaise, anorexia, abdominal pain, and vomiting, may be noted, especially in younger children





Treatment :

Streptococcal pharyngitis usually is self-limited and resolves spontaneously within 3 to 4 days after onset of symptoms. The oral antibiotic of choice for group A streptococci is either penicillin V or amoxicillin. Other choices for penicillin-allergic patients include azithromycin, clindamycin, cephalosporins and macrolides (such as, erythromycin or clarithromycin).

Scarlet Fever (Scarlatina)

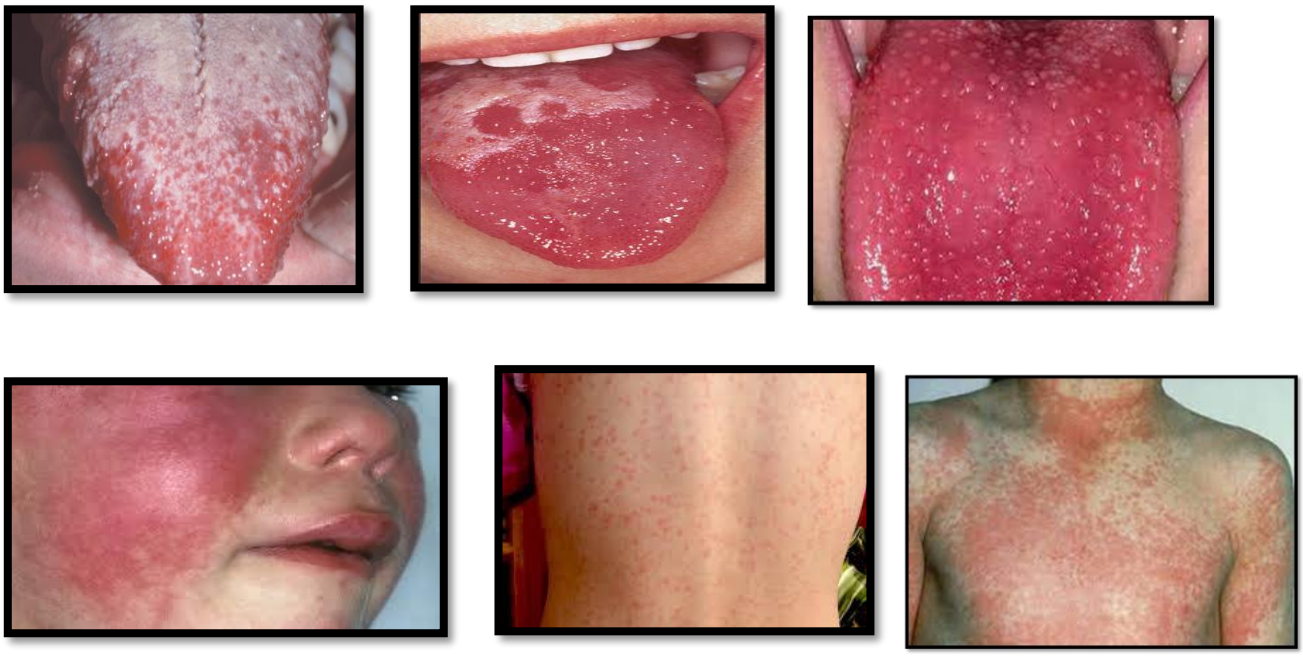
Scarlet fever is a systemic infection produced by group A,β-hemolytic streptococci. The disease begins as a streptococcal tonsillitis with pharyngitis in which the organisms elaborate an erythrogenic toxin that attacks the blood vessels and produces the characteristic skin rash.

Clinical Features:

Scarlet fever is most common in children from the ages of 3 to 12 years. The tonsils, soft palate, and pharynx become erythematous and edematous, and the tonsillar crypts may be filled with a yellowish exudate. In severe cases, the exudates may become confluent and can resemble diphtheria . Scattered petechiae may be seen on the soft palate in up to 10% of affected patients. During the first 2 days, the dorsal surface of the tongue demonstrates a white coating through which only the fungiform papillae can be seen; this has been called white strawberry tongue . By the fourth or fifth day, red strawberry tongue develops when the white coating desquamates to reveal an erythematous dorsal surface with hyperplastic fungiform papillae. Classically, in untreated cases, fever develops abruptly around the second day. The patient's temperature peaks

at approximately 103° F and returns to normal within 6 days. Abdominal pain, headache, malaise, nausea, and vomiting frequently are present.

The exanthematous rash develops within the first 2 days and becomes widespread within 24 hours. The classic rash of scarlet fever is distinctive and often is described as a "sunburn with goose pimples." Pinhead punctate areas that are normal in color project through the erythema, giving the skin of the trunk and extremities a sandpaper texture. The rash is more intense in areas of pressure and skin folds. In contrast, the skin of the face usually is spared or may demonstrate erythematous cheeks with circumoral pallor. The rash usually clears within 1 week, and then a period of desquamation of the skin occurs.



Treatment:

The oral antibiotic of choice for group A streptococci is either penicillin V or amoxicillin. Other choices for penicillin-allergic patients include azithromycin, clindamycin, cephalosporins such as, cefadroxil or cephalexin), and macrolides (such as, erythromycin or clarithromycin). Ibuprofen can be used to reduce the fever and relieve the associated discomfort.

Necrotizing Ulcerative Gingivitis

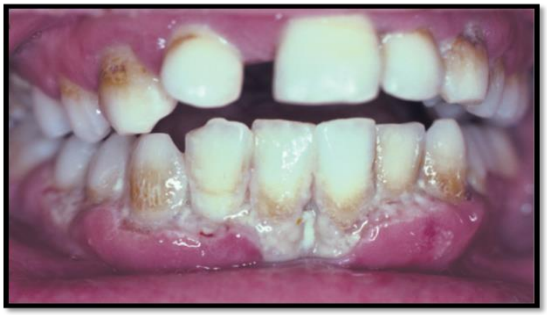
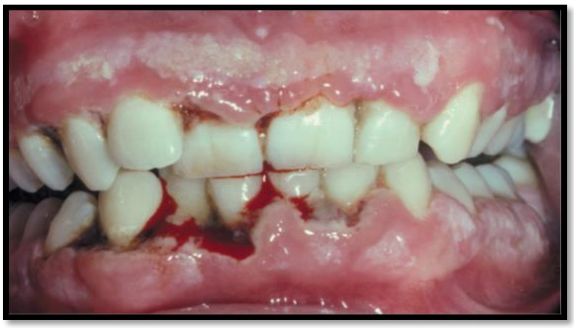
Necrotizing ulcerative gingivitis is a relatively rare specific infectious gingival disease of young persons. Fusobacterium nucleatum, Treponema vincentii, and probably other bacteria play an important role. Predisposing factors are emotional stress, smoking, poor oral hygiene, local trauma, and HIV infection.

Clinical features:

The characteristic clinical feature is painful necrosis of the interdental papillae and the gingival margins, and the formation of craters covered with a gray pseudo-membrane. Spontaneous gingival bleeding, halitosis, and intense salivation are common. Fever, malaise, and lymphadenopathy are less common. Rarely, the lesions may extend beyond the gingiva (necrotizing ulcerative stomatitis).

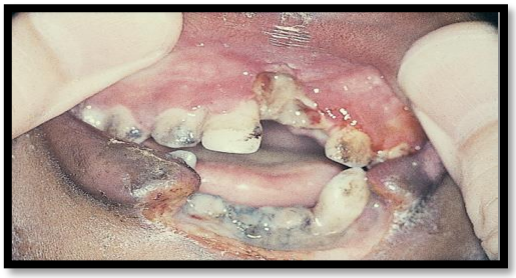
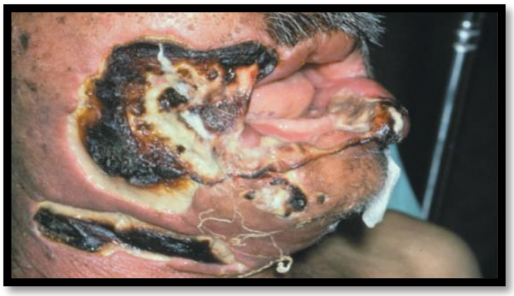
Treatment:

Systemic metronidazole and oxygen-releasing agents topically are the best therapy in the acute phase, followed by a mechanical gingival treatment.

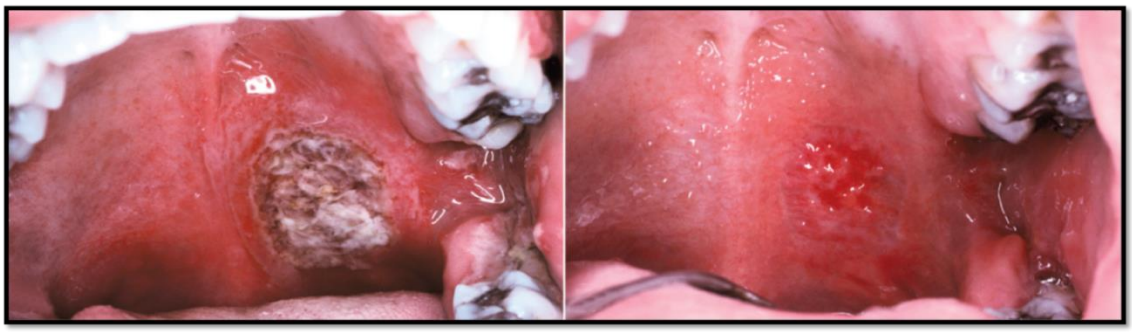
Noma

Noma, also known as cancrum oris and gangrenous stomatitis, is a devastating disease of malnourished children that is characterized by a destructive process of the orofacial tissues. The condition is rare in developed countries. Necrosis of tissue occurs as a consequence of invasion by anaerobic bacteria such as Fusobacterium necrophorum, Prevotella intermedia and spirochaetes in a host whose systemic health is significantly compromised.

Clinical Features **:** It typically affects children. also can occur in adults with a major debilitating disease (e.g., diabetes mellitus, leukemia, lymphoma, or HIV infection).The initial

lesion of noma is a painful ulceration, usually of the gingiva or buccal mucosa, which spreads rapidly and eventually becomes necrotic. Denudation of involved bone may follow, eventually leading to necrosis and sequestration. Teeth in the affected area may become loose and may exfoliate. Penetration of organisms into the cheek, lip, or palate may also occur, resulting in fetid necrotic lesions.

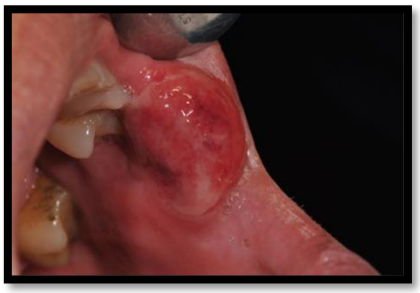


Treatment: Therapy involves treating the underlying predisposing condition, as well as the infection itself. Therefore fluids, electrolytes, and general nutrition are restored, along with the introduction of antibiotics.

Syphilis

Syphilis is a relatively common sexually transmitted disease Caused by Treponema pallidum.

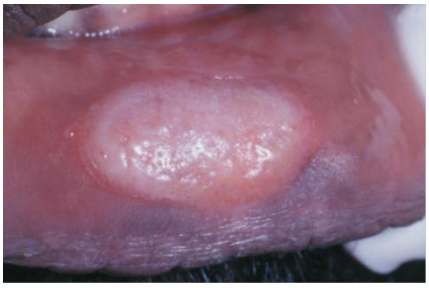
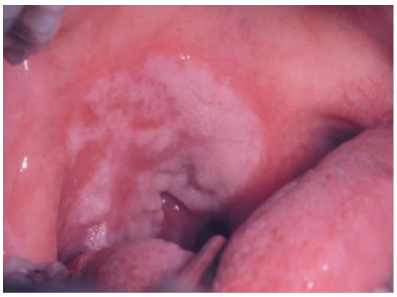
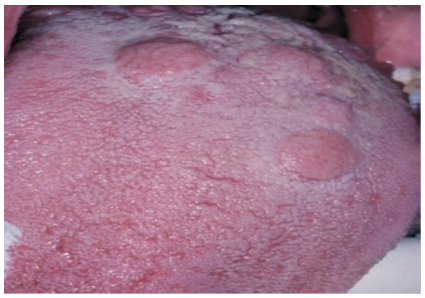
Clinical features: Syphilis may be acquired (common) or congenital (rare). Acquired syphilis is classified as primary, secondary and tertiary. The characteristic lesion in the primary stage is the chancre that appears at the site of inoculation, usually three weeks after the infection. Oral chancre appears in about 5–10% of cases, and clinically presents as a painless ulcer with a smooth surface, raised borders, and an indurated base. Regional lymphadenopathy is a constant finding.



Oral Chancre

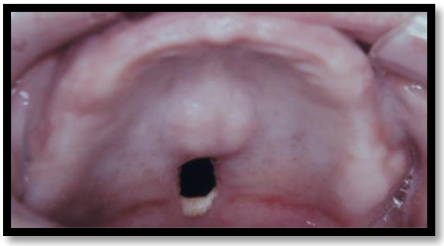
The secondary stage begins 6–8 weeks after the appearance of the chancre, and lasts for 2–10 weeks. Oral lesions are mucous patches (common), macular syphilids, and condylomata lata (rare). Constitutional symptoms and signs (malaise, low-grade fever, headache, lacrimation, sore throat, weight loss, myalgias and multiple arthralgias, generalized lymphadenopathy) as well as

cutaneous manifestations (macular syphilids, papular syphilids, condylomata lata, nail involvement, hair loss, atypical rash, etc.) are constant findings.

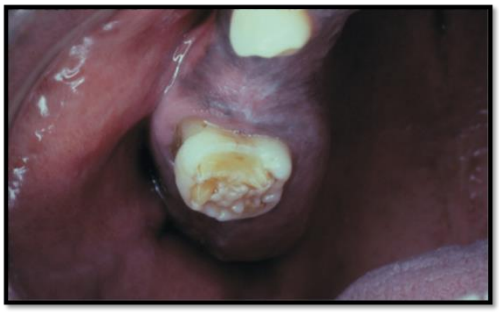
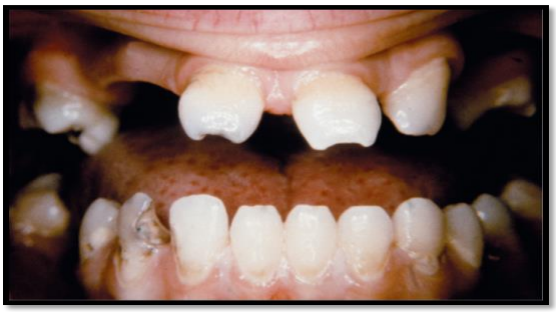
mucous patches condylomata lata

Tertiary syphilis begins after a period of 4–7 years. Oral lesions are gumma, atrophic glossitis, and interstitial glossitis.



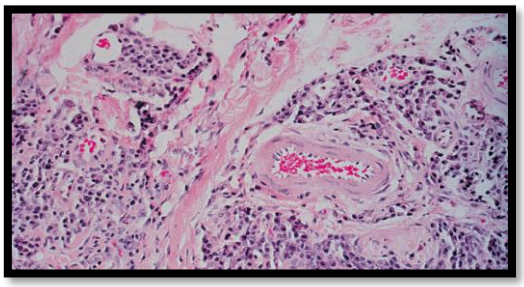
Gumma

The most common oral lesions in congenital syphilis are a high-arched palate, short mandible, Hutchinson's teeth, and Moon's or mulberry molars.

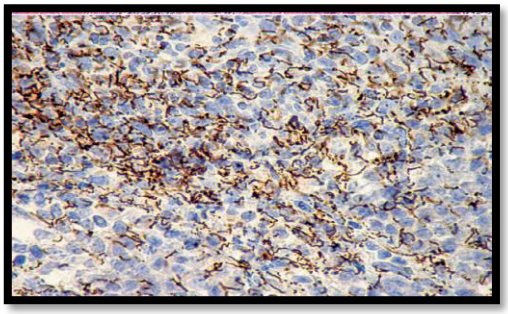



Histopathology. The basic tissue response to T. pallidum infection consists of a proliferative endarteritis and infiltration of plasma cells. Spirochetes can be demonstrated in the tissues of various lesions of syphilis using silver stains, although they may be scant in tertiary lesions. Gumma may show necrosis and greater numbers of macrophages, resulting in a granulomatous

lesion that is similar to other conditions, such as tuberculosis (TB).



A chronic perivascular inflammatory infiltrate of plasma cells and lymphocytes.



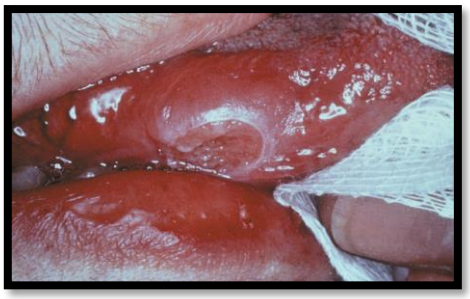
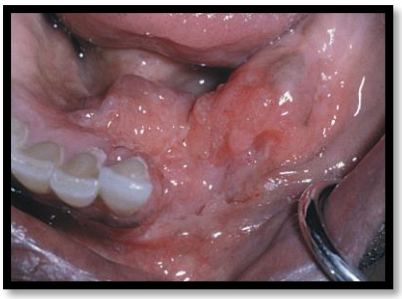
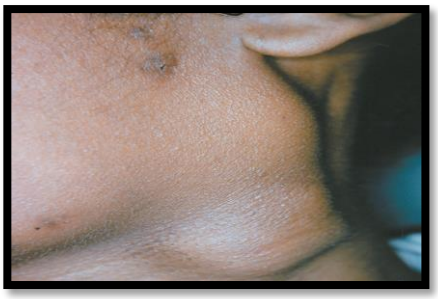
Immunoperoxidase reaction for Treponema pallidum demonstrating numerous spirochetes in the epithelium.

Treatment. Penicillin is the antibiotic of choice. Erythromycin or cephalosporins are good alternatives

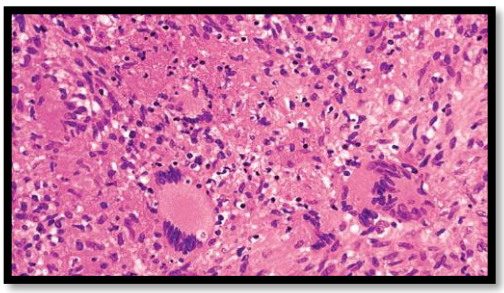
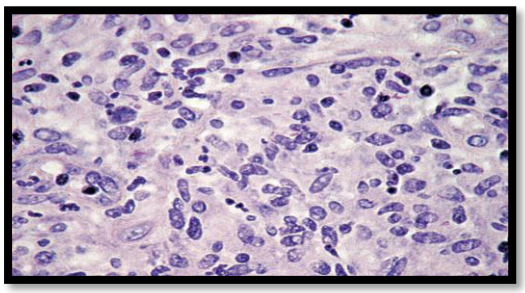
Tuberculosis

Tuberculosis is a chronic, granulomatous, infectious disease that primarily affects the lungs, caused by Mycobacterium tuberculosis.

***Clinical features*:** The oral lesions are rare, and usually secondary to pulmonary tuberculosis. The tuberculous ulcer is the most common feature. Clinically, the ulcer is painless and irregular, with a thin undermined border and a vegetating surface, usually covered by a gray-yellowish exudate. The surrounding tissues are inflamed and indurated. The dorsum of the tongue is the most commonly affected site, followed by the lip, buccal mucosa, and palate. Osteomyelitis of the jaws, periapical granuloma, regional lymphadenopathy, and scrofula are less common oral manifestations.

Histopathology.The basic microscopic lesion of TB is granulomatous inflammation, in which granulomas show central caseous necrosis. In tissues, M. tuberculosis incites a characteristic macrophage response, in which focal zones of macrophages become surrounded by lymphocytes and fibroblasts. The macrophages develop an abundant eosinophilic cytoplasm, giving them a superficial resemblance to epithelial cells; for this reason, they are frequently called epithelioid cells. Fusion of macrophages results in the appearance of Langerhans giant cells, in which nuclei are distributed around the periphery of the cytoplasm. As the granulomas age, central necrosis occurs; this is usually referred to as caseous necrosis because of the gross cheesy texture of these zones. A Ziehl-Neelsen or Fite stain must be used to confirm the presence of the organism in the granulomas, because several infectious and noninfectious conditions may produce a similar granulomatous reaction.

A  B 

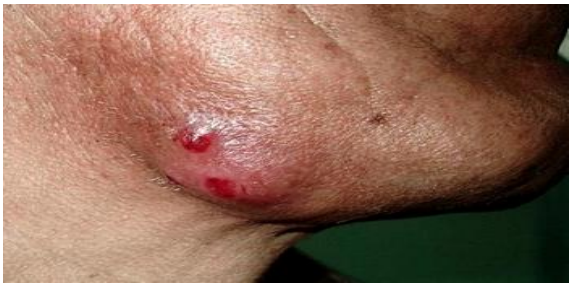
Sheets of histiocytes are intermixed with multinucleated giant cells and areas of necrosis.(B) Acid-fast stain exhibiting scattered mycobacterial organisms presenting as small red rods.

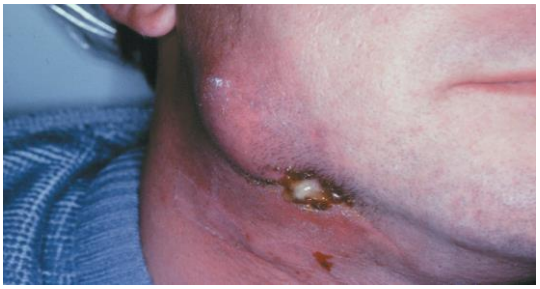
Actinomycosis

Actinomycosis is a chronic bacterial disease caused by Actinomyces israelii, an anaerobic , gram-positive bacterium. Infection usually appears after trauma, surgery, or previous infection.

Clinically: It typically presents as swelling of the mandible that may simulate a pyogenic infection. The lesion may become indurated and eventually may form one or more draining sinuses, leading from the medullary spaces of the mandible to the skin of the neck. The clinical course ranges from acute to chronic. The skin lesions are indurated and are described as having a

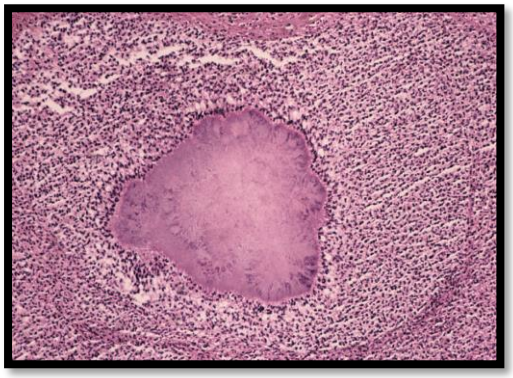
“woody hard” consistency. Pus draining from the chronic lesion may contain small yellow granules, known as sulfur granules, which represent aggregates of A. israelii organisms. Radiographically, this infection presents as a lucency with irregular and ill-defined margins.

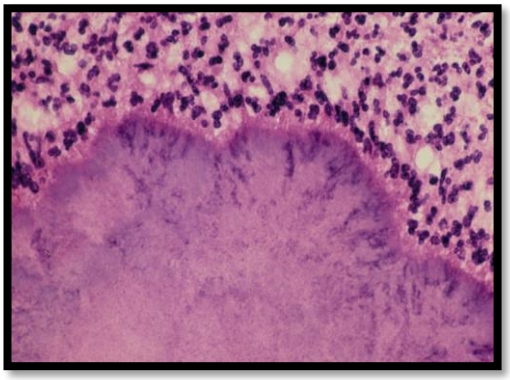




Histopathology. A granulomatous inflammatory response with central abscess formation is seen in actinomycosis. At the center of the abscesses, distinctive colonies of gram-positive organisms may be seen. Radiating from the center of the colonies are numerous filaments with clubbed ends.

Treatment. Long-term, high-dose penicillin or penicillin analogs are the required antibiotic regimen for actinomycosis.





Oral pathology

Viral Infection

HERPES SIMPLEX VIRUS

HSV-1 is spread predominantly through infected saliva or active perioral lesions . HSV-2 is adapted best to the genital zones, is transmitted predominantly through sexual contact, and typically involves the genitalia and skin below the waist.

Herpes simplex virus (HSVs) infections occur in two forms—primary (systemic)and secondary (localized). Both forms are self-limited, but recurrences of the secondary form are common because the virus can remain within ganglionic tissue in a latent state.

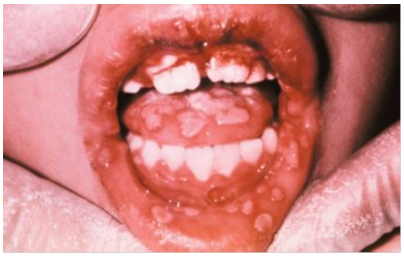
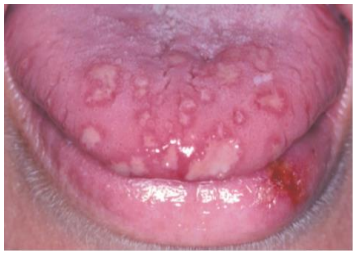
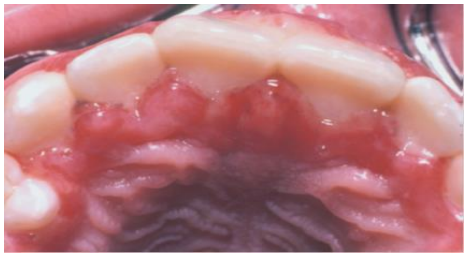
Primary infection refers to initial exposure of an individual without antibodies to the virus. Primary infection with HSV-1 typically occurs at a young age, often is asymptomatic . After primary infection the virus remains in a latent state in trigeminal ganglion.

Recurrent (secondary or recrudescent) infection occurs with reactivation of the virus. Old age, ultraviolet light, physical or emotional stress, fatigue, heat, cold, pregnancy, allergy, trauma, dental treatment, respiratory illnesses, fever, menstruation, systemic diseases, and malignancy have been associated with reactivation.

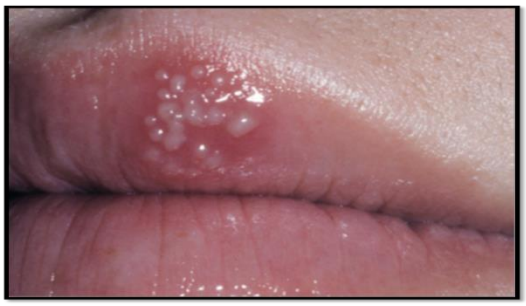
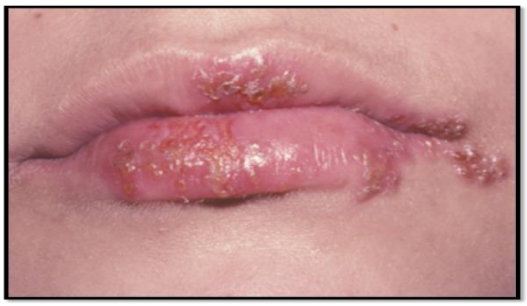
Clinical Features

Acute herpetic gingivostomatitis (primary herpes) is the most common pattern of symptomatic primary HSV infection, and more than 90% of cases are caused by HSV-1. Most affected individuals are children between the ages of 6 months and 5 years . The onset is abrupt and often accompanied by anterior cervical lymphadenopathy, chills, fever , nausea, anorexia, irritability, and sore mouth lesions.

Initially the affected mucosa develops numerous pinhead vesicles, which rapidly collapse to form numerous small, red lesions. These lesions enlarge slightly and develop central ulceration covered by yellow fibrin ulcerations may coalesce to form larger, shallow, irregular ulcerations . Mild cases usually resolve within 5 to 7 days; severe cases may last 2 weeks.

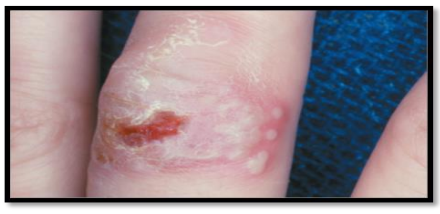




Recurrent herpes simplex infections (secondary herpes) may occur either at the site of primary inoculation or in adjacent areas of surface epithelium supplied by the involved ganglion. The most common site of recurrence for HSV-1 is the vermilion border and adjacent skin of the lips. This is known as herpes labialis (**"cold sore" or "fever blister"**). In some patients, ultraviolet light or trauma can trigger recurrences. Prodromal signs and symptoms (e.g., pain, burning, itching, tingling, localized warmth, and erythema of the involved epithelium) arise 6 to 24 hours before the lesions develop. Multiple small erythematous papules develop and form clusters of fluid-filled vesicles. The vesicles rupture and crust within 2 days. Healing usually occurs within 7 to 10 days. Symptoms are most severe in the first 8 hours.

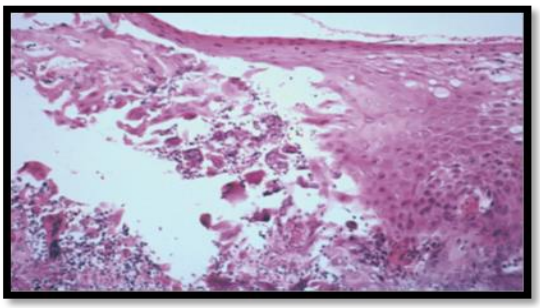



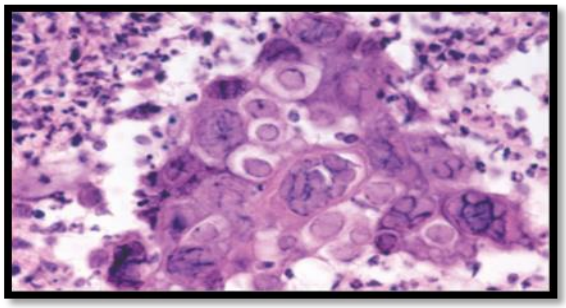
The lesions begin as 1- to 3-mm vesicles that rapidly collapse to form a cluster of erythematous macules that may coalesce or slightly enlarge . The damaged epithelium is lost, and a central yellowish ulceration develops. Healing occurs within 7 to 10 days. Several less common presentations also exist

Primary or recurrent HSV infection of the fingers is known as **herpetic whitlow (herpetic paronychia)**. This condition may result from self-inoculation in children with orofacial HSV-1 infection or adults genital HSV-2 infection.Recurrent digital infection may result in paresthesia and permanent scarring.



Histopathological Features: HSV-infected epithelial cells exhibit acantholysis, nuclear clearing, and nuclear enlargement (termed ballooning degeneration).The acantholytic epithelial cells may be referred to as Tzanck cells. (This term refers to free-floating epithelial cells in any intraepithelial vesicle and is not specific for herpes.) Multinucleated epithelial cells are formed by fusion between adjacent cells .





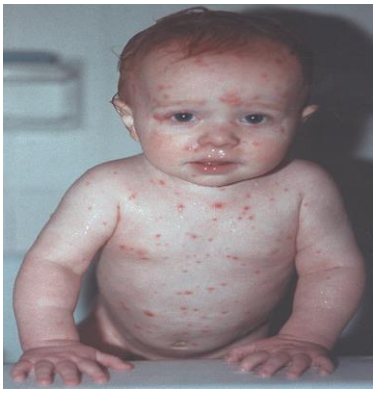
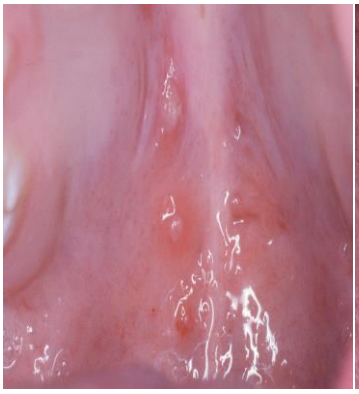
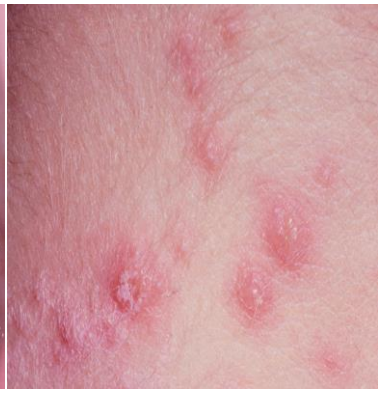
Treatment and Prognosis: Symptomatic. In severe cases, systemic aciclovir or valaciclovir. Non-steroidal anti-inflammatory drugs (NSAIDs) used for more immediate pain relief.

VARICELLA (CHICKENPOX):

Varicella (chickenpox) represents primary infection with the varicella-zoster virus (VZV or HHV-3). Secondary or reactivated disease is known as **herpes zoster** .The virus may be spread through air droplets or direct contact with active lesions. In contrast to primary HSV infection, most cases of primary VZV infection are symptomatic.

Clinical Features A maculopapular, cutaneous rash with only a small number of lesions, few or no vesicles, low or no fever, and a shortened disease course of approximately 4 to 6 days are characteristic findings. Patients are contagious until no new lesions appear within a 24-hour period. The symptomatic phase of primary VZV infection usually begins with malaise, pharyngitis, and rhinitis. In older children and adults, additional symptoms (e.g., headache, myalgia, nausea, anorexia, and vomiting) occasionally are seen. This is followed by a characteristic, intensely pruritic exanthem. The rash begins on the face and trunk and spreads to the extremities. Each lesion rapidly progresses through stages of erythema, vesicle, pustule, and hardened crust.

The vesicular stage is the classic presentation. Each vesicle is surrounded by a zone of erythema and has been described as “a **dewdrop on a rose petal**.” In contrast to herpes simplex, the lesions typically continue to erupt for 4 or more days.

Perioral and oral manifestations are fairly common and may precede the skin lesions. The vermilion border and palate are involved most often, followed by the buccal mucosa. Occasionally, gingival lesions resemble those noted in primary HSV infection, but distinguishing between the two is not difficult because the lesions of varicella tend to be relatively painless. The lesions begin as 3- to 4-mm, white, opaque vesicles that rupture to form 1- to 3-mm ulcerations.

Treatment and Prognosis

Supportive therapy is generally indicated. Warm baths with soap, application of calamine lotion; and systemic antihistamine still are used to relieve pruritus. Acetaminophen is the preferred antipyretic for childhood cases. Peroral antiviral medications (such as, acyclovir, valacyclovir,) .

HERPES ZOSTER (SHINGLES)

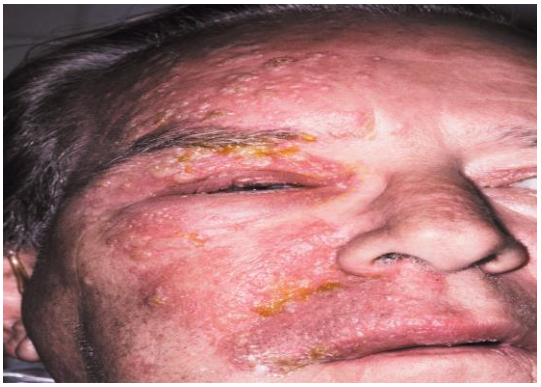
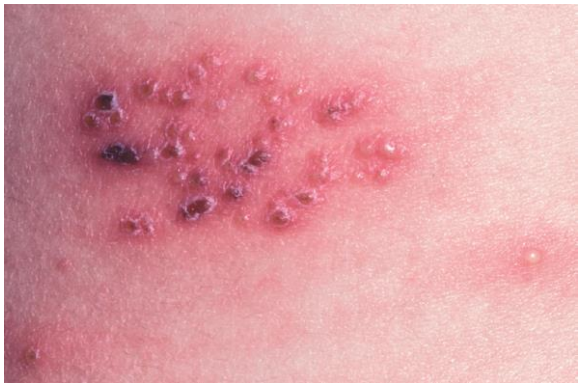
Herpes zoster develops after reactivation of the virus, with involvement of the distribution of the affected sensory nerve. The prevalence of attacks increases with age, apparently due to age-related decline in cell-mediated immunity. Immunosuppression, HIV infection, treatment with cytotoxic or immunosuppressive , radiation, malignancy, old age, alcohol abuse, stress(emotional or physical), and dental manipulation are additional predisposing factors for reactivation.

Clinical Features

The clinical features of herpes zoster can be grouped into three phases: prodromal , acute, and chronic. During initial viral replication, ganglionitis develops with resultant neuronal necrosis and severe neuralgia. This inflammatory reaction is responsible for the prodromal pain present in more than 90% of cases. The pain intensifies and has been described as burning, tingling, itching, boring, prickly, or knifelike. and may be accompanied by fever,

malaise, and headache. This prodromal pain normally precedes the acute phase rash by 1 to 4 days and, depending on which dermatome is affected, may masquerade as sensitive teeth, otitis media, migraine headache, myocardial infarction, or appendicitis.

The acute phase begins as the involved skin develops clusters of vesicles set on an erythematous base . Within 3 to 4 days, the vesicles become pustular and ulcerate, with crusts developing after 7 to 10 days. The exanthem typically resolves within 2 to 3 weeks in otherwise healthy individuals. On healing, scarring with hypopigmentation or hyperpigmentation is not unusual.

Infrequently, there is dermatomal pain without development of a rash; this pattern is called **zoster sine herpete**(zoster without rash).

Oral lesions occur with trigeminal nerve involvement and may be present on the movable or bound mucosa. Like varicella, the individual lesions manifest as 1- to 4-mm vesicles or pustules that rupture to form shallow ulcerations . Reactivation of VZV in the geniculate ganglion may cause Ramsay Hunt syndrome. Approximately 15% of patients progress to the chronic phase of herpes zoster (termed **postherpetic neuralgia**), which is characterized by persistent pain after resolution of the rash.

Treatment and Prognosis

Supportive therapy for herpes zoster may include antipruritics. Antiviral medications, such as acyclovir and valacyclovir has been found to accelerate healing of mucocutaneous lesions and reduce pain .

Hand-foot and- mouth disease

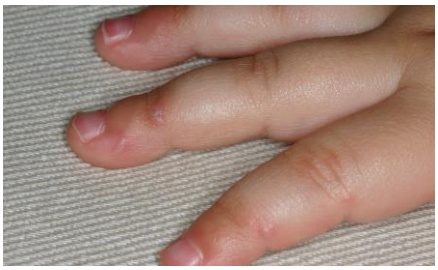
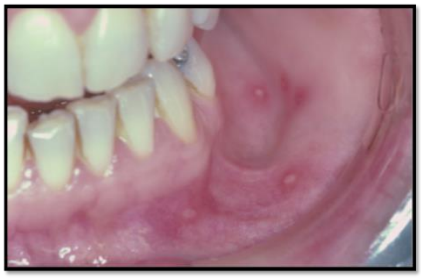
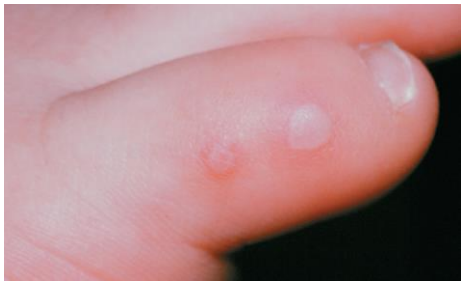
Hand-foot-and-mouth disease is the best-known presentation of enterovirus infection. It is caused by coxsackievirus A16, but also may arise from coxsackie virus A5, A9, or A10.

Clinical Features

The skin rash and oral lesions typically are associated with flulike symptom (e.g., sore throat, dysphagia, and fever), occasionally accompanied by cough, rhinorrhea, anorexia, vomiting, diarrhea, myalgia, and headache. The name fairly well describes the location of the lesions.

Oral and hand lesions almost always are present. The oral lesions arise without prodromal symptoms and precede the development of the cutaneous lesions. Sore throat and mild fever usually are present also. The cutaneous lesions range from a few to dozens and primarily affect the borders of the palms and soles and the ventral surfaces and sides of the fingers and toes . The cutaneous lesions begin as erythematous macules that develop central vesicles and heal without crusting.

The oral lesions begin as numerous red macules, which form fragile vesicles that rapidly ulcerate and involve anterior regions of the mouth. The number of lesions ranges from 1 to 30. The buccal mucosa, labial mucosa, and tongue are the most common sites. The individual lesions typically measure 2 to 7 mm in diameter but may be larger than 1 cm. The lesions rapidly ulcerate and then typically heal within 1 week.

Treatment and Prognosis

In most instances, enterovirus infections are self-limiting and without significant complications. Therapy is directed toward symptomatic relief; non-aspirin antipyretics and topical anesthetics, such as dyclonine hydrochloride, often are beneficial.

MEASLES (RUBEOLA):

Measles (rubeola) is a highly contagious infection produced by a virus in the family Paramyxoviridae and genus Morbillivirus.

Clinical Features: Most cases of measles arise in late winter or spring and are spread through respiratory droplets. The average incubation period is 14 days, and affected

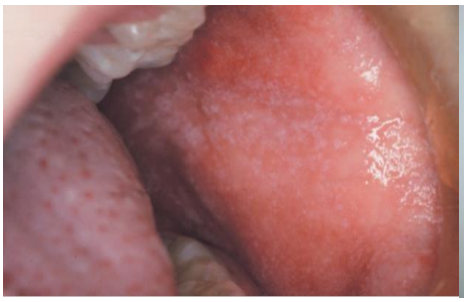
individuals are infectious from 4 days before until 4 days after appearance of the associated rash. The virus is associated with significant lymphoid hyperplasia that often involves the lymph nodes, tonsils, adenoids, and Peyer patches.

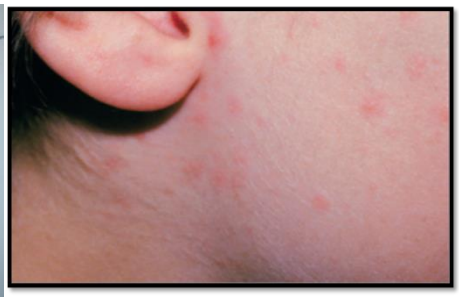
There are **three stages** of infection, with each stage lasting 3 days—hence the designation 9-day measles.

The first 3 days are dominated by the three Cs: coryza (runny nose), cough (typically brassy and uncomfortable), and conjunctivitis (red, watery, and photophobic eyes). Fever typically accompanies these symptoms. During this initial stage, the most distinctive oral manifestation, **Koplik spots**, is seen. These lesions represent foci of epithelial necrosis and appear as numerous small, blue-white macules (or "grains of salt) surrounded by erythema . Typical sites of involvement include the buccal and labial mucosa, and less often the soft palate.

As the second stage begins, the fever continues, the Koplik spots fade, and a maculopapular and erythematous (**morbilliform**) rash begins. The face is involved first, with eventual downward spread to the trunk and extremities. Ultimately, a diffuse erythematous eruption is formed, which tends to blanch on pressure .

In the third stage, the fever ends. The rash begins to fade,with downward progression and replacement by brown pigmentation. Ultimately, desquamation of the skin is noted in areas previously affected by the rash.





. **Treatment :**

No specific treatment for measles is known. Supportive therapy of bed rest, fluids, adequate diet, and analgesics generally suffices.

Fungal infections

Candidal infection (Candidiasis)

Candidiasis is the most common oral fungal infection. It is usually caused by Candida albicans.

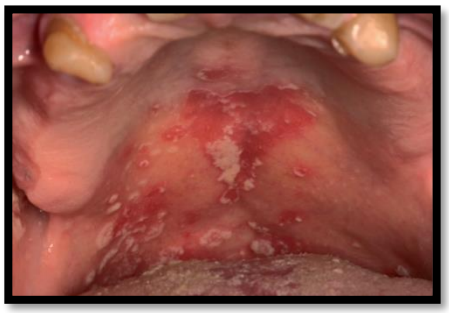
Predisposing factors are **local** (poor oral hygiene, xerostomia,mucosal damage, dentures, antibiotic mouthwashes) and **systemic** (broad-spectrum antibiotics, steroids, immunosuppressive drugs, radiation, HIV infection,hematological malignancies, neutropenia, iron-deficiency anemia, cellular immunodeficiency, endocrine disorders).

Clinical features

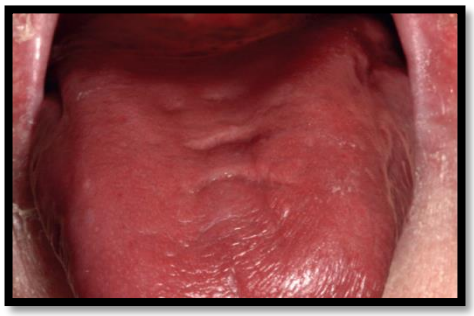
Oral candidiasis is classified as **primary**, consisting of lesions exclusively on the oral and perioral area, and **secondary**, consisting of oral lesions of mucocutaneous disease.

Primary candidiasis includes many clinical varieties:

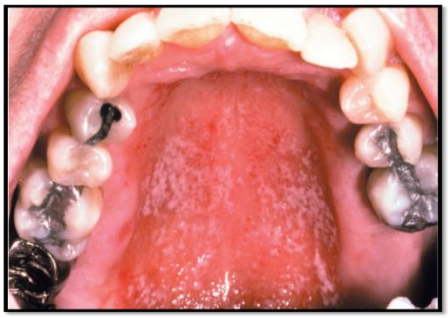
pseudomembranous (thrush) , erythematous(papillary hyperplasia of the palate), Chronic Hyperplastic Candidiasis , and Candida-associated lesions (angular cheilitis, median rhomboid glossitis, denture stomatitis) .



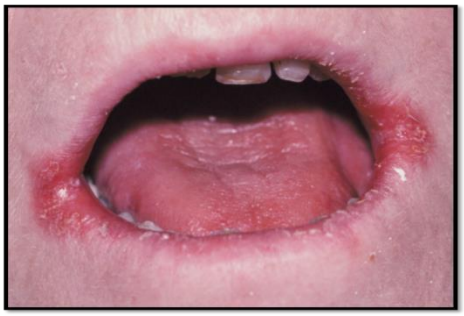
-Pseudomembranous Candidiasis



- Erythematous Candidiasis



-Papillary hyperplasia of the palate



- Angular cheilitis

Histopathology: In acute candidiasis, fungal pseudohyphae are seen penetrating the upper layers of the epithelium at acute angles. Neutrophilic infiltration of the epithelium with superficial microabscess formation is typically seen.

Treatment: dealing with predisposing factors + topical and/or systemic antifungals.

Deep fungal infections

Deep fungal infections are characterized by primary involvement of the lungs. Infections may disseminate from this focus to involve other organs.Deep fungal infections having a significant incidence of oral involvement include histoplasmosis, coccidioidomycosis, blastomycosis, mucormycosis, and cryptococcosis

Clinical Features: Initial signs and symptoms of deep fungal infection are usually related to lung involvement and include cough, fever, night sweats, weight loss, chest pain, and hemoptysis. The usual oral lesion is ulcerative. Whether single or multiple, lesions are non-healing, indurated, and frequently painful.

Histopathology. The basic inflammatory response in a deep fungal infection is granulomatous. In the presence of these microorganisms, macrophages and multinucleated giant cells dominate the histologic picture

Treatment : Treatment of deep mycotic infection generally consists of antifungals such as ketoconazole, fluconazole, and amphotericin B .

Human immunodeficiency virus (HIV) infections and AIDS

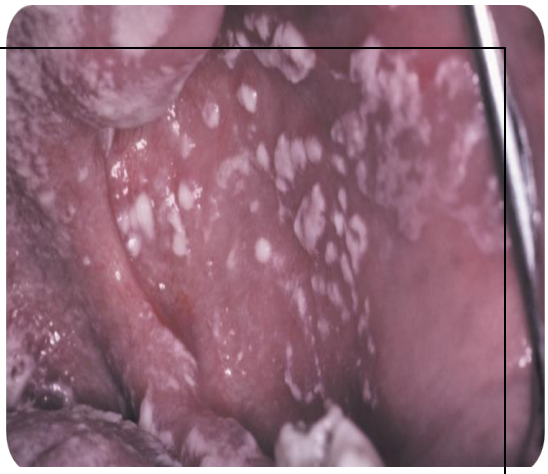
The oral manifestation of HIV infection are numerous and have been divided into three groups based on the strength of their association with HIV infection. the main lesions in each group are listed in table below

Group 1-Lesions strengthly associated with HIV infections

- Candidiasis
  - Erythematous
  - Hyperplastic
  - Pseudomembranous
- Hairy leukoplakia (EB virus)
- HIV associated periodental disease
  - HIV gingivitis
  - Necrotizing ulcerative gingivitis
  - HIV associated periodontitis
  - Necrotizing stomatitis
- Kaposis sarcoma
- Non-Hodgkins lymphoma

Group 2-lesions less commonly associated with HIV infections

- Atypical ulceration

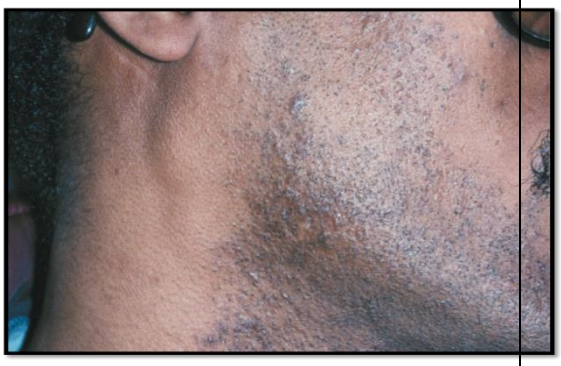


- ❖ Ideopathic thrombocytopenic purpura
- ❖ Salivary gland disorders (Dry mouth, decreased salivary flow rate Unilateral or bilateral swelling of major glands
- ❖ Viral infection other than (EB virus)
    - Cytomegalo virus
    - Human papilloma virus
    - Varicella zoster virus

Group 3-lesions possibly associated with HIV infection

- ❖ Bacterial infections other than gingivitis/periodontitis
- ❖ Fungal infection other than candidiasis
- ❖ Melanotic hyperpigmentation
- ❖ Neurologic disturbances
- ❖ Facial palsy
- ❖ Trigeminal neuralgia

Oral Manifestaton of Aquired immunodyficiency system (AIDS)



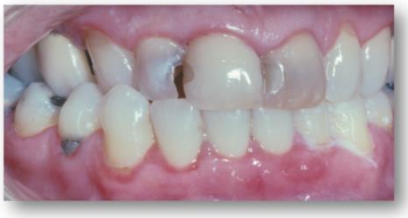
Persistent generalized lymphadenopathy.

HIV lymphadenitis may be seen in the HIV scale, later in the course of the disease lymph node biopsies may be necessary to rule out lymphoma.

Candidiasis. Oral candidiasis is the most common intra oral manifestation of HIV infection and often is the presenting sign that leads to the initial diagnosis, Its presence in a patient infected with HIV is not diagnostic of AIDS but appears to be predictive for the subsequent development of full-blown AIDS in untreated patients with in 2 years. The following four clinical patterns of oral candidiasis are seen:

- •Pseudomembranous
- •Erythematous
- •Hyperplastic
- •Angular cheilitis

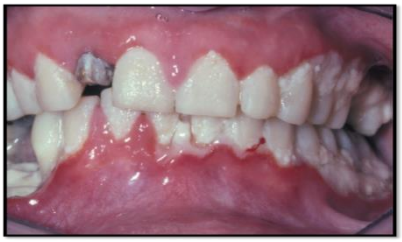
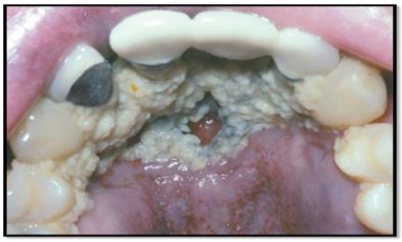
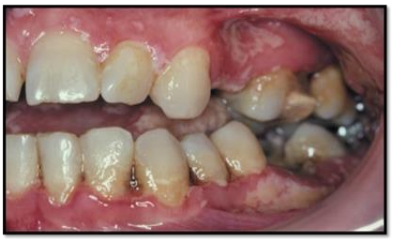
HIV-associated periodontal disease. Three patterns of periodontal disease are associated strongly with HIV infection:



- Linear gingival erythema
- Necrotizing ulcerative gingivitis
- Necrotizing ulcerative periodontitis

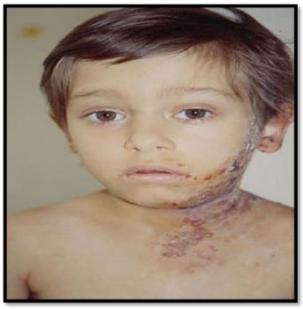
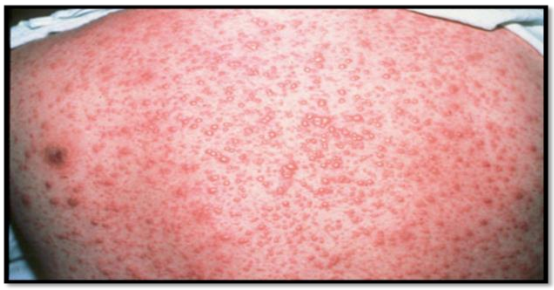
Linear gingival erythema initially was termed HIV" Iated gingivitis but ultimately was noted in association with other disease processes.

Necrotizing ulcerative gingivitis (NUG) Refers to ulceration and necrosis of one or more interdental papillae with no loss of periodontal attachment. Necrotizing ulcerative periodontis (NUP) was previously termed HIV-associated periodontitis; however, it has not been seemed to be specific for HIV infection. NUP is characterized by gingival ulceration and necrosis associated with rapidly progressing loss of periodontal attachment. Although severe cases can affect all teeth.

Herpes simplex virus (HSV). Recurrent HSV infections occur in about the same percentage of HIV-infected patients as they do in the immunocompetent population (10% to 15%); however, the lesions are more widespread, occur in an atypical pattern, and may persist for months.

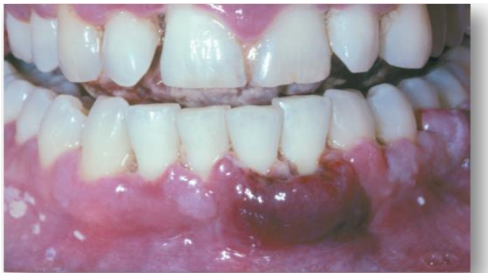
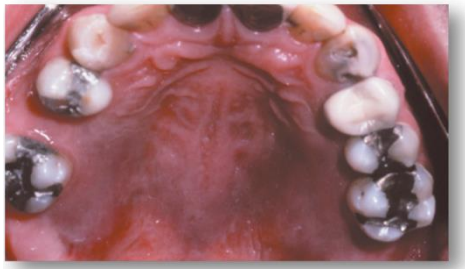
Varicella-zoster virus (VZV). Recurrent VZV infection (herpes zoster) is fairly common in HIV-infected patients, oral involvement often is severe and occasionally leads to bone sequestration and loss of teeth. Associated pain typically is intense.

Epstein-Barr virus (EBV).

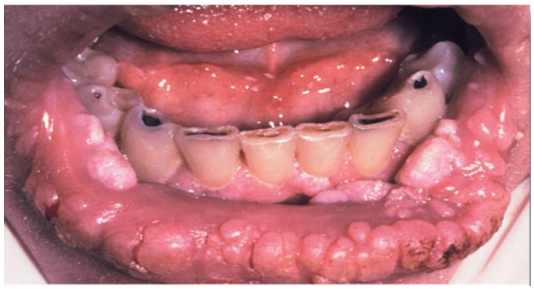
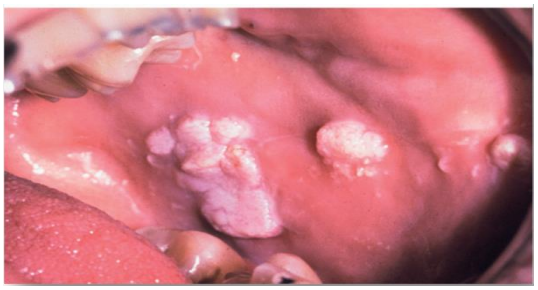
Although EBV is thought to be associated with several forms of lymphoma in HIV infected patients, the most common EBV-related lesion in patients with AIDS is oral hairy leukoplakia (OHL). This lesion has a somewhat distinctive (but not diagnostic)pattern of hyperkeratosis and epithelial hyperplasia that is characterized by white mucosal lesions that do not rub off.

Kaposi's sarcoma (KS): KS is a multifocal neoplasm of vascular endothelial cell origin, KS begins with single or, more frequently. Multiple lesions of the skin or oral mucosa. The trunk, arms, head, and neck are the most commonly involved anatomic sites. Oral lesions are seen in approximately 50% of affected patients and are the initial site of involvement in 20% to 25%. Although any mucosal site may be involved, the hard palate, gingiva, and tongue are affected most frequently the neoplasm mean invade bone and create tooth mobility.

Aphthous ulcerations. Lesions that are similar clinically to aphthous ulcerations occur with increased frequency in patients infected with HIV. All three forms (minor, major, and herpetiform) are seen.

Human papillomavirus (HPV) HPV is responsible for several facial and oral lesions in immunocompetent patients.The most frequent of which are the verruca vulgaris (common wart) and oral squamous papilloma.

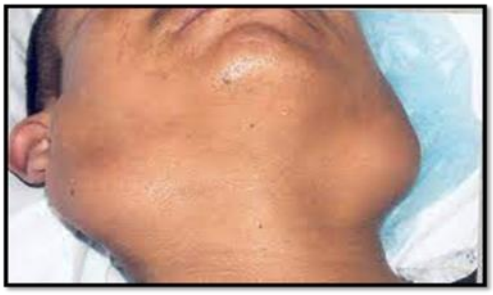



Histoplasmosis.

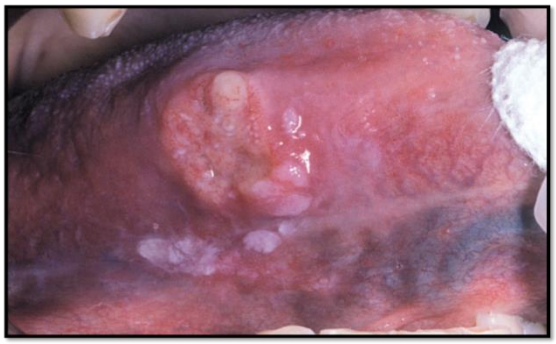
Histoplasmosis is produced by Histoplasma capsulatum. In healthy patients. The infection typically is subclinical and self-limiting, but clinically evident infections do occur in immunocompromised individuals. Although a number of deep fungal infections are possible in patients with AIDS.

HIV-associated salivary gland disease.

Clinically obvious salivary gland disease is noted in approximately 5% of HIV infected patients, with a greater prevalence noted in children. The main clinical sign is salivary gland enlargement, particularly affecting the parotid. Bilateral involvement is seen in about 60% of the patients with glandular changes and often is associated with cervical lymphadenopathy.



Oral squamous cell carcinoma. Squamous cell carcinoma of the oral cavity, pharynx, and larynx has been reported in HIV-infected patients.



Oral Pathology

Lec. 18+ lec.19

Epithelial Pathology

❖ Squamous cell papilloma and other benign lesion associated with human papilloma (HPV)

HPV are DNA viruses and more than 130 types are now recognized, of which at least 30 have been isolated from oral lesions. The majority are low-risk types (e.g. 6, 11, 13, and 32) which are associated with benign lesions of the skin and oral mucosa, such as verruca vulgaris, condyloma accuminatum, and focal epithelial hyperplasia. However, certain types of HPV may be present in clinically healthy oral mucosa and the identification of HPV in a lesion does not necessarily imply a causal relationship.

SQUAMOUS CELL PAPILLOMA

This common benign tumor is usually a solitary lesion and can occur anywhere on the oral mucosa. Most occur in adults but they may also be seen in children. Papillomas vary in size and may be either pedunculated or sessile. They present as **warty or cauliflower-like growths with a white or pink surface depending on the amount of keratin present**. Histological examination shows **finger-like processes of proliferating stratified squamous epithelium supported by thin cores of vascular connective tissue. The epithelium may show hyperkeratosis**. Mitotic figures are often seen in the basal layer of the epithelium, but features of epithelial dysplasia are not present. Malignant change has not been described in a squamous cell papilloma of the oral mucosa and it is not a premalignant lesion.

VERRUCA VULGARIS (COMMON WART)

Clinically, these lesions present as squamous cell papillomas and may be sessile or pedunculated, single or multiple. They appear white because of hyperkeratosis and are seen most often in children when they may be associated with auto inoculation from warts on the fingers and lips. Histologically, they consist of papillary processes of proliferating, acanthotic, hyperkeratotic squamous epithelium supported by thin cores of vascular connective tissue. The hyperplastic rete ridges around the margins usually slope inwards towards the corner of the lesion. Common warts on the skin are usually associated with HPV types 2 or 4 infection.

CONDYLOMA ACUMINATUM (VENEREAL WART)

Characteristically these warts occur in the ano- genital region but they may be seen on the oral mucosa. Clinically, they present as multiple pink nodules which grow and coalesce firm soft, pink, pedunculated or sessile papillary lesions similar in color to the surrounding mucosa. In some patients they are an oral manifestation of HIV infection.

Histologically

The dominant epithelial feature is a prominent acanthosis with marked broadening and elongation of the rete ridges. Keratinization is not a feature although there may be a surface layer of parakeratoric cells. Condyloma acuminatum is associated with HPV types 6.

FOCAL EPITHELIAL HYPERPLASIA (HECK'S DISEASE)

This rare disease was originally described in native North Americans and India but occurs in other ethnic groups and in some immunocompromised patients. It is characterized by multiple small elevated epithelial plaques or polypoid lesions most frequently involving the lower lips and buccal mucosa.

Histological examination shows hyperparakerarosis and acanthosis of the oral epithelium. HPV types I3 and 32 appear to be specific to oral focal epithelial hyperplasia. Lesions of the oral mucosa, which are white, result from the scattering of light through a thickened layer of keratin, epithelial hyperplasia, intracellular epithelial

edema, and/or reduced vascularity of subjacent connective tissue. White or yellow-white lesions may also be due to fibrinous exudates covering an ulcer, submucosal deposits, surface debris, or fungal colonies.

MOLLUSCUM CONTAGIOSUM

is a virus-induced epithelial hyperplasia produced by the molluscum contagiosum virus, a member of the DNA poxvirus group. At least 6% of the population (more in older age groups) has antibodies to this virus, although few ever develop lesions. After an incubation period of 14 to 50 days, infection produces multiple papules of the skin or, rarely, mucous membranes. These remain small for months or years and then spontaneously involute

Verruciform xanthoma is a hyperplastic condition of the epithelium of the mouth, skin, and genitalia, with a characteristic accumulation of lipid-laden histiocytes beneath the epithelium. The lesion probably represents an unusual reaction or immune response to localized epithelial trauma or damage The lesion appears as a well-demarcated, soft, painless, sessile, slightly elevated mass with a white, yellow white, or red color and a papillary or roughened (verruciform) surface Rarely, flat-topped nodules are seen without surface projections. Most lesions are smaller than 2 cm in greatest diameter

❖ EPHELIS

An ephelis is a common small hyper pigmented macule of the skin that represents a region of increased melanin production Ephelis are seen most often on the face, arms, and back of fair-skinned, blue-eyed, redor light-blond haired persons.

❖ MELASMA (MASK OF PREGNANCY)

is an acquired, symmetrical hyperpigmentation of the sun-exposed skin of the face and neck. The exact cause is unknown, but UV light exposure and hormonal influences appear to be important etiologic factors. Melasma classically is associated with pregnancy.

❖ ORAL MELANOTIC MACULE (FOCAL MELANOSIS)

is a flat, brown, mucosal discoloration produced by a focal increase in melanin deposition and, possibly, a concomitant increase in the number of melanocytes. The cause remains unclear. Unlike the cutaneous ephelis (freckle), the melanotic macule is not dependent on sun exposure histopathology: increased melanin pigmentation distributed along basal epithelial layer.

❖ ORAL MELANOACANTHOMA

is an uncommon, benign, acquired pigmentation of the oral mucosa characterized by dendritic melanocytes dispersed throughout the epithelium. The lesion appears to be a reactive process; in some cases, an association with trauma has been reported.

❖ ACQUIRED MELANOCYTIC NEVUS (NEVOCELLULAR NEVUS; MOLE

The generic term nevus refers to congenital or developmental malformations of the skin (and mucosa). Nevi may arise from the surface epithelium or underlying connective tissue.

The most commonly recognized nevus is the acquired melanocytic • nevus, or common mole—so much so that the simple term nevus often is used synonymously for this pigmented lesion. However, many other developmental nevi also are recognized.

• The congenital melanocytic nevus affects approximately 1% of newborns in the United States. The trunk and extremities are involved most commonly, although approximately 15% of lesions arise in the head and neck area. Intraoral involvement is rare.

❖ HALO NEVUS (SUTTON NEVUS; LEUKODERMA ACQUISITUM CENTRIFUGUM)

The halo nevus is a melanocytic nevus with a hypopigmented border, apparently resulting from nevus cell and melanocyte destruction by the immune system. The cause of the immune attack is unknown, but regression of the nevus usually results. Interestingly, multiple halo nevi may develop in patients who have had a recent excision of a melanoma.

❖ BLUE NEVUS (DERMAL MELANOCYTOMA)

The blue nevus is an uncommon, benign proliferation of dermal melanocytes, usually deep within the connective tissue. Mucosal lesions may involve the oral mucosa, conjunctiva, and, rarely, sinonasal mucosa. Oral lesions almost always are found on the palate. The lesion usually occurs in children and young adults

❖ FOCAL FRICTIONAL HYPERKERATOSIS (reactive lesions)

Etiology: Focal (frictional) hyperkeratosis is a white lesion that is related to chronic rubbing or friction against an oral mucosal surface. This results in a presumably protective hyperkeratotic white lesion that is analogous to a callus on the skin.

Clinical Features

Friction-induced hyperkeratoses occur in areas that are commonly traumatized, such as the lips, lateral margins of the tongue, buccal mucosa along the occlusal line, and edentulous alveolar ridges. Chronic cheek or lip chewing may result in opacification (keratinization) of the affected area. Chewing on edentulous alveolar ridges produces the same effect.

Histopathology.

As the name indicates, the primary microscopic change is hyperkeratosis. A few chronic inflammatory cells may be seen in the subjacent connective tissue.

Diagnosis

Careful history taking and examination should indicate the nature of this lesion. If the practitioner is clinically confident of a traumatic cause, no biopsy may be required. Patients should be advised to discontinue the causative habit or the offending tooth or denture should be smoothed. The lesion should resolve or at least should be reduced in intensity over time, confirming the clinical diagnosis. Resolution of the lesion would allow unmasking of any underlying lesion that may not be related to trauma. If the clinical diagnosis is in doubt, a biopsy should be taken.

Treatment: Observation is generally all that is required for simple frictional hyperkeratotic lesions. Control of the habit causing the lesion should result in clinical improvement. No malignant potential exists.

❖ KERATOACANTHOMA

Is a self-limiting, epithelial proliferation with a strong clinical and histopathologic similarity to well differentiated squamous cell carcinoma. Indeed, many dermatopathologists consider it to represent an extremely well-differentiated squamous cell carcinoma. Cutaneous lesions presumably arise from the infundibulum of hair follicles. Intraoral lesions have been reported, but they are rare; in fact, some authorities do not accept keratoacanthoma as an intraoral disease.

The exact cause is unknown. An association with sun damage is suggested by the fact that most solitary lesions are found on sun-exposed skin in older adults. Additional potential contributing factors include tar exposure, HPV, immunosuppression, certain drugs (such as, BRAF inhibitors and tyrosine kinase inhibitors), tattooing, and burns or other trauma. Keratoacanthoma shows a male predilection and rarely occurs before 45 years of age. Almost 95% of solitary lesions involve sunexposed skin, and 8% of all cases involve the outer edge of the vermilion border of the lips, with equal frequency on the upper and lower lip.

Oral pathology

Lec.19

Epithelial hyperplasia, atrophy, and dysplasia

SMOKELESS TOBACCO KERATOSIS

Marked geographic and gender differences in tobacco use have been identified. In the United States, a relatively high prevalence of smokeless tobacco users is found in the southern and western states. Use by men in New York and Rhode Island is less than 1% of the population, but in West Virginia, use exceeds 20%. Among teenagers, whites are the predominant users of smokeless tobacco, with males making up nearly this entire group. Smokeless tobacco is also used in Sweden in the form of snus, a non-fermented type of tobacco with lower concentrations of harmful nicotine and tobacco derivatives versus those types of fermented smokeless tobaccos traditionally used in the United States. In regions such as the Indian subcontinent and Southeast Asia, use is even more common and the materials more destructive. The tobacco-containing preparations generally are of a higher (alkaline) pH and often are mixed with other ingredients, including shredded areca (betel) nut; they may also contain lime, camphor, and spices.

The general increase in smokeless tobacco consumption has been related to both peer pressure and increased media advertising, which often glamorizes the use of smokeless tobacco, or snuff dipping. In addition, individuals who have been intense smokers and those who wish to avoid smoking may gravitate to this alternative. The clinical results of long term exposure to smokeless tobacco include the development of oral mucosal white patches with a slightly increased malignant potential, dependence, alterations of taste, acceleration of periodontal disease, and significant amounts of dental abrasion.

Etiology: A causal relationship has been documented between smokeless tobacco and white tissue changes. Although all forms of smokeless tobacco may cause alterations in the oral mucosa, snuff (particulate, finely divided, or shredded tobacco) appears to be much more likely to cause oral lesions than does chewing tobacco. Oral mucosa responds to the topically-induced effects of tobacco with inflammation and keratosis.

At the molecular level, altered cell signaling and subsequent cell damage have been demonstrated. Dysplastic changes may follow, with a low potential risk of malignant change. Smokeless tobacco–induced alterations in tissues are thought to be a response to tobacco constituents and perhaps other agents that are added for flavoring or moisture retention. Carcinogens such as nitro son or nicotine, an organic component of chewing tobacco and snuff, have been identified in smokeless tobacco. The pH of snuff, which ranges between 8.2 and 9.3, may be another factor that contributes to the alteration of mucosa.

Duration of exposure to smokeless tobacco that is necessary to produce mucosal damage is measured in terms of years. It has been demonstrated that leukoplakia can be predicted with the use of three tins of tobacco per week or duration of the habit of longer than 2 years.

Clinical Features

White lesions associated with smokeless tobacco develop in the immediate area where the tobacco is habitually placed. The most common area of involvement is the mucobuccal fold of the mandible in the incisor or the molar region. The mucosa develops a granular to wrinkled appearance. In advanced cases, a heavy, folded character may be seen. Less often, an erythroplakic or red component may be admixed with the white keratotic component. The lesions are generally painless and asymptomatic, and their discovery is often incidental to routine oral examination.

Histopathology.

Slight to moderate parakeratosis, often in the form of spires or chevrons, is noted over the surface of the affected mucosa. Superficial epithelium may demonstrate vacuolization or edema. A slight to moderate chronic inflammatory cell infiltrate is typically present. Epithelial dysplasia may occasionally develop in these lesions, especially among long-time users of smokeless tobacco. On occasion, a diffuse zone of basophilic stromal alteration may be seen, usually adjacent to inflamed minor salivary glands.

Treatment and Prognosis

With discontinuation of smokeless tobacco use, some lesions may disappear after several weeks. It would be prudent to perform a biopsy on persistent lesions. A long period of exposure to smokeless tobacco increases the risk of transformation to verrucous or squamous cell carcinoma, although this risk is probably low.

NICOTINE STOMATITIS

Etiology: Nicotine stomatitis is a common tobacco-related form of keratosis. It is typically associated with pipe and cigar smoking, with a positive correlation between intensity of smoking and severity of the condition. The importance of the direct topical effect of smoke can be appreciated in instances in which the hard palate is covered by a removable prosthesis, resulting in sparing of the mucosa beneath the appliance and hyperkeratosis of exposed areas. The combination of tobacco carcinogens and heat is markedly intensified in reverse smoking (lit end positioned inside the mouth), adding significant risk for malignant conversion.

Clinical Features

The palatal mucosa initially responds with an erythematous change followed by keratinization. Subsequent to opacification or keratinization of the palate, red dots surrounded by white keratotic rings appear. The dots represent inflammation surrounding the minor salivary gland excretory ducts.

Histopathology.

Nicotine stomatitis is characterized by epithelial hyperplasia and hyperkeratosis. The minor salivary glands in the area show inflammatory change, and excretory ducts may show squamous metaplasia.

Treatment and Prognosis

This condition rarely evolves into malignancy, except in individuals who reverse smoke. Although the risk of carcinoma development in the palate is minimal, nicotine stomatitis is a marker or indicator of intense tobacco use and hence may indicate increased risk of epithelial dysplasia and neoplasia elsewhere in the oral cavity, oropharynx, and respiratory tract.

Therefore, nicotine stomatitis should be viewed as a potential indicator of significant epithelial change at sites other than the hard palate.

ACTINIC CHEILITIS

Actinic, or solar, cheilitis represents accelerated tissue degeneration of the vermilion (dry mucous membrane) of the lips, especially the lower lip, as a result of chronic exposure to sunlight; it is considered to represent a potentially premalignant condition. This condition occurs almost exclusively in whites and is especially prevalent in those with fair skin.

Etiology and Pathogenesis. The wavelengths of light most responsible for actinic cheilitis and, in general, other degenerative actinically-related skin conditions are usually considered to be those between 2900 and 3200 nm (ultraviolet B [UVB]). This radiant energy affects not only the epithelium, but also the superficial supporting connective tissue.

Clinical Features

The affected vermilion of the lips takes on an atrophic, pale to silvery gray, glossy appearance, often with fissuring and wrinkling at right angles to the cutaneous-vermilion junction. Slightly firm, bilateral swelling of the lower lip is common. In advanced cases, the junction is irregular or totally effaced, with a degree of epidermization of the vermilion. Mottled areas of hyperpigmentation and keratosis are often noted, as well as superficial scaling, cracking, erosion, ulceration, and crusting.

Histopathology

The overlying epithelium is typically atrophic and hyperkeratotic. Basophilic changes in the submucosa (altered elastin that replaces normal collagen) and telangiectasia are also seen.

Treatment

Because of the positive relationship between exposure to UV light and carcinoma, lip protection is indicated. The use of lip balm containing a sunscreen agent such as para-aminobenzoic acid (PABA) or its derivatives is indicated during periods of sun exposure in high-risk patients.

Sun-blocking agents such as titanium dioxide or zinc oxide provide complete protection from both ultraviolet A (UVA) and UVB rays. Chronic sun damage mandates periodic examination and a biopsy if ulceration persists or if induration occurs. If atypical changes are noted within the epithelium, a vermilionectomy may be

performed in association with mucosal advancement to replace the damaged vermilion. This operation is associated with some morbidity, primarily related to lip paresthesia, therefore prompting some to advocate wedge excision for suspicious lesions. Acceptable results are attainable with the use of laser surgery or cryosurgery, as well as with topical 5-fluorouracil. Topical imiquimod, an immune stimulant, has been used with clearing of lesions noted within 4 weeks of treatment completion.

ACTINIC KERATOSES (SOLAR KERATOSES)

Actinic keratoses of the skin, the cutaneous counterpart of actinic cheilitis, are epithelial changes noted typically in light-complexioned individuals who have had long-term exposure to sunlight. A small percentage of these lesions develop into squamous cell carcinoma. Outdoor workers and individuals participating in extensive outdoor recreation are particularly prone to the development of actinic keratosis Oval plaques, usually smaller than 1 cm in diameter, are typically found on the forehead, cheeks, temples, ears, and lateral portions of the neck. The color may vary from yellow-brown to red, and the texture is usually rough and sandpaper-like.

Common to the many actinic keratosis microscopic subtypes are nuclear atypia, an increased nuclear-cytoplasmic ratio, and atypical proliferation of basal cells. The dermis generally contains a lymphocytic inflammatory cell infiltrate. Elastotic or basophilic changes in collagen and irregular clumps of altered elastic fibers and regenerated collagen are noted in these areas.

Individual actinic keratoses may be treated with cryotherapy. However, in patients with confluent actinic keratoses, the therapeutic mainstay is topical application of 5 fluorouracil. Additional treatment modalities include curettage and surgical excision. For lesions that are indurated or nodular, or that demonstrate marked inflammation, a biopsy to rule out invasive squamous cell carcinoma is necessary.

ORAL SUBMUCOUS FIBROSIS

Oral submucous fibrosis is a high-risk, precancerous condition characterized by chronic, **progressive scarring of the oral mucosa**. It is seen primarily in the Indian subcontinent, Southeast Asia, Taiwan, southern China, The condition affects more than 5 million people in India alone. Cases among Asian communities in North America, Europe, and Africa also have been reported.

The pathogenesis of oral submucous fibrosis is hypothesized to involve the disruption of collagen metabolism by components of the areca nut. Oral submucous fibrosis often manifests in young adult betel quid users. Typical chief complaints include an inability to open the mouth (trismus) and a generalized oral burning sensation (stomatopyrosis). The mucosa develops a blotchy, marblelike pallor and progressive stiffness. Submucosal fibrous bands are palpable on the buccal mucosa, soft palate, and labial mucosa.

LEUKOPLAKIA

Leukoplakia is a clinical term indicating a white patch or plaque of oral mucosa that cannot be rubbed off and cannot be characterized clinically as any other disease. This excludes lesions such as lichen planus, candidiasis, leukoedema, WSN, and obvious frictional keratosis.

Leukoplakias may have similar clinical appearances but have a considerable degree of microscopic heterogeneity. Because leukoplakia may range microscopically from benign hyperkeratosis to invasive squamous cell carcinoma, a biopsy is mandatory to establish a definitive diagnosis.

Etiology and Pathogenesis

Many cases of leukoplakia are etiologically related to the use of tobacco in smoked or smokeless forms and may regress after discontinuation of tobacco use. Other factors, such as alcohol abuse, trauma, and C. albicans infection, may have a role in the development of leukoplakia. Nutritional factors have been cited as important, especially relative to iron deficiency anemia and development of sideropenic dysphagia (Plummer-Vinson or Paterson-Kelly syndromes).

Rates of transformation to squamous cell carcinoma have varied from study to study as a result of differences in the underlying pathology and differences in the use of putative carcinogens such as tobacco. Geographic differences in the transformation rate, as well as in the prevalence and location of oral leukoplakias, are likely related to differences in tobacco habits in various parts of the world. In U.S. populations, a majority of oral leukoplakias are benign and probably never become malignant.

Approximately 5% of leukoplakias are malignant at the time of first biopsy, and approximately 5% of the remainder undergo subsequent malignant transformation. From 10% to 15% of dysplasias that present as clinical leukoplakia will develop into squamous cell carcinoma. Wide ranges in risk of transformation have been observed from one anatomic site to another, such as the floor of the mouth, where transformation rates are comparatively high, although paradoxically many show only minimal amounts of epithelial dysplasia.

Clinical Features

Leukoplakia is a condition associated with middle-aged and older populations. A vast majority of cases occur after the age of 40 years. Over time, a shift in gender predilection has been noted, with near parity in the incidence of leukoplakia, apparently as a result of the change in smoking habits of women.Predominant sites of occurrence have changed through the years. At one time, the tongue was the most common site for leukoplakia, but this area has given way to the mandibular mucosa and the buccal mucosa, which account for almost half of leukoplakias. The palate, maxillary ridge, and lower lip are somewhat less often involved, and the floor of the mouth and retromolar sites are involved less often.

The relative risk of neoplastic transformation varies from one region to another. Although the floor of the mouth accounts for a relatively small percentage (10%) of leukoplakias, a large percentage of leukoplakias at this site are found to be dysplasia, carcinoma in situ, or invasive carcinoma when examined microscopically. Leukoplakia of the lips and tongue also exhibits a relatively high percentage of dysplastic or neoplastic change. In contrast to these sites, the retromolar area exhibits these changes in only about 10% of cases. On visual examination, leukoplakia may vary from a barely evident, vague whiteness on a base of uninflamed, normal-appearing tissue to a definitive white, thickened, leathery, fissured, verrucous (wartlike) lesion. Red zones may also be seen in some leukoplakias, prompting use of the term speckled leukoplakia (erythroleukoplakia). Risk of malignant transformation of speckled leukoplakia is greater than lesions that are homogeneous. On palpation, lesions may be soft, smooth, or finely granular. Other lesions may be roughened, nodular, or indurated. Proliferative verrucous leukoplakia (PVL) has been segregated from other leukoplakias. This type of leukoplakia begins as simple keratosis and eventually becomes verrucous in nature. Lesions tend to be persistent, multifocal, recurrent, and sometimes locally infiltrative. Metastasis to regional lymph nodes is uncommon. The cause of PVL is unknown, although early reports suggest a relationship in some lesions with human papillomavirus, but this has not been substantiated. The typical patient with PVL more often is female than male, and traditional risk factors attributed to oral cancer such as tobacco and alcohol use are strongly lacking. The diagnosis is determined clinicopathologically and usually is made retrospectively. Malignant transformation to verrucous or squamous cell carcinoma from precursor lesions is greater than in epithelial dysplasia and may occur in up to 80% of cases.

Histopathology: Histologic changes range from hyperkeratosis, dysplasia, and carcinoma in situ to invasive squamous cell carcinoma. The term dysplasia indicates abnormal epithelium and disordered growth, whereas atypia refers to abnormal nuclear features. Increasing degrees of dysplasia are designated as mild, moderate, and severe and are subjectively determined microscopically.

Oral Pathology

Lec. 20

Precancerous or premalignant conditions

A precancerous lesions is defined as a morphologically altered tissue in which cancer is more likely to occur than in its normal counterpart ,for example leukoplakia ,that is the lesion itself undergoes malignant transformation .In contrast, a precancerous condition is a generalized disorder associated with a significantly increased risk of cancer developing somewhere in the mouth ,for Example oral submucous fibrosis ,however , it must be remembered that relatively few oral carcinoma are preceded by a recognizable premalignant lesion or condition**.**

The precancerous lesions of the oral mucosa**-** :

1-Precancerous lesions

a-Leukoplakia-homogeneous, non-homogeneous, nodular, and speckled types, including candida associated lesions (chronic hyperplasitc candidosis and proliferative verrucous leukoplakia**)**

b- Erythroplakia

c- carcinoma in situ

2 –Precancerous conditions

a-Oral submucous fibrosis

b-Lichen planus-0.1% erosive type

c-Other conditions associated with epithelial atrophy, e.g. sideropenic dysphagia.

Epithelial dysplasia: ‘‘Dysplasia’ ’is the term that is used within the context of mucosal premalignancies. For the sake of clarity, one has to distinguish between cellular changes and architectural changes**.**

Histological features of epithelial dysplasia- :

1– Increased and abnormal mitoses. Mitoses may be increased in number, occur in higher number in the epithelium that is usual way from basal (supra basal mitoses).

2-Basal cell hyperplasia. The presence of several layers of cells of basaloid appearance. It is often associated with drop-shaped reteridegs.

3-Drop-shaped reteridegs. The rete-pegs are wider at their deepest part than they are more superficially.

4-Distributed polarity of the basal cell layers or loss of cellular orientation.

5-Alteration (invariably an increase) is seen in the nuclear/cytoplasmic ratio by either area or volume.

6-Nuclear hyperchromatism. Nuclear staining which is abnormally intense

7-Prominent and enlarged nucleoli

8-Irregular epithelial stratification or disturbed maturation. The cells no longer show proper sequence of morphological and maturational changes as they pass from the basal layer to the surface

9-Nuclear and cellular pleomorphism. Nuclei and cells are of different size and shape.

10 –A abnormal keratinization. Keratinization occurring below the normal keratin layer, either as individual cell keratinization within the stratum spinosum or as disturbed maturation of groups of cells.

11-loss or reduction of intercellular adhesion (or cohesion). This may be difficult to distinguish from intercellular odema.

❖ WHO Dysplasia Classification.

Dysplasia with Three Grades

Mild Dysplasia Architectural disturbance is limited to the lower third of the epithelium and is accompanied by cytological atypia.

Moderate Dysplasia Architectural disturbance that extends into the middle third of the epithelium is the initial criterion for recognizing this category of dysplasia. However, consideration of the degree of cytological atypia may require up grading to severe dysplasia.

Severe Dysplasia Architectural disturbance with associated cytological atypia is greater than two thirds of the epithelium.

Erythroplakia: is defined as a brighter red velvety plaque on the oral mucosa which cannot be categorized clinically or pathologically a being due to any other conditions, erythroplakia lesions may be homogeneous with a well-defined but irregular outline, or may be intermingled with patches of leukoplakia-such lesions are often called speckled leukoplakia or erythroplakia, histologically erythroplakia may represent carcinoma in situ or even invasive carcinoma.

Carcinoma in situ

This term is used to describe severe epithelial dysplasia in which the whole , or almost the whole , thickness of the epithelium is involved but the basement membrane is intact and there is no invasion of the lamina propria ,Oral carcinoma in situ usually presents clinically as leukoplakia or erythroplakia .It is a precancerous(premalignant) lesion , but its natural history is not well understood .In some patients the lesion may progress to invasive carcinoma but in other sit remains static for long periods and ,in some ,the degree of dysplasia may regress or fluctuate with time. It is common to find histological changes of dysplasia, including carcinoma in situ, in the epithelium surrounding an invasive carcinoma, even though this may appear clinically healthy. This suggests that in some patients there may be a field of potentially precancerous change involving a wide area of mucosa. It is probable that some carcinomas thought to be recurrent tumors represent new primary lesions arising in such afield change.

Squamous cell carcinoma(SCC)

Epidemiology Squamous cell carcinoma accounts for 90 percent or more of all oral malignant neoplasms. The incidence of oral cancer varies enormously around the world, in both the United Kingdom and the USA oral cancer accounts for less than 4 percent of all cancers, but in India and South east Asia it accounts for up to 40 percent of all malignant tumors. It is a malignant neoplasm of stratified squamous epithelium that is capable of locally destructive growth and distant metastasis. OSCC is often begin as epithelial dysplasia and progressing until the dysplastic epithelial cells reach the basement membrane and invade into the underlying connective tissue. OSCC most commonly occurs in middle aged and older individuals, although a disturbing number of these malignancies also being documented in younger adults. From an epidemiological and clinicopathological perspective, OSCC can be divided into three categories:

- Carcinoma of the oral cavity
- Carcinoma of the lip vermilion
- Carcinoma arising in the oropharynx

Intraoral and oropharyngeal tumors are more common among men than women, with a male: female ratio of over2:1.

Etiological factors in oral cancer

Tobacco smoking: Much in direct clinical evidence implicates the habit of tobacco smoking in the development of oral squamous cell carcinoma.

The proportion of smokers (80%) among patients with oral carcinoma is two to three times greater than the general population. Pipes Smokeless(spit) tobacco. Smokeless or "spit" tobacco use in Western cultures may increase a chronic user's risk for oral carcinoma, cigars, cigarettes. Reverse smoking in reverse smoking, the burning end of a handmade cigar or cigarette is held inside the mouth. This habit considerably elevates one's

risk for oral cancer. Where reverse smoking is practiced as many as 50% of all oral malignancies are found on the hard palate, as it usually spared by this disease.

Smokeless tobacco: Snuff dipping, tobacco sachets and tobacco chewing Betel chewing, betelquid, areca nut: The betel or paanquid is a compound of natural substances (i. e., areca palm nuts, betel leaf. Slakedlime. perhaps tobacco leaf) chewed for their Psycho stimulating effects, this habit is also associated with significant development of precancers, such as leukoplakia, Alcohol, Spirits, Wines and beers and tobacco synergism. This habit does However appear to be a significant potentiator or promoter for other causative factors especially tobacco and its effects are significant when it is understood that most heavy drinkers are also heavy smokers.

Diet and nutrition: Iron deficiency and vitamins A and C deficiency. Vitamin A deficiency produces excessive keratinization of the skin and mucous membranes .and it has been suggested that the vitamin may play a protective or preventive role in oral precancer and cancer.

Dental factors: Poor oral hygiene, faulty restoration, sharp edges of teeth, and ill-fitting dentures have been incriminated in an etiology of oral cancer

Ultraviolet light and Radiation: The effects of ultraviolet radiation on the lips x-irradiation, decreases immune reactivity and produces abnormalities in chromosomal material. It should not seem surprising that radio therapy to the head and neck area increases the risk of the later development of a new primary oral malignancy either a carcinoma or a sarcoma**.**

Viruses

Herpes simplex viruses: Laboratory experiments have shown that HSV can be carcinogenic or carcinogenic under certain circumstances and so must be considered as possible a etiological agents in oral carcinoma.

Human papilloma viruses HPV types 16 and 18 are important factors in the etiology of squamous cell carcinoma of the uterine cervix, but their role in oral carcinomas is less clear. HPV genes code for proteins which can bind and inactivate the products of the tumor suppressor genes p53 and Retinablastoma gene, so they thought to be significant in the development of oral cancer

Epstein-Barrvirus: It has an a etiological role in the development of some nasopharyngeal lymphoma, this virus has been demonstrated more frequently in carcinoma than in normal epithelium human immunodeficiency virus

Immunosuppression. It has been reported that risk of carcinoma of the lip in patients following renal and other organ transplantation due to immune suppressive therapy that such patients receive.

Chronic infections

Candidiosis: Hyperplastic candidiasis frequently is cited as an oral precancerous condition. Because this lesion appears as a white plaque that cannot be rubbed off, however this has not been proven.

Syphilis; Syphilis (tertiary stage) has long been accepted as having a strong association with the development of dorsal tongue carcinoma.

Occupation

Outdoors workers are at risk of high exposure to ultraviolet light which is an important factor in squamous cell carcinoma of the lip, other occupational and environmental factors, such as atmospheric pollution by chemicals and dusts.

Oncogenes and tumour-suppressor genes.

Oral cancer has a multifactorial etiology and is the result of genetic damage allowing uncontrolled proliferation of cells. It is a multistep process involving multiple sequential mutations which accumulate within the cell. Mutations in the genes which regulate cell growth and proliferation are particularly important. These genes are the growth-promoting proto-oncogenes found in normal cells, and the tumor suppressor genes that encode for growth inhibitory proteins. Under normal circumstances cellular proliferation is controlled by the balance between these growth-promoting and growth inhabiting genes. During carcinogenesis a proto-oncogene may undergo mutation and become an activated oncogene, resulting in enhanced activity, and/or tumor-suppressor genes may be mutated or their products in activated The result in both cases leads to deregulation of cell proliferation and tumor formation.

Oncogenes (for example, the c-mycandras families) encode for arrange of growth-promoting proteins such as growth factor receptors, signal transmitting proteins, and stimulatory cell-cycle regulating proteins. In contrast, tumor-suppressor genes encode for growth-inhibitory proteins, such as p53 which plays a vital role in inhibiting the cell cycle and, if necessary, arresting the cycle and switching cells into apoptosis. The most important oncogenes and tumor-suppressor genes so far identified appear to influence pathways controlling the first stages of the cell cycle, i.e. The progression through the G1phase(the phase before DNA synthesis) into S phase (the phase of DNA synthesis).Most oncogenic agents probably exert significance affects during the G1 phase of the cell cycle and the G1,to S transition carefully regulated by inhibitory proteins, particularly p53 Thus ,cells with damaged DNA are normally blocked at this G1, check point this allows time for repair of the damaged DNA ,or ,if that fail to switch the cell into apoptosis ,so preserving the integrity of the genome .Mutations of the p53 gene can therefore result in loss of regulation of the checkpoint , allowing cells with damaged DNA to undergo replication . Mutation of the p53 gene is a common and significant event in many cancers throughout the body.

Clinical presentation

In the oral cavity, the majority of cancers are concentrated in the lower part of the mouth, particularly lateral border of the tongue, the adjacent floor of the mouth and the lingual aspect of the alveolar margins, forming a U-shaped are an extending back towards the oropharynx. Two major factors help to explain why this region is at such a high risk:

First- any carcinogen may mix with saliva, pool in the floor of the mouth, and constantly bathe these anatomicsites

Second- these regions of the mouth are covered by a thin non keratinized mucosa which provides less protection from carcinogens. Less frequently, the gingival and alveolar ridge is the site of origin, the buccal mucosa especially above the occlusal line is seldom involved. Compare with other intraoral sites, carcinoma arising on the hard palate and dorsum of the tongue are relatively rare. Early lesions are usually asymptomatic. Common modes of presentation area white patch, a small exophytic growth which in the early stages may show no ulceration or erythema, a small indolent ulcer, or an area of erythroplakia pain is seldom present.

Clinical features which should arouse suspicion of an early carcinoma are persistent ulceration, induration, and fixation of affected tissue to underlying structures in duration is rubbery hardness caused by invasion of the carcinoma resulting in loss of the normal elasticity and compliance of the oral mucosa.

Fixation is caused by the carcinoma infiltrating through and binding together (tethering) different natural tissue planes. Underlying bone destruction may also be detected in the case of carcinomas arising from the alveolar mucosa. Lymph node involvement may occur early in oral carcinomas, but enlarged regional nodes do not necessarily indicate metastatic spread as they may show only non-specific changes of reactive hyperplasia. Carcinom a developing on the vermilion border of the lip is clearly visible and so may be noticed at a nearly stage as a slightly raised swelling or a crusty, inconspicuous lesion resembling delayed healing of herpes labialis. An advanced lesion may present as a broad-based, exophytic mass with a rough, nodular, warty, hemorrhagic, or necrotic surface or as a deeply destructive and craterlike ulcer with raised, rolled everted edges. Infiltration of the oral musculature may result in functional disturbances particularly if the tumor involves the tongue or floor of mouth. Because of reduced mobility of the tongue patients may complain of impaired speech or of difficulty in swallowing. Pain may be a feature of an advanced lesion. Bone invasion may be detected on radiographs and may be suggested clinically by mobility of teeth, and in the mandible, by altered sensation over the distribution of the mental nerve, or pathological fracture. It is important to note that the size of the surface lesion does not indicate the extent of underlying invasion.

Histopathology

It is customary to grade squamous cell carcinoma into well differentiated, moderately differentiated, and poorly differentiated types. In well-differentiated tumors, the neoplastic epithelium is obviously squamous in type and consists of masses of prickle cells with a limiting layer of basal cells a round, the periphery. Intercellular bridges are readily recognizable Keratin pearls are often found within the masses of infiltrating cells, each pearl consisting of a central area of keratin surrounded by whorls of prickle cells. Nuclear and cellular pleomorphism is not prominent and there are relatively few mitotic. Moderately differentiated tumors how less keratinization and more nuclear and cellular pleomorphism and mitotic activity, but are still readily identified as squamous in type.

In contrast, in poorly differentiated tumors keratinization is usually absent and the cells show prominent nuclear and cellular pleomorphism and abundant, often bizarre, mitoses. It must be appreciated that the assessment of grade is entirely subjective process and that a degree of overlap between them is inevitable,

depending on the area of the tumor sampled and the individual pathologist's criteria for evaluation. Moreover, clinical staging seems to correlate much better with the prognosis than microscopic grading. In some poorly differentiated tumors the cells may be so abnormal as to hardly be recognizable as epithelial cells.

There is variable lymphocytic and plasma cell infiltration in the stroma supporting the invasive malignant epithelium, which probably represents are action by the host immune system to tumor antigens as well as a response of tumor necrosis and ulceration. The lymphatic spread to the regional lymph nodes is a variable feature, but the frequency of cervical metastasis tends to increase with increasing size of the primary tumor. As the metastatic carcinoma destroy and replaces the nodal lymphoid tissue it may also invade through the capsule of the node into the surrounding tissue, resulting in fixation of the node on clinical examination, extracapsular spread is an important which a has an adverse effect on prognosis, blood borne metastases occur later in the clinical course of the disease.

Histopathological variants of squamous cell carcinoma

- Verrucous carcinoma (snuff dipper's cancer; ackerman's tumor)
- Spindle cell carcinoma (sarcomatoid squamous cell carcinoma; polypoidsquamouscellcarcinoma)
- Basaloid squamous carcinoma (basaloid squamous cell carcinoma)
- Adenosquamous carcinoma

Verrucous carcinoma

This is an uncommon but distinctive pathological variety of low-grade squamous cell carcinoma which presents as slow growing, thick, white, warty plaque of heaped-up tissue.

Histologicaliy, it is a very well differentiated, heavily keratinizing squamous cell carcinoma with little or no cytological atypia. It is predominantly an exophytic tumour but also has a slowly advancing, pushing, cohesive invasive front causing local destruction. It has a good prognosis and is said not no metastasize. The diagnosis of verrucous carcinoma is difficult and strict criteria must be adopted. The tumor must be differentiated from a well-differentiated papillary squamous cell carcinoma or from leukoplakic lesions with warty surfaces variously called verrucous hyperplasia or verrucous leukoplakia.

Treatment

Because metastasis is an extremely rare event in verrucous carcinoma, the treatment of choice is surgical excision without radical neck dissection. The surgery generally need not be as extensive as that required for routine squamous cell carcinoma of a similar size. With this treatment ,90% of patients are disease free after 5years. Although some patients will require at least one additional surgical procedure during that time.

Basal cell carcinoma(rodent ulcer)

This is a common neoplasm of the skin of the face, particularly in elderly patients with a history of long exposure to ultraviolet radiation, occasionally, basal cell carcinoma a presents on the lips, but many are probably skin tumors that have spread to involve the vermilion. Multiple nevoid basal cell carcinoma arising at

a younger age and on non-exposed sites are a characteristic feature of the naevoid basal cell carcinoma syndrome.

The typical basal cell carcinoma presents as a slow-growing nodule that eventually ulcerates centrally. Histologically it consists of cytologically malignant basaloid cells, arranged in a variety of patterns, invading adjacent tissue.

Oral Pathology

Connective tissue lesions and neoplasms

Part I

► Tumors of fibrous tissue: -

A) Hyperplastic lesions: -

1- Peripheral fibroma include:
-Fibroma.
-Peripheral ossifying fibroma.
-Peripheral odontogenic fibroma.
-Giant cell fibroma.
2-Generalized gingival hyperplasia.
3-Focal fibrous hyperplasia.
4-Denture-induced fibrous hyperplasia.

B) Neoplasms:-

1- Myxoma.
2- Nodular fasciitis.
3- Fibrous histoicytoma
4- Fibromatosis.
5- Fibrosarcoma.

Reactive hyperplasia comprised a group of fibrous connective tissue lesions that commonly occurs in oral mucosa as a result of injury. They represent a chronic process in which granulation tissue and scar follows injury. As a group these lesions present as submucosal masses that may become secondarily ulcerated when-traumatized during mastication.

A - Hyperplastic lesions

1.Peripheral fibroma :-

Clinical features

It's a reactive hyperplastic mass that occurs on the gingiva and is believed to be derived from connective tissue of the submucosa or periodontal ligament. It may occur at any age, although young aged groups are mostly affected. Females more commonly affected than do males, the gingiva anterior to the permanent molars. Fibroma, presents clinically, as either a pedunculated or a sessile mass that is similar in color to the surrounding connective tissue, ulceration may be noted.

Histopathology

a) ***Fiybroma (Traumatic fibroma):*** Is a focal fibrous hyperplasia "hyperplastic scar". It's highly collagenous and relatively avascular, and it may contain a mild to moderate chronic inflammatory cell infiltrate. This lesion is basically the gingival counterpart to traumatic fibroma occurring in other mucosal sites.

b) ***Peripheral ossifying fibroma*****:** Is a gingival mass in which islands of woven "immature bone" and osteoid are seen. The bone formed is surrounded by a lobular proliferation of plump benign fibroblasts. Chronic inflammatory cells tend to be seen around the margins of the lesion. The surface is ulcerated.

c) ***Peripheral odontogenic fibroma***: Is a gingival mass composed of well-vascularized, non-encapsulated fibrous connective tissue. The distinguishing feature of this variant is the presence of strands of odontogenic epithelium, often abundant, throughout the connective tissue, amorphous hard tissue resembling tertiary dentine "dentinoid" maybe seen. It's usually non-ulcerated.

d) ***Giant cell fibroma***: Is a focal fibrous hyperplasia in which connective tissue cells, many of which are multinucleated, assume a stellate shape. It has been shown by immunohistochemical studies that most of these cells are fibroblast. Histologically is a mass of vascular connective tissue with numerous large stellate fibroblast (with several nuclei) in the superficial connective tissue. The retrocuspid papilla is a developmental anomaly with similar histopathological features. It affect lower gingiva behind the lower canine, unilateral or bilaterally. No treatment is required.

Differential diagnosis

Pyogenic granuloma and peripheral giant cell granuloma.

Treatment

By local excision that include periodontal ligament if involved and any other possible etiologic agent such as calculus or other foreign material. Recurrence may occasionally be seen in peripheral ossifying fibroma. Re-excision to the periosteum or periodontal ligament prevents further recurrence.

2.Focal fibrous hyperplasia:-

Is a reactive lesion usually caused by chronic trauma to oral mucous membranes, over production of fibrous connective tissue results in a clinically evident submucosal mass. Although the terms traumatic fibroma and oral fibroma are applied to these entities, they are misnomers, since these lesions are not benign tumors of fibroblasts, as the term fibroma implies.

Clinical features

It's a very common reactive hyperplasia that is typically found in frequently traumatized areas, such as the buccal mucosa, lateral border of the tongue and lower lip. It's a painless, broad swelling that is paler than the surrounding tissue because of its relative lack of vascular channels. The surface may occasionally be ulcerated traumatically, particularly in larger lesions, they usually don't exceed 1-2 cm in diameter.

Histopathology

Collagen overproduction is the basic process that dominates the microscopy of this lesion. Fibroblasts are mature and widely scattered in a dense collagen matrix. Occasional chronic inflammatory cells may be seen. Overlying epithelium is often hyperkeratotic because of chronic irritation.

Differential diagnosis

In tongue → Neurofibroma, neurilemmoma, and granular cell tumor. In lower lip + buccal mucosa → lipoma, mucocele and salivary gland tumor.

Treatment

By surgical excision The term fibrous hyperplasia is synonymous with peripheral fibroma, traumatic fibroma, irritation fibroma, hyperplastic scar, inflammatory fibrous hyperplasia.

3.Denture-induced fibrous hyperplasia

Denture-induced fibrous hyperplasia is related to chronic trauma produced by an illfitting denture. The process is essentially the same as the one that leads to traumatic fibroma, except that a denture is specifically identified as the causative agent, this lesion has been named by several synonyms: inflammatory hyperplasia, denture hyperplasia, epulis fissuratum.

Clinical feature

It is a common lesion that occurs in the vestibular mucosa and less commonly along the mandibular lingual sulcus where the denture flange contacts tissue. Chronic trauma and irritation may cause fibrous connective tissue reparative response, which resulted in the appearance of painless folds of fibrous tissue surrounding the overextended denture flanges.

Treatment

Removal of the denture, surgical excision of the hyperplastic scar and construction of a new denture.

B- Neoplasm of fibrous tissue

1-Myxoma:-

Clinical features

Is a soft tissue neoplasm composed of a gelatinous material that has a myxoid appearance histologically. Oral tumors are rare and present as a slow growing asymptomatic submucosal mass, usually in the palate.

Histopathology

The tumor is not encapsulated and may exhibit infiltration into surrounding soft tissue. Stellate and spindle shaped fibroblasts are found in a loose myxoid stroma.

Treatment

Surgical excision, recurrence is not uncommon.

2. Nodular fasciitis, fibrous histoicytoma and fibromatosis.

Nodular fasciitis:-

Clinical features

Also known as pseudosarcomatous fasciitis, is a well-recognized entity representing a fibrous connective tissue growth. Trauma is believed to be important in many cases because of the location of the lesions over bony prominence such as the angle of the mandible and the zygoma. Although traditionally considered a reactive condition, recent molecular evidence suggests that the cells in nodular fasciitis are clonal, thus supporting the concept that the lesion is a benign neoplasm. Clinically they present as a firm mass in the submucosa and exhibits rapid growth with pain and tenderness, young adults and adults are mainly affected, 10% of these lesions appear in the head and neck region, usually in the skin of the face, and the parotid sheath, intra-orally the buccal mucosa is the most common affected site, the lesion is benign.

Histopathology

A nodular growth of plump fibroblast and myofibroblasts with vesicular nuclei in a haphazard to storiform arrangement.

Differential diagnosis

Fibromatosis, fibrohistocytoma and Fibrosarcoma.

Fibromatosis →More infiltration, grow in fascicles, produce more collagen and less cellular.

Fibrous histiocytoma → More cellular with storiform pattern.

Fibrosarcoma →Is infiltrative and exhibit a herringbone pattern, with nuclear pleomorphism, hyperchromatism and abundant mitoses.

Treatment

Nodular fasciitis and fibrous histocytorna —»by surgical excision Fibromatosis —»by aggressive surgery

3-Fibrosarcoma

Malignant spindle cell tumor showing a herringbone or interlacing fascicular pattern and no expression of other connective tissue cell markers.

Clinical features

Rare soft tissue and bone malignancy results from proliferation of malignant mesenchymal cells at the site of origin, it may become secondarily ulcerated. Mainly affects young adults. The tumor is infiltrative locally destructive more than a metastatic one.

Histopathology

Malignant appearing fibroblasts, with herringbone or interlacing fascicular pattern, collagen may be sparse and mitotic figures frequent. The margins are illdefined.

Treatment

Wide surgical excision, with high recurrence rate.

4-Benign and malignant fibrous histocytoma (B & MFH)

BFH:-

Is a fibroblastic neoplasm that uncommonly occur in oral soft tissues. Mainly affects adults with fifth decade of life and presents as painless masses that maybe ulcerated.

Histopathology

Well demarcated tumor, there is a storiform (cartwheel or mat-like) growth pattern of spindle cells "fibroblasts" with vesicular nuclei admixed with some inflammatory cells, tumor giant cells may be seen. No atypia, mitoses are infrequent or not present.

Treatment Surgical excision.

MFH:-

A soft tissue malignant tumor with different clinical and histological features.

Clinical features

It's an infrequently reported lesion in the head and neck region. It has a significant recurrence and metastatic potential. It occurs in late adult life and is rare in children.

Histopathology

Proliferation of pleomorphic spindle cells showing fibroblastic morphology, abnormal and frequent mitotic figures, necrosis and extensive cellular atypia. The storiform pattern is seen in some cases.

Treatment

Wide surgical excision.

► Vascular lesions:-

1- Pyogenic granuloma:

Represents an exuberant connective tissue proliferation to a known stimulus or injury. It appears as a red mass because it is composed predominantly of hyperplastic granulation tissue in which capillaries are very prominent, and hence the term lobular capillary hemangioma. The original term pyogenic granuloma is a misnomer in that it's not pus producing, and it does not represent granulomatous inflammation. Hence the new term is lobular capillary hemangioma and currently considered as vascular tumor.

Clinical features

Mostly seen on the gingiva, where they are presumably caused by calculus or foreign material within the gingival cervice. Hormonal changes of puberty and pregnancy may modify the gingival reparative response to injury, producing what was called "pregnancy tumor". Other parts of oral mucosa may else be affected, such as lower lip, buccal mucosa, and the tongue. Pyogenic granuloma is typically red. Occasionally they may become ulcerated because of secondary trauma.

Histopathology

Microscopically, consist of lobular masses of hyperplastic granulation tissue, some scarring may be noted in some of these lesions, suggesting that occasionally there may be some maturation of the connective tissue repair process. Numerous small and large endothelium-lined channels are formed organized in lobular aggregate. Admixedinflammatory cells infiltration is evident.

Differential diagnosis

Peripheral giant cell granuloma, ossifying fibroma, rarely metastatic malignancy.

Treatment

Surgical excision, which includes the connective tissue from which the lesion arises as well as removal of local etiologic features, some lesions have recurrence potential.

2- Congenital hemangioma and vascular malformations: The term congenital hemangioma is used to identify benign congenital neoplasms of proliferating endothelial cells, congenital vascular malformation includes lesions resulting from abnormal vessels morphologies.

The term congenital hemangioma and congenital vascular malformations have been used as a generic designation for many vascular proliferation and they have also been used

interchangeably. Because of the difference in clinical as well as behavioral characteristic it is important to separate one from another:-

	Criteria	Congenital Hemangioma	Vascular malformation
1	Description	Benign congenital neoplasms of pr endothelial cells	Lesions resulting from abnormal vessels morphologies
2	Elements	Results in increase in No. of capillaries	A mix of arteries, veins, capillaries
3	Growth	Rapid congenital growth	Growth with patient
4	Boundaries	Often circumscribed, rarely affects b	Poorly circumscribed, may affects b
5	Involution	Spontaneously involutes	Does not
6	Resection	Persistent lesion resection	Difficult to be resect
7	Recurrence	Uncommon	Common.

Clinical features

Congenital hemangioma , also called strawberry nevus, usually appears around the time of birth, but may not be apparent until early childhood. It exhibit a rapid growth phase, which is followed several years later by an involution phase. While congenital malformation are persistent. Both types maybe flat, nodular or bosselated. Lesions are most commonly found on the lips, tongue, and buccal mucosa. Lesions that affect bone are probably congenital vascular malformations rather than congenital hemangioma.

Histopathology

Congenital hemangiomas are composed of abundant capillary spaces lined by endothelium without muscular support. Congenital vascular malformation may consist not only of capillaries, but also of venous, arteriolar and lymphatic channels.

Treatment

● Congenital hemangioma → spontaneous involution during early childhood if not → surgery, arterial embolization, and sclerosant therapy and laser therapy.

● Congenital vascular malformation →the same → difficult to eradicate.

Sturge-weber syndrome (Encephalotrigeminal Angiomatosis)

A condition that includes vascular malformations, venous malformation involves the leptomeninges of the cerebral cortex, with similar vascular malformations of the face. The associated face lesion is called as port-wine stain, which involves the skin innervated by one or more branches of the trigeminal nerve. The patient may complain from mental retardation, hemiparalysis and seizure disorders, oral mucosal and eye lesions may also be present.

Lymphangioma

Regarded as a congenital lesion, usually appears within the 1st 2 decades of life. Involution doesn't occur.

Clinically

Presents as painless nodular vesicle-like swelling when superficial, and as a submucosal mass when located deeper. The color range, from lighter than the surrounding tissue to red-blue

when capillaries, are part of the congenital malformation. The tongue is the most common intraoral site, and the lesion maybe responsible for macroglossia when diffusely distributed throughout the submucosa.

▪ Lymphangioma of the lip cause a macrocheilia.

▪ Lymphangioma of the neck, known as cystic hygroma, hygroma colli or cavernous Lymphangioma, which is a diffuse soft tissue swelling that may be life threatening because it involves vital structures of the neck.

Histopathology

Endothelial-lined lymphatic channels are diffusely distributed in the submucosa. The channels contain eosinophilic lymph that occasionally includes RBC s.

Treatment → surgical removal

Malignant vascular lesions:-

1-Angiosarcoma.

2-Kaposi's sarcoma.

1-Angiosarcoma:-

Rare neoplam of endothelial cell origin arise from either blood or lymphatic vesseles. More than 50% occur in head and neck with scalp and forehead being the most common site. Oral cavity may be involved in rare instances. Hemagioendothelioma is a term used to describe vascular tumors with microscopic features intermediate between those of hemagiomas and angiosarcoma.

Clinical features

Angiosarcoma affect elderly patients resemble a simple 0000. continue to enlarge resulting in a nodular lesion which could be multifocal.

Histopathology

An unencapsulated proliferation of anaplastic endothelial cells enclosing irregular luminal spaces.

Treatment

Aggressive clinical course leading to poor diagnosis.

2.Kaposi's sarcoma:-

It is a proliferation of endothelial cell origin. Recently discovered herpesvirus known as human herpesvirus 8 (HHV8) or Kaposis sarcoma herpesvirus (KSHV) is found in all Kaposis lesions, as well as in acquired immmunodeficiency syndrome (AIDS).

Clinical features

Three different clinical patterns of Kaposi's sarcoma are described

a- Kaposis sarcoma in older men living in mediterranean basin appear as multifocal reddish brown nodules in skin and lower extremities, Oral lesions are rare.

b- Endemic Kaposi's sarcoma in Africa which affect skin of extremities mostly of black people. Oral lesions also rarely seen.

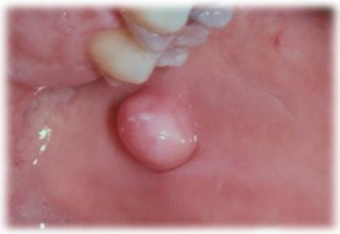
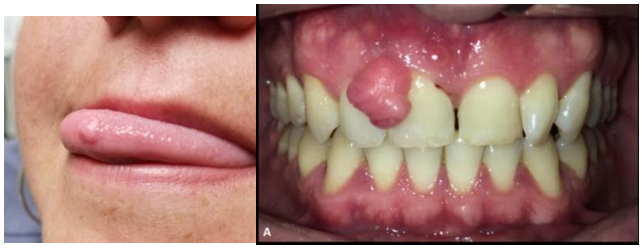
c- Kaposi's sarcoma in patients with immunodeficiency states especially (AIDS). Skin lesions are not limited to the extremities, oral and lymph node lesions are common, younger age group people is affected

Histopathology

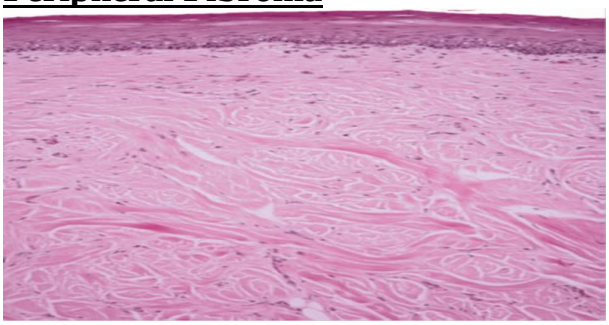
Hypercellular foci of bland-appearing spindle cells with ill-defined vascular channels and extravasated red blood cells are seen in Kaposi's sarcoma.

Treatment

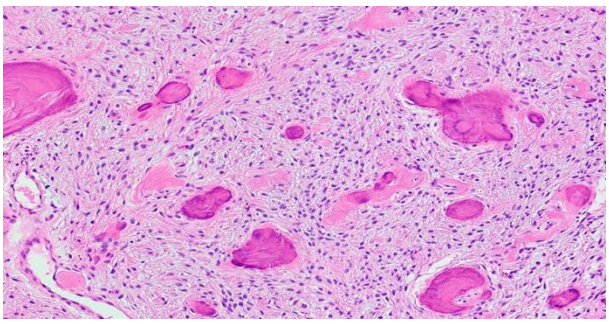
For localized lesions surgery with low dose and intralesional chemotherapy could be beneficial, while for larger and multifocal lesions systemic chemotheraputic regimens are being used.

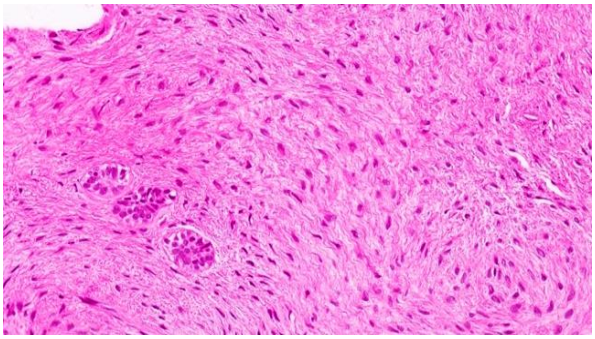
Peripheral Fibroma



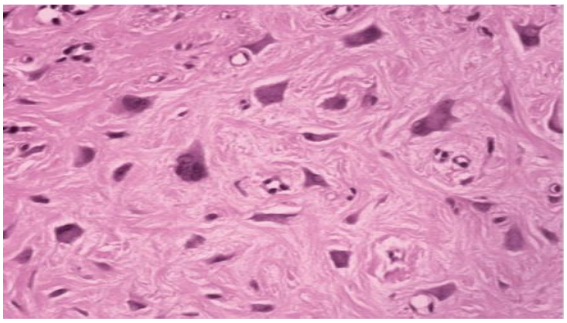
Traumatic fibroma



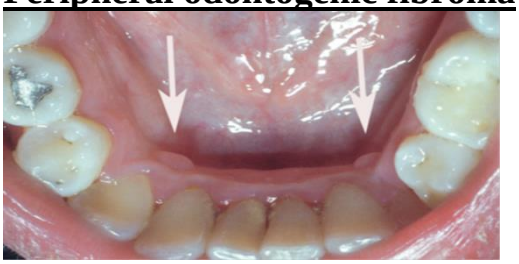
peripheral ossifying fibroma



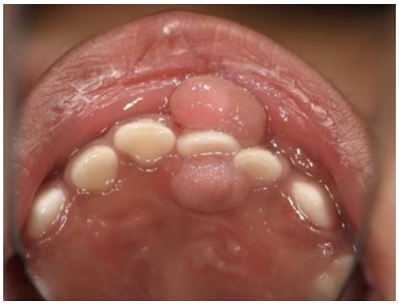
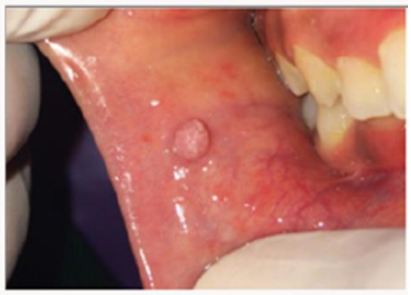
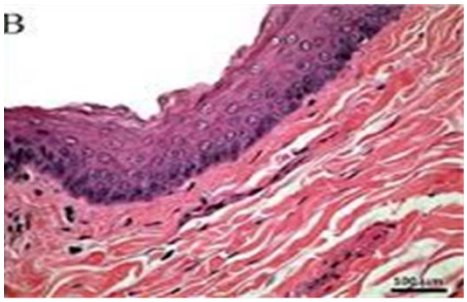
Peripheral odontogenic fibroma



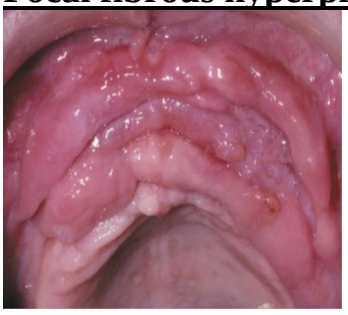
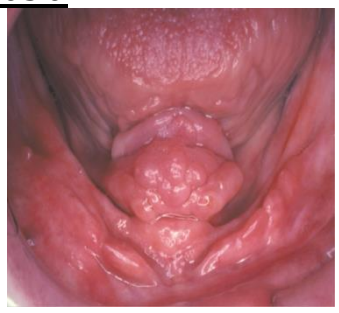
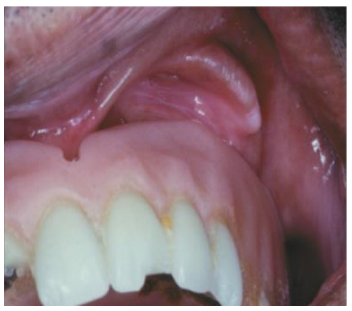
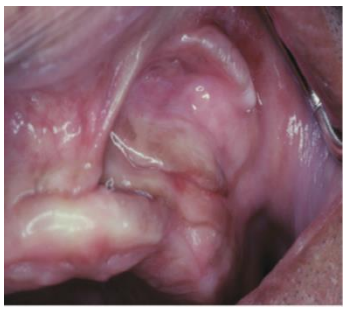
Giant cell fibroma



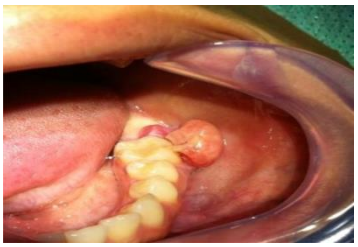
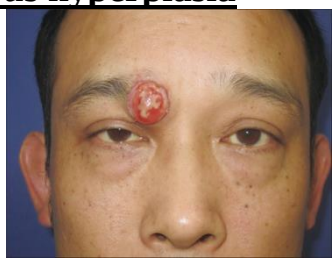
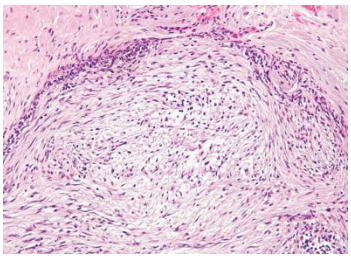
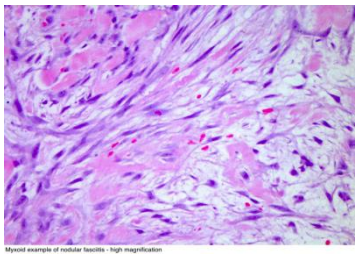
Retrocuspid papilla

Focal fibrous hyperplasia

Denture induced fibrous hyperplasia

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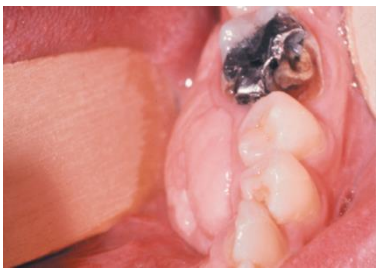
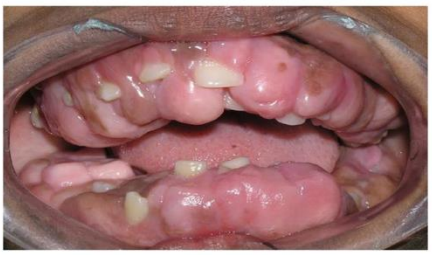
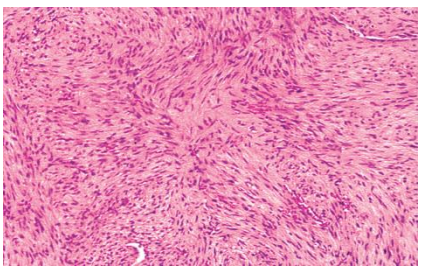
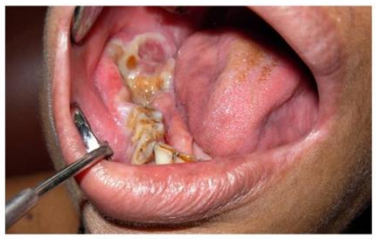
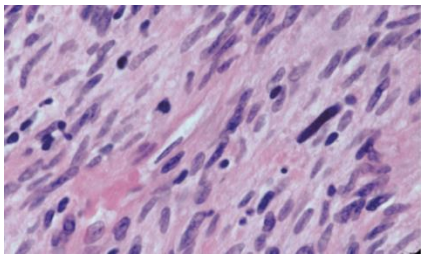
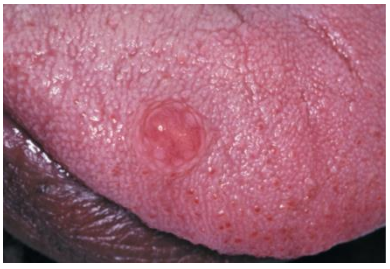
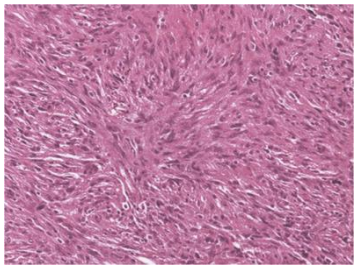
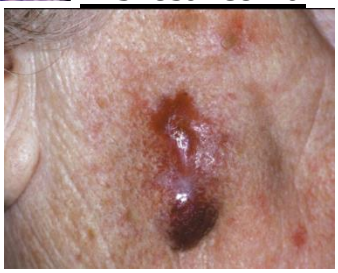
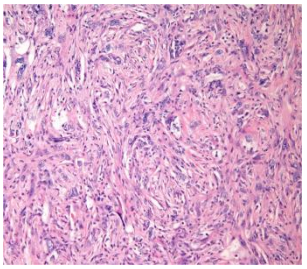




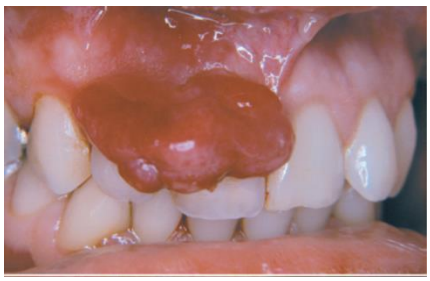
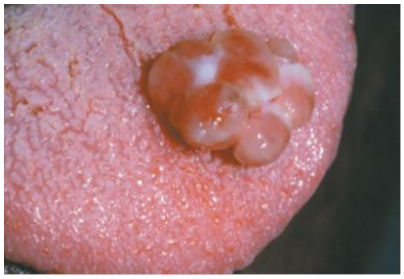
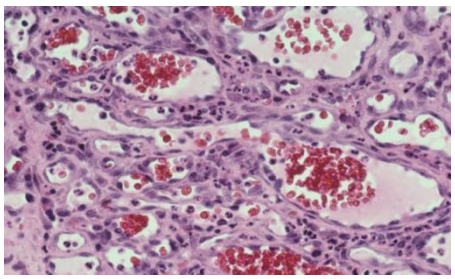
Fibromatosis

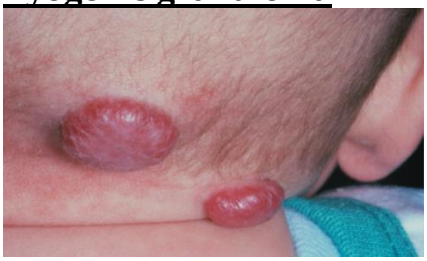
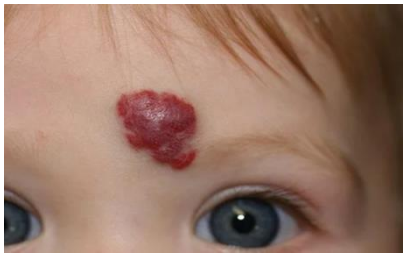
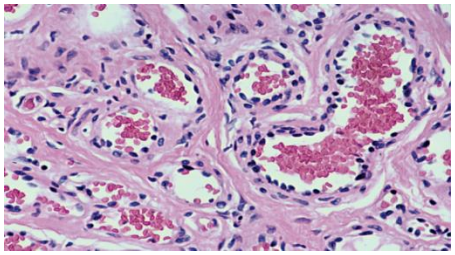
Fibrosarcoma

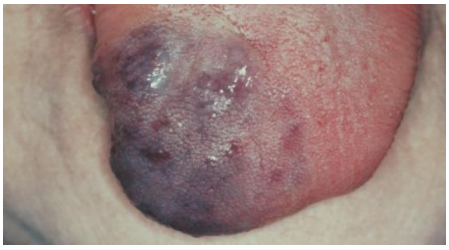
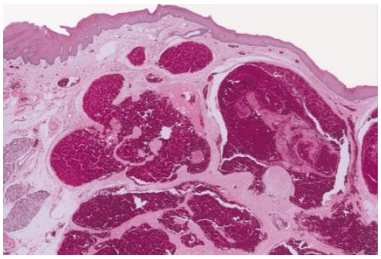
Benign fibrous histocytoma **Malignant fibrous histocytoma**

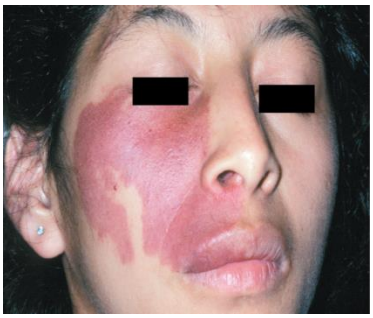
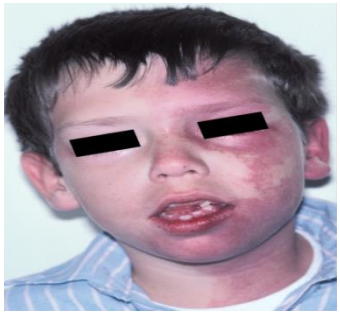
Pyogenic granuloma

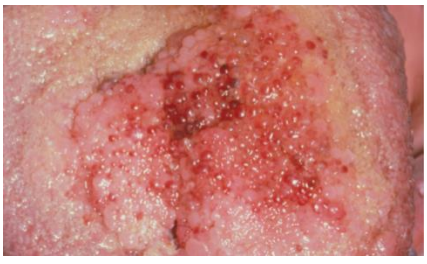
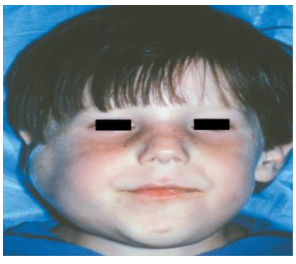
Congenital heamangioma

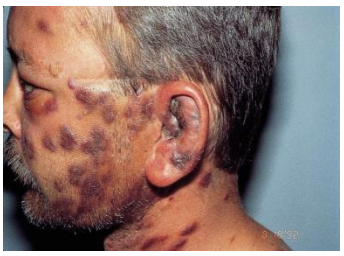
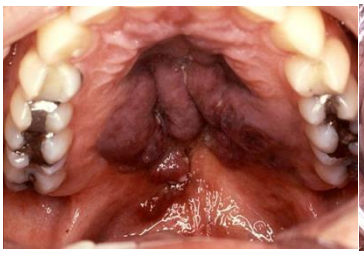
Vascular malformation

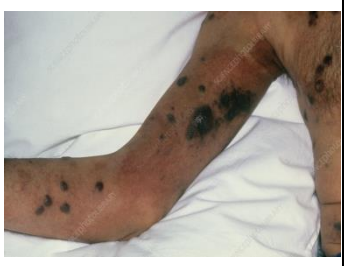



Sturge-weber syndrome

lymphangioma



Kaposi's sarcoma

Oral Pathology

Connective tissue lesions and neoplasms

Part II

► Neural lesions

1-Reactive lesions: -

Traumatic neuroma:

Caused by injury to a peripheral nerve, such as a tooth extraction, from local anesthetic injection, or from an accident. Transection of a sensory nerve can result in inflammation and scarring in the area of injury. As the proximal nerve segment proliferates in an attempt to regenerate into to the distal segment, it becomes entangled and trapped in the developing scar, resulting in a mass of fibrous tissue, Schwann cells and axons.

Clinical features

Pain ranges from occasional tenderness to constant, severe pain. Injection of local anesthesia relieves the pain. The mental foramen is the most common location, followed by extraction site, in the anterior maxilla and posterior mandible. The lower lip, tongue, buccal mucosa and palate are also relative common soft tissue locations.

Histopathology

Bundles of nerves in a haphazard or tortuous arrangement are found admixed with dense collagenous fibrous tissue.

Treatment → surgical removal.

2-Neoplasms:-

Granular cell tumor:

Uncommon benign tumor of unknown cause. It is believed to be of neural origin (Schwann cells). A related lesion of dispute origin is the congenial epulis which is composed of cells that are light microscopically identical to those of granular cell tumors with slight differences.

a)Granular cell tumor:

Clinical features

- Benign tumor of neural sheath origin,
- Any age, females slightly more than males,
- Any site, usually tongue.
- Asymptomatic submucosal mass (1-2 cm).
- Same or lighter than mucosal color.
- Intact overlying epithelium.

Histopathology

Large, uniform cells with granular cytoplasm, with indistinct cytoplasmic borders, overlying pseudoeptheliomatous hyperplasia. Cells are positive for neural-associated proteins and negative for muscle protein. Treatment —> excision, no recurrence.

b)Congenital epulis:

Clinical features

- Benign tumor or disputed origin.
- Infants only, gingiva only, usually pedunculated, non ulcerated mass.

Histopathology

Large, uniform cells with granular cytoplasm no overlying pseudoeptheliomatous hyperplasia. Cells are negative for neural and muscle proteins.

Treatment

Excision → no recurrence

C) Schwannoma (neurilemmoma) and Neurofibroma:

Schwannoma: Is a benign neoplasm that is derived from a proliferation and Schwann cells, or nerve sheath.

Clinical features

The lesion is an encapsulated submucosal mass. The tongue is the most common site

Histopathology

Encapsulated tumor, spindle cells exhibiting two different patterns: in one pattern, the so called Antoni-A areas consist of spindle cells organized in palisaded manner. These cells often surround an acellular eosinophilic zone "Verocay body", which represent reduplicated basement membrane. The other pattern is the so called Antoni-B tissue consisting of spindle cells haphazardly distributed in a delicate fibrillar microcystic matrix.

Treatment → surgical excision

d) Neurofibroma:

May appear as a solitary lesion or as multiple lesions as part of the syndrome "neurofibromatosis" (von-Recklinghausen's disease of skin) which is inherited as an autosomal-dominant trait.

Clinically:

1.Solitary neurofibroma —► present at any age as an uninflamed asymptomatic, submucosal mass. The tongue, buccal mucosa, and vestibule are the oral regions most commonly affected.

2.In fibromatosis —►it includes multiple neurofibromas cutaneous cafe-au-lait macules, bone abnormalities, CNS changes.

Histopathology: Spindle shaped cells, with fusiform or wavy nuclei found in a delicate connective tissue matrix, the matrix maybe myxoid, mast cells are characteristically scattered throughout the lesion

Comparison between Schwannoma and neurofibroma

	Criteria	Schwannoma	Neurofibroma
1	Cell of origin	Schwwanna cells	Schwwana cells and perineural fibrob
2	Site	Any Especially tongue	Any Especially tongue ,buccal mucosa or
3	Number	Solitary	Solitary or multiple

Treatment → Surgical excision.

e) Neurofibromatosis

Common hereditary condition and at least eight forms have been recognized but the most common is neurofibromatosis type I (NFI) or von Recklinghausen disease of the skin

Clinically

1- Six or more café au lait macules with variable size depend on puberty
2- Two or more neurofibromas of any type
3- Freckling in the axillary or lingual regions
4- Optic glioma
5- Two or more Lisch nodules

Treatment

No specific therapy for NFI, prevention of complication which the development of cancer, most often Neurofibrosarcoma and malignant schwannoma

f) Pigmented neuroectodermal tumor of infancy

It is rare benign neoplasm of primitive pigment-producing cells. Like melanocytes and nevus cells,

Clinically

it is found in infants usually younger than 6 months of age and occurs typically in the maxilla, although the mandible and the skull have been involved. This lesion usually presents as a non-ulcerated and occasionally darkly pigmented mass due to melanin production by tumor cells.

Histologically

This neoplasm exhibits an alveolar pattern (i.e., nests of tumor cells with small amounts of intervening connective tissue) . The variably sized nests of round to oval cells are found within a well-defined connective tissue margin. Cells located centrally within the neoplastic nests are dense and compact, resembling neuroendocrine cells; peripheral cells are larger and often contain melanin.

Treatment → Surgical excision

g) Malignant peripheral nerve sheath tumor:

Rare malignant tumor that develops, either from a pre-existing neurofibroma or denovo.

Clinically

appears as an expansible mass that is usually asymptomatic, pain or paresthesia may accompany the lesion in bone.

Histopathology

The lesion is composed of abundant spindle cells with variable numbers of abnormal mitotic figures. Streaming and palisading of nuclei are often seen.

Treatment → wide surgical excision, recurrence is common.

► Muscle lesions

(Rhabdomyoma and Rhabdomyosarcoma) Rhabdomyomas:

Are rare lesions, but they have a predilection for the soft tissue of the head and neck. Orally, the floor of the mouth, soft palate, tongue and buccal mucosa.

Microscopically

The neoplastic cells closely mimic their normal counterpart in adult patients. The fetal type, the neoplastic cells are elongated and less differentiated.

Rhabdomyosarcoma: have three principal microscopical forms, (embryonal &alveolar) and pleomorphic .

◊ Embryonal type consists of primitive round cells, spindle cells. (Botryoid Type)

◊ Alveolar variant consists of round cells to oval cells separated by fibrous septa. These cells demonstrate a central loss of cohesiveness, which results in an alveolar pattern.

◊ Pleomorphic type consists of sharp or spindle cells.

Embryonal & Alveolar : mainly found in children in head and neck region.

Pleomorphic : less than 5% and show peak prevalence in patients older than 40 years of age and primarily occur on the extremities.

Treatment → surgery, radiation and chemotherapy.

► Tumor of Adipose tissue

- **Lipoma**
- **Liposarcoma**

Lipoma

Uncommon neoplasm of oral cavity, tongue, buccal mucosa and floor of the mouth among common locations. Appear as asymptomatic, yellowish submucosal mass,overlying epithelium is intact and superficial blood vessels are evident over the tumor.Histologically it composed of a well-circumscribed lobulated mass of adipocytes in various degree of maturation,

Liposarcoma

Is a rare slow growing malignant neoplasm of soft tissue of head and neck, variation in its microscopic findings led to subclassification of liposarcoma into four types:

- Well differentiated
- Myxoid
- Round cell
- pleomorphic

Treatment of liposarcoma is by surgery or radiation and prognosis is fair to good.

► Tumor of smooth muscle origin

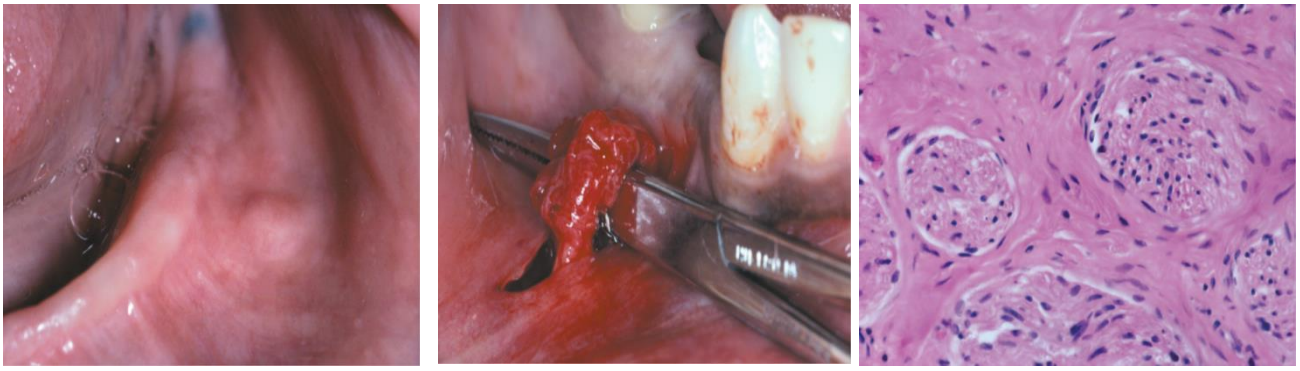
- **Leiomyoma**
- **Leiomyosarcoma**

Leiomyoma and Leiomyosarcoma

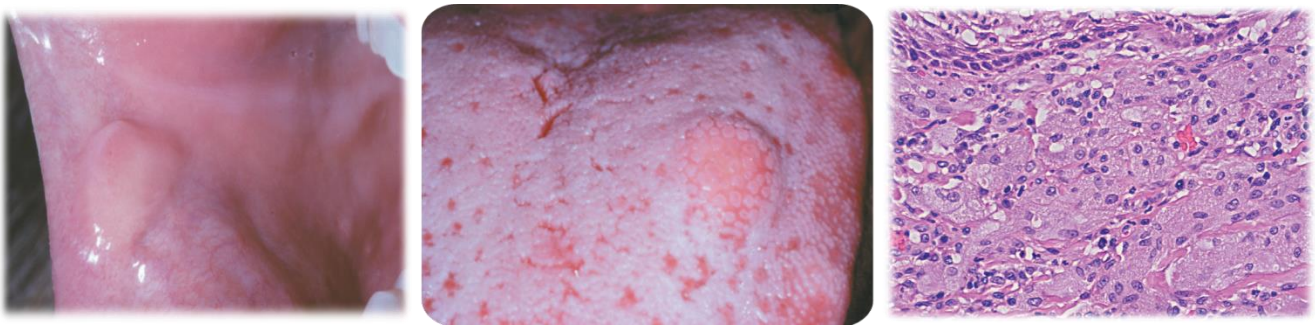
In the oral cavity both are rare smooth muscle neoplasm, appear as a slow growing, asymptomatic sbumucosal masses, usually in the tongue, hard palate or buccal mucosa. Occur in all age groups. Histologically both composed of spindle cell proliferation shares many similarities with neurofibroma, fibromatosis, myofibroma and shwanoma. Treatment by surgical excision with unexpected recurrence.

Metastatic Tumors

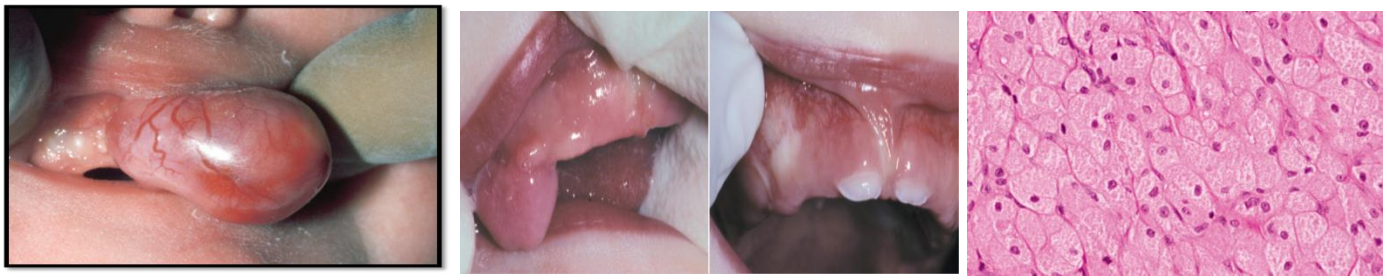
Metastatic disease to the jaws is unusual, approximately 80% of these metastases are to the mandible and 14% to the maxilla. Occasionally metastatic deposits are seen in gingiva simulate pyogenic granuloma. Occur in older age groups (5th & 6th decades of life) associated with bone pain and swelling, loosening of teeth, lip parasthesia, gingival mass and pathologic fracture.



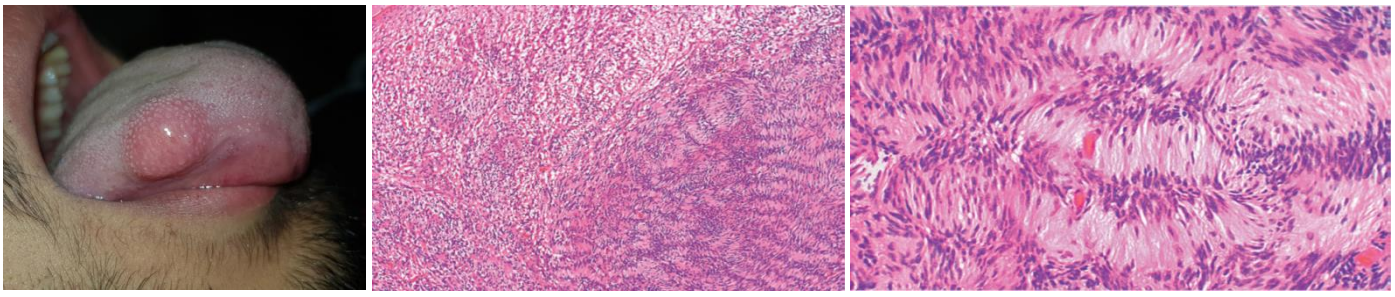
Traumatic neuroma:



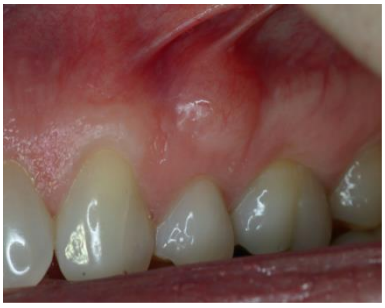
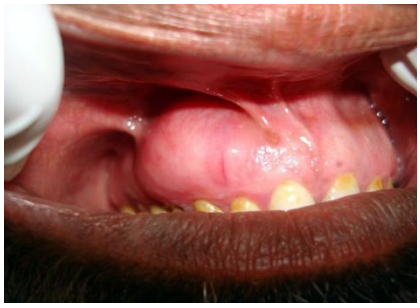
Granular cell tumor



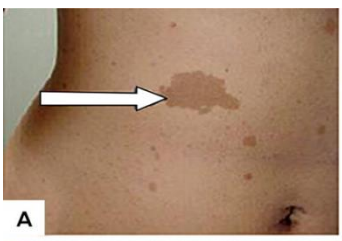
Congenital epulis

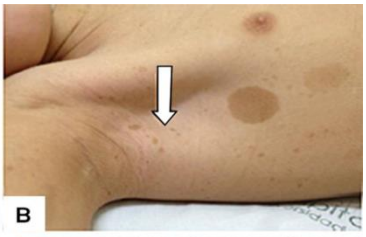


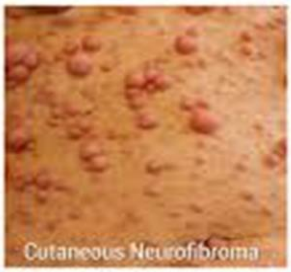
Schwannoma (neurilemmoma)

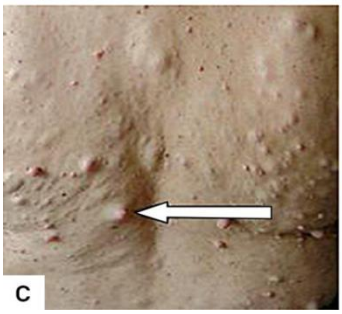



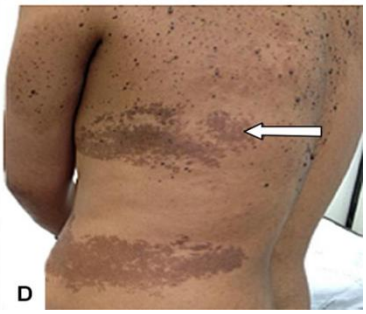
Neurofibroma

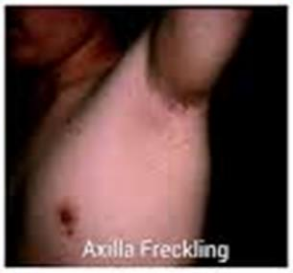


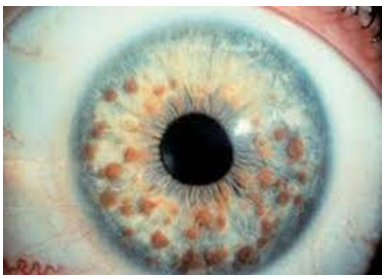
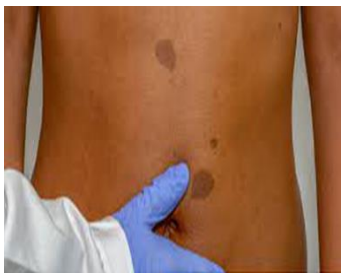
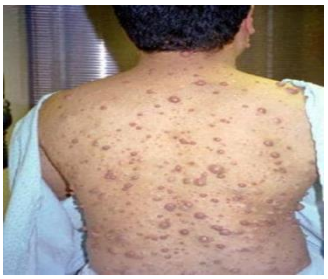




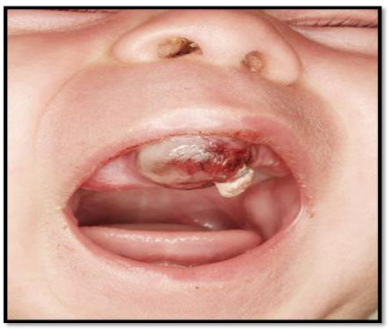
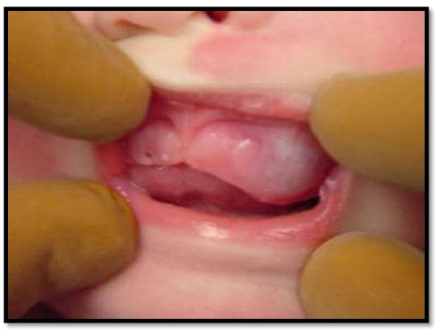
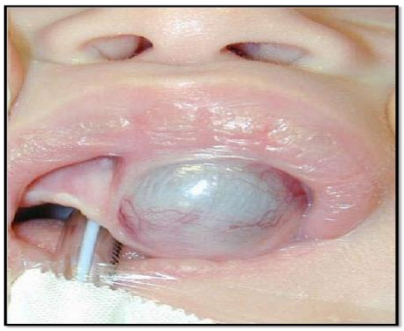




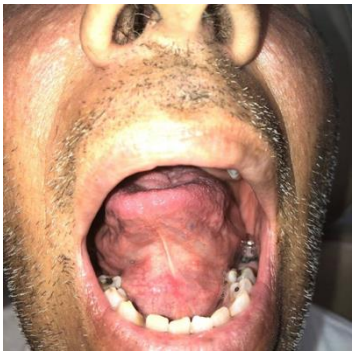
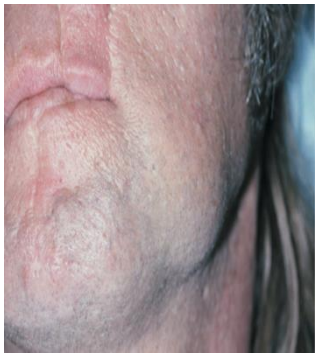
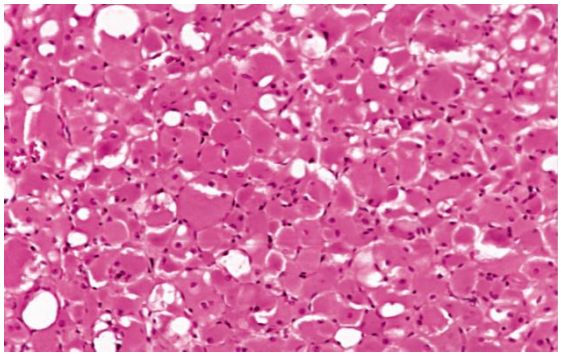


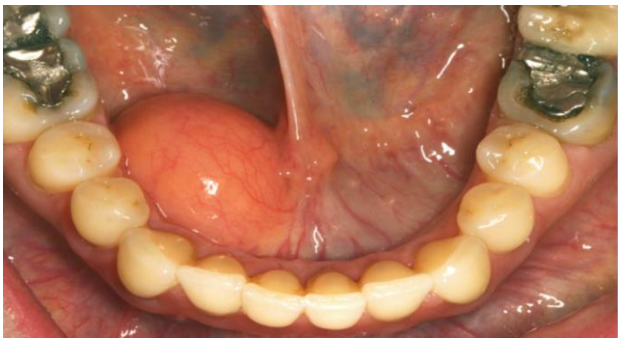
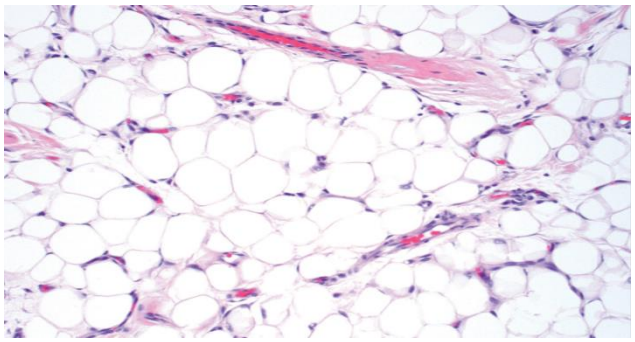
Neurofibromatosis

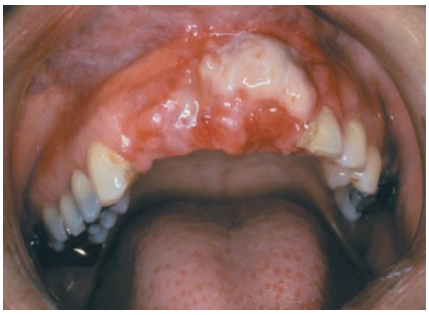
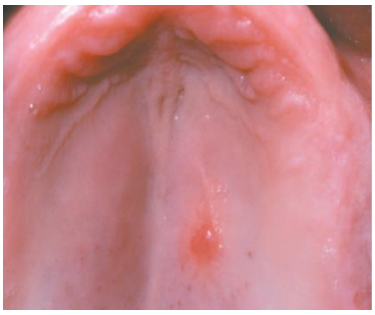
Pigmented neuroectodermal tumor of infancy

Rhabdomyoma

Lipoma

Leiomyoma and Leiomyosarcoma

Oral pathology

Immune-mediated disorder

❖ Recurrent Aphthous Stomatitis (Recurrent Aphthous Ulcerations)

Recurrent aphthous stomatitis (RAS) is a common disease in humans. Within the oral cavity, RAS is the most common condition affecting the mucosal soft tissue.

Etiology:

The cause appears to be "different things in different people". Although no single triggering agent is responsible, the mucosal destruction appears to represent a T cell–mediated immunologic reaction with production of tumor necrosis factor-alpha (TNF-α). This factor is a major inflammatory cytokine and assists in the ultimate targeting of the surface epithelium for destruction by cytotoxic T cells .

The following all have been reported to be responsible in certain subgroups of patients

- Allergies
- Genetic predisposition
- Hematologic abnormalities
- Hormonal influences
- Immunologic factors
- Infectious agents
- Nutritional deficiencies
- Smoking cessation
- Stress (mental and physical)
- Trauma

Systemic Disorders Associated with Recurrent Aphthous Stomatitis

- Bechtel syndrome
- Celiac disease
- Cyclic neutropenia
- Immunoglobulin A (IgA) deficiency
- Immunocompromised conditions, including human immunodeficiency virus (HIV)
- Inflammatory bowel disease
- MAGIC syndrome (mouth and genital ulcers with inflamed cartilage)
- Reactive arthritis

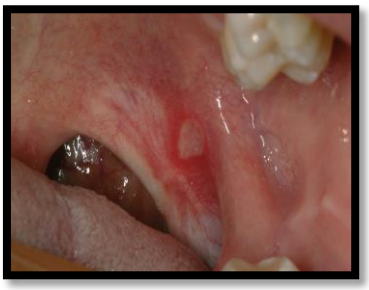
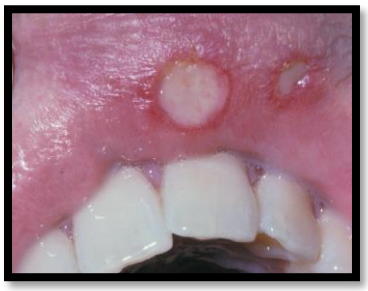
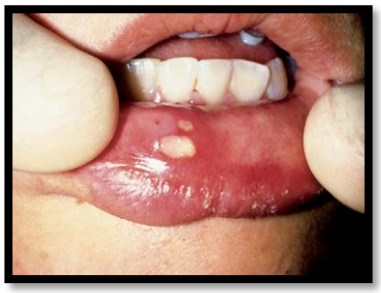
Clinical Features

Three forms of RAU have been recognized :

1. **Minor aphthous ulcer**

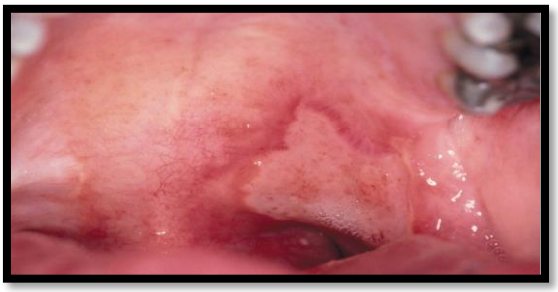
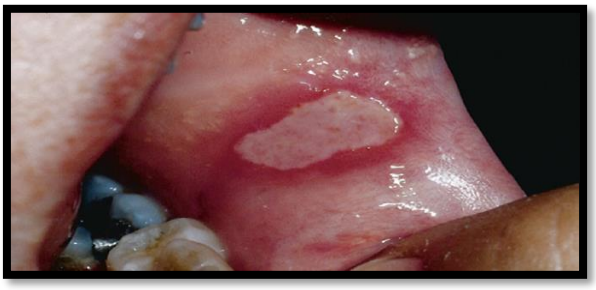
Minor aphthos ulcers are the most commonly encountred form .Patients with minor aphthous ulcerations experience the fewest recurrences, and the individual lesions exhibit the shortest duration of the three variants. The ulcers arise almost exclusively on non-keratinized mucosa and may be preceded by an erythematous macule in association with prodromal symptoms of burning, itching, or stinging. The ulceration demonstrates a yellow-white, removable fibrinopurulent membrane that is encircled by an erythematous halo.

Classically, the ulcerations measure between 3 and 10 mm in diameter, and heal without scarring in 7 to 14 days. From one to five lesions typically are present during a single episode, and the pain often is out of proportion for the size of the ulceration. The buccal and labial mucosae are affected most frequently, followed by the ventral surface of the tongue and mucobuccal fold, floor of the mouth, and soft palate.

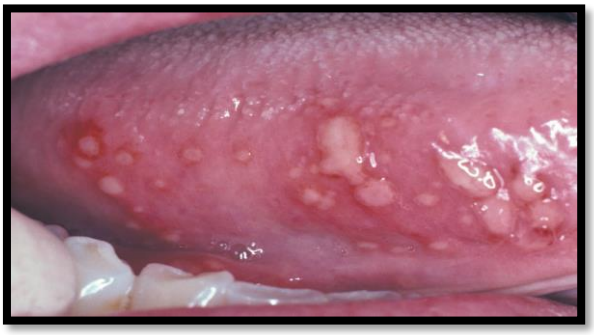
2. **Major aphthous ulcer**

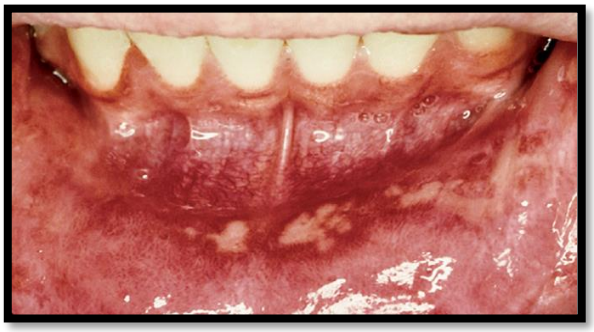
Major aphthous ulcerations are larger than minor aphthae and demonstrate the longest duration per episode. The ulcerations are deeper than the minor variant, measure from 1 to 3 cm in diameter, take from 2 to 6 weeks to heal, and may cause scarring . The number of lesions varies from 1 to 10. Any oral surface area may be affected, but the labial mucosa, soft palate, and tonsillar fauces are involved most commonly .

3. Herpetiform aphthous ulcer

Herpetiform aphthous ulcerations demonstrate the greatest number of lesions and the most frequent recurrences. The individual lesions are small, averaging 1 to 3 mm in diameter,with as many as 100 ulcers present in a single recurrence.Because of their small size and large number, the lesions bear a superficial resemblance to a primary HSV infection. It is common for individual lesions to coalesce into larger irregular ulcerations . The ulcerations heal within 7 to 10 days, but the recurrences tend to be closely spaced. Although the non-keratinized, movable mucosa is affected most frequently.





Histopathology :

Biopsies is usually unnecessary because the diagnosis is evident clinically . The early ulcerative lesions demonstrate a central zone of ulceration, which is covered by a fibrinopurulent membrane. Deep to the area of ulceration, the connective tissue exhibits an increased vascularity and a mixed inflammatory cellular infiltrate that consists of lymphocytes, histiocytes, an polymorphonuclear leukocytes. The epithelium at the margin of the lesion demonstrates spongiosis and numerous mononuclear cells in the basilar one-third. A band of lymphocytes intermixed with histiocytes is present in the superficial connective tissue and surrounding deeper blood vessels.

Treatment :

The patient's medical history should be reviewed for signs and symptoms of any systemic disorder . Most patients with mild aphthosis receive either no treatment, or therapy with a number of anesthetics or protective bioadhesive products .

In patients with mild disease, the mainstay of therapy is the use of topical corticosteroids. Most patients with diffuse minor or herpetiform aphthae respond well to dexamethasone solution (0.5 mg/5 mL) used in a rinse-and-expectorate method.

Patients with localized ulcerations can be treated successfully with 0.05% augmented betamethasone dipropionate gel or 0.05% fluocinonide gel.

Major aphthous ulcerations are more resistant to therapy and the individual lesions may be injected with triamcinolone acetonide or covered with 0.05% clobetasol propionate gel .

Triamcinolone tablets also can be dissolved directly over the lesions. In resistant cases, systemic corticosteroids may be required .

Widely accepted topical alternatives drugs include amlexanox paste, chlorhexidine , tetracycline oral suspension. Frequently mentioned systemic therapies include a number of immunomodulatory agents, such as colchicine, dapsone, pentoxifylline, and thalidomide.

Although laser ablation shortens the duration and decreases associated symptoms.

Chemical cautery with silver nitrate continues to be suggested as an effective therapy.

❖ Behçet's syndrome

Behçet syndrome is an uncommon complex multisystem condition that is diagnosed by means of clinical criteria. The main features as consisting of oral and genital aphthae, pustular vasculitic cutaneous lesions, and ocular and GI vasculitic lesions.

The cause of Behçet syndrome is unknown. Immune factors, infectious agents, and immune effector mechanisms have been implicated where represent an abnormal immune process triggered by an infectious or environmental antigen in a genetically predisposed individual.

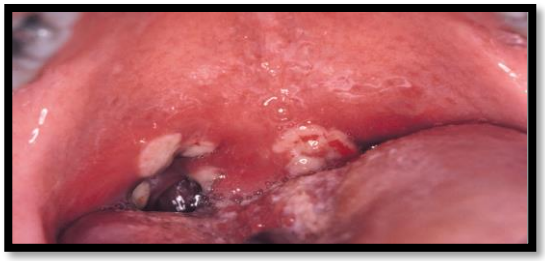
Clinical Features:

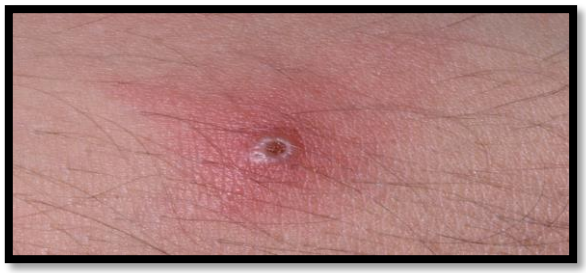
Behçet syndrome usually arises in the third and fourth decades . Men exhibit a slightly increased prevalence . Virtually all affected patients demonstrate oral lesions 100% , genital ulcerations (75 % of cases) and eye lesions . Other less frequently associated features include cutaneous lesions, arthritis, uveitis, thrombophlebitis, gastrointestinal manifestations, and central nervous system (CNS) involvement.

The oral lesions are similar to aphthous ulcerations and demonstrate the same duration and frequency. All three forms of oral aphthous stomatitis may be seen.

The genital lesions in males, approximately 90% of the lesions involve the scrotum, whereas those in females are most frequent on the vulva, vagina, or uterine cervix. perianal involvement . Ocular involvement occurs in up to 70% of the cases and is more frequent and severe in males. The most common findings are posterior uveitis, conjunctivitis, corneal ulceration, and arteritis. The most common secondary ocular complications are cataracts, glaucoma.Common cutaneous lesions include erythematous papules, pustules acneiform eruptions, and erythema nodosum–like lesions .Arthritis is one of the more common minor manifestations of the disease and is usually self-limiting and non-deforming. Although the vascular disease may involve arteries, veins are affected more

frequently and present as superficial and deep thrombophlebitis.Gastrointestinal disease is variable and includes abdominal pain, anorexia, diarrhea, dyspepsia, and vomiting. CNS involvement is not common but, when present, is associated with a poor prognosis.





Diagnosis :

Criteria for the Diagnosis of Behçet Disease:

- Recurrent oral ulceration ⟶ Minor, major, or herpetiform aphthae

Plus two of the following:

- Recurrent genital ulcerations
- Eye lesions (Anterior or posterior uveitis, cells in vitreous on slit-lamp examination, or retinal vasculitis).
- Skin lesions (Erythema nodosum, pseudofolliculitis or papulopustular lesions, or acneiform nodules noted in postadolescent patients not receiving corticosteroids).
- Positive pathergy test Read by physician at 24 to 48 hours.

Histopathology: The histopathologic features are not specific for Behçet syndrome and can be seen in many disorders, including aphthou stomatitis. The pattern most frequently seen is called leukocytoclastic vasculitis. The ulceration is similar in appearance to that seen in aphthous stomatitis, but the small blood vessels classically demonstrate intramural invasion by neutrophils, karyorrhexis of neutrophils, extravasation of red blood cells, and fibrinoid necrosis of the vessel wall.

Treatment : No single medication is universally effective with variable responses seen in different groups of patients. Systemic medications include azathioprine, colchicine, corticosteroids, cyclosporine, dapsone, interferon-α, methotrexate, pentoxifylline, thalidomide, and anti-TNF-α medications . The oral and genital ulcerations typically respond well to potent topical or intralesional corticosteroids or topical tacrolimus.

❖ Erythema Multiforme

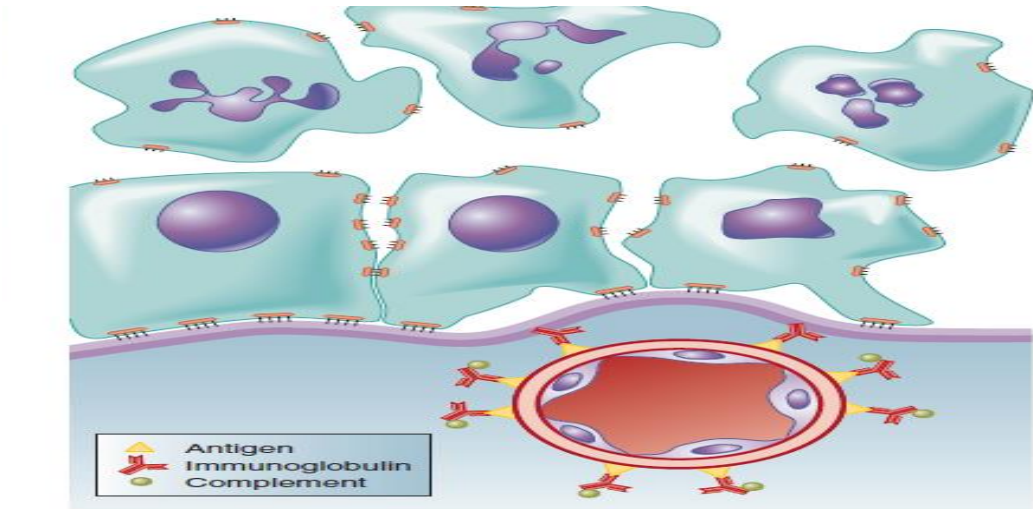
Erythema multiforme (EM) is an inflammatory disease of immune origin that affects the skin and mucous membranes and is a blistering, ulcerative mucocutaneous condition. It has been divided into two subtypes : Erythema multiforme minor and Erythema multiforme major.

The common precipitating factors are :

1. Infections such as herpes simplex, mycoplasma pneumonia.
2. Drugs (mostly sulfas, penicillin, Dilantin, barbiturates and iodines)
3. GI conditions (Crohn disease and ulcerative colitis).
4. Conditions such as malignancy, radiation therapy, and recent vaccination.

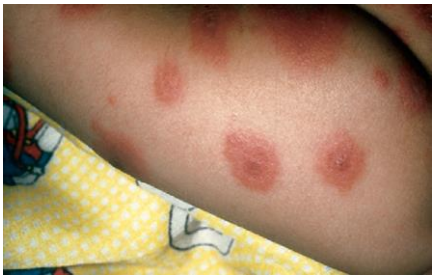
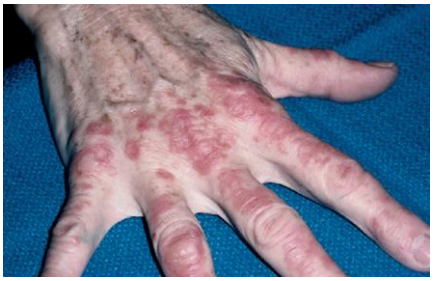
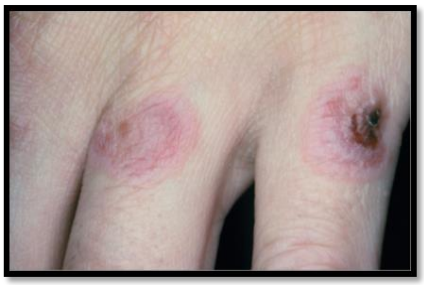
The pathogenesis of EM is mostly unknown. Research has identified circulating immune-related complexes that appear after patients have encountered some infections and after allergic reactions to medications.

Antibodies form against an exogenous antigen and the complex circulates in the blood being filtered in the walls of blood vessels; there they cause a vasculitis , which results in small areas of thrombosis and ischemic necrosis. The resulting skin and mucosal reactions range from a mild erythema to widespread necrosis with sloughing of the epithelial layer, depending on the intensity of the immune response to the antigen.

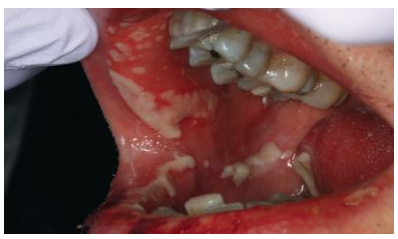
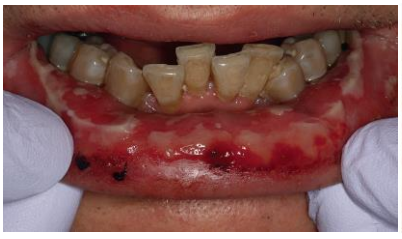
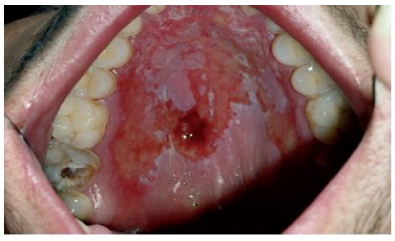


Clinical Features:

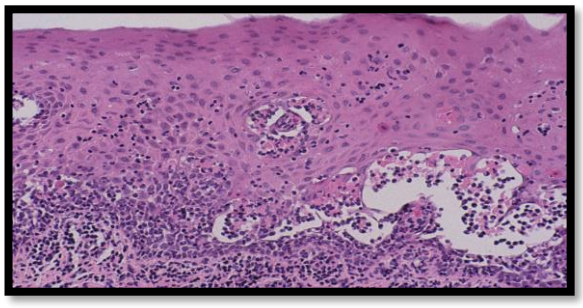
Erythema multiforme typically has an acute onset and usually affects young adults with a slight female predilection . Prodromal symptoms are often present and include fever, malaise, headache, cough, and sore throat, occurring approximately 1 week before onset. Erythema multiforme minor, usually begin with the development of slightly elevated, round, dusky-red patches on the skin of the extremities. These lesions may have a variety of appearances. Some of these skin lesions develop features that are highly characteristic for the disease. These lesions appear as concentric circular erythematous rings resembling a target or bull's-eye (target lesions) .In more severe cases, these may evolve into bullae with necrotic centers.

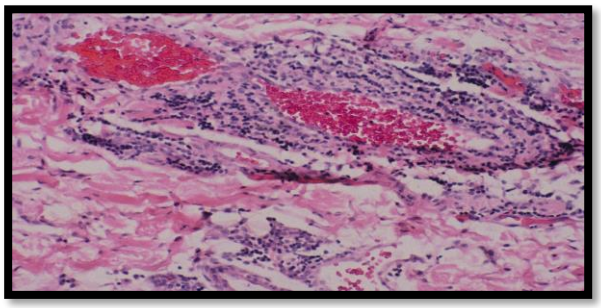




The oral cavity is the most frequently involved mucosal site, although the conjunctival, genitourinary, and respiratory mucosa also may be affected. The oral lesions begin as erythematous patches that undergo epithelial necrosis and evolve into large, shallow erosions and ulcerations with irregular borders . Hemorrhagic crusting of the vermilion zone of the lips is common . Sometimes patients are dehydrated because they are unable to ingest liquids as a result of mouth pain.The ulcerations often have a diffuse distribution. The lips, labial mucosa, buccal mucosa, tongue, floor of the mouth, and soft palate are the most common sites of involvement. Usually, the gingivae and hard palate are relatively spared. Erythema Multiforme Major their diagnosis can be made if two or more mucosal sites are affected in conjunction with widespread skin lesions. In most cases the oral mucosa is involved in addition to either the ocular or genital mucosae. With severe ocular involvement, scarring symblepharon formation may occur, similar to that in cicatricial pemphigoid .

Histopathology: Histopathologic examination is not pathognomonic. Subepithelial or intraepithelial vesiculation may be seen in association with necrotic basal keratinocytes . A mixed inflammatory infiltrate is present, consisting of lymphocytes, neutrophils, and often eosinophils. Sometimes these cells are arranged in a perivascular orientation .





Treatment:

The disease is self-limiting, usually lasting 2 to 6 weeks . Treatment in mild cases is symptomatic and consists of antihistamines, analgesics, and antipyretics combined with oral rinses of antihistamine or the use of a topical steroid . If a causative drug is identified or suspected, then it should be discontinued immediately.

If the patient is dehydrated as a result of an inability to eat because of oral pain, then IV rehydration may be necessary along with topical anesthetic agents to decrease discomfort.

If disease is triggered by herpes simplex, then continuous oral acyclovir or valacyclovir therapy can prevent recurrences.

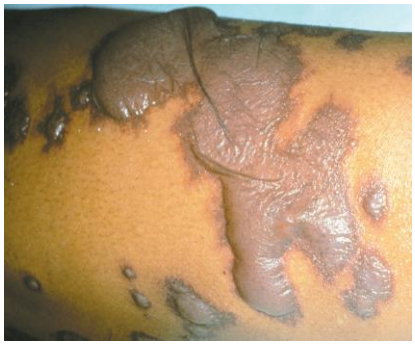
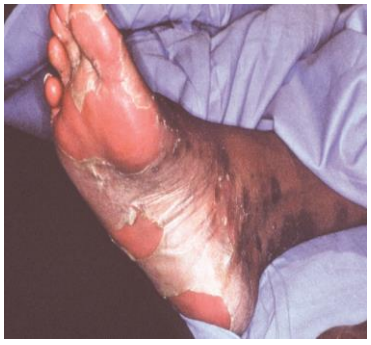
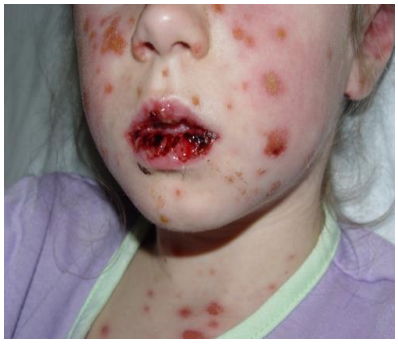
❖ Stevens-johnson syndrome and Toxic epidermal necrolysis

In the past, many dermatologists considered Stevens- Johnson syndrome and toxic epidermal necrolysis to represent the most severe end of the erythema multiforme but now is consider as separated entity . Although the inciting event in erythema multiforme is usually a herpes virus infection, Stevens-Johnson syndrome and toxic epidermal necrolysis are almost always triggered by drug exposure. Recent studies have shown that the damage to the epithelium is due to increased apoptosis of the epithelial cells, and several mechanisms have been postulated to account for this phenomenon.

Clinical Features: The difference between Stevens-Johnson syndrome and toxic epidermal necrolysis is the degree of skin involvement, with Stevens-Johnson syndrome having less than 10% of the body surface affected by lesions, and toxic epidermal necrolysis having more than 30% involvement.

In contrast to Stevens-Johnson syndrome, which is usually seen in younger patients, toxic epidermal necrolysis tends to occur in people over 60 years of age. A female predilection is observed. These patients usually have flu-like prodromal signs and symptoms, including fever, malaise, sore throat, headache, and loss of appetite.

Within a few days, skin lesions begin to develop, but unlike erythema multiforme, the cutaneous lesions of Stevens-Johnson syndrome and toxic epidermal necrolysis initially appear on the trunk, presenting as erythematous macules (completely flat). Within 1 to 14 days, however, sloughing of the skin and flaccid bullae develop. If the patient survives, then the cutaneous process resolves in 3 to 5 weeks; however, oral lesions may take longer to heal, and significant residual ocular damage is evident in half of the patients.

Treatment :

Most identifying and immediately discontinuing any drug that might be initiating the condition. Management of patients of these lesions in the burn unit of the hospital is recommended.

❖ Lupus Erythematosus

Lupus erythematosus (LE) is a classic example of an immunologically mediated condition, and is the most common of the so-called collagen vascular or connective tissue diseases . It may exhibit any one of several clinicopathologic forms.

Systemic lupus erythematosus (SLE) is a serious multisystem disease with a variety of cutaneous and oral manifestations. There is an increase in the activity of the humoral limb (B lymphocytes) of the immune system in conjunction with abnormal function of the T lymphocytes. Although genetic factors probably play a role in the pathogenesis of SLE, the precise cause is unknown. Undoubtedly, interplay between genetic and environmental factors occurs.

Chronic cutaneous lupus erythematosus (CCLE) may represent a different, but related, process. It primarily affects the skin and oral mucosa, and the prognosis is good.

Subacute cutaneous lupus erythematosus (SCLE) is a third form of the disease, which has clinical features intermediate between those of SLE and CCLE.

Clinical Features:

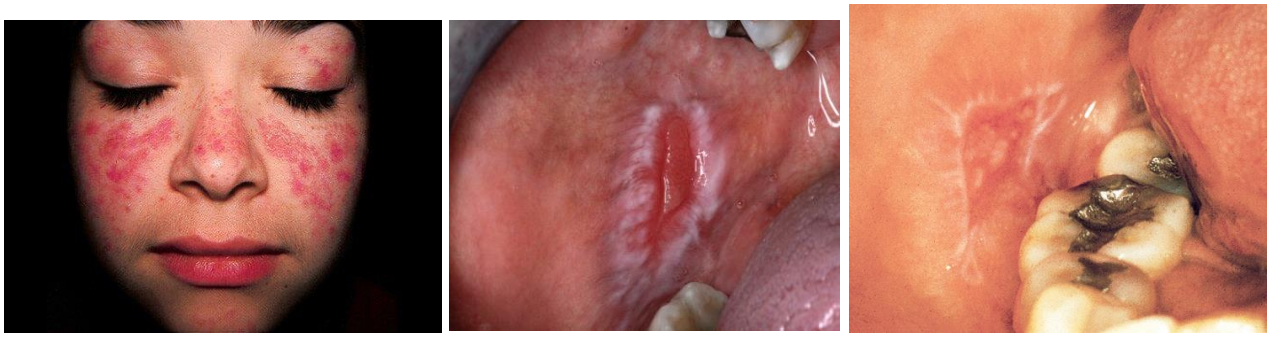
1.**Systemic Lupus Erythematosus**

SLE can be a very difficult disease to diagnose in its early stages because it often appears in a nonspecific, vague fashion, frequently with periods of remission or disease inactivity. Women are affected nearly 8 to 10 times more frequently than men. The average age at diagnosis is 31 years.Common findings include fever, weight loss, arthritis, fatigue, and general malaise. In 40% to 50% of affected patients, a characteristic rash, having the pattern of a butterfly, develops over the malar area and nose ,typically sparing the nasolabial folds. Sunlight often makes the lesions worse.

The kidneys are affected in approximately 40% to 50% of SLE patients. This complication may ultimately lead to kidney failure; thus it is typically the most significant aspect of the disease.

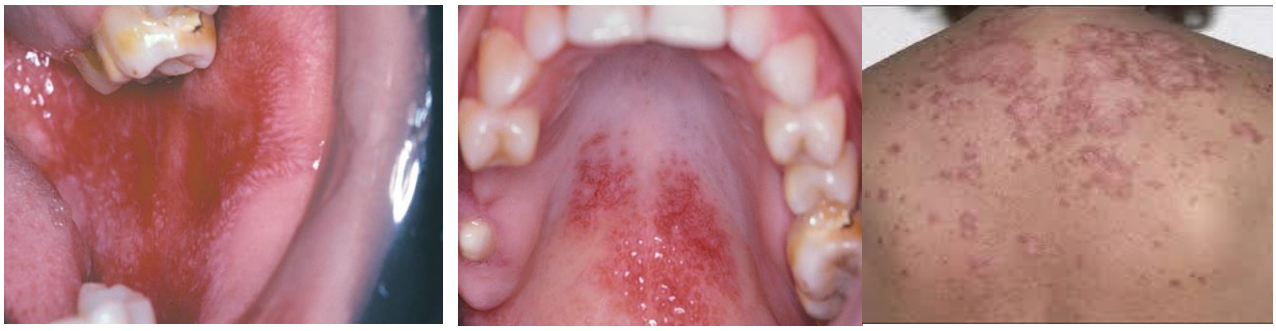
Cardiac involvement is also common, with pericarditis being the most frequent complication.

Oral lesions of SLE develop in 5% to 25% of these patients, although some studies indicate prevalence as high as 40%. The lesions usually affect the palate, buccal mucosa, and gingivae. Sometimes they appear as lichenoid areas, but they may also look nonspecific or even somewhat granulomatous . Involvement of the vermilion zone of the lower lip (lupus cheilitis) is sometimes seen. Varying degrees of ulceration, pain, erythema, and hyperkeratosis may be present. Other oral complaints such as xerostomia, stomatodynia, candidiasis, periodontal disease, and dysgeusia have been described, but the direct association of these problems with SLE remains to be proven.



2. Chronic Cutaneous Lupus Erythematosus

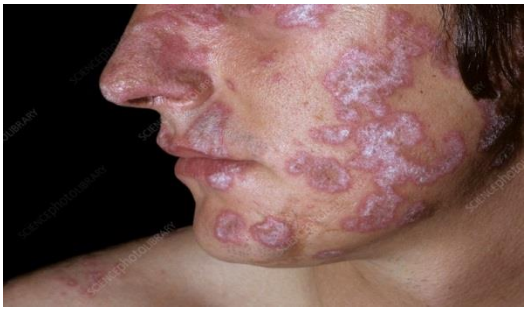
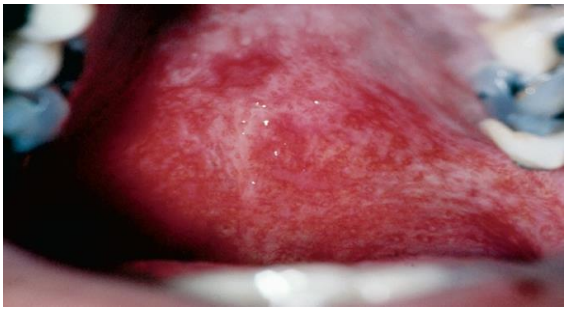
Patients with CCLE usually have few or no systemic signs or symptoms, with lesions being limited to skin or mucosal surfaces. The skin lesions of CCLE most commonly present as discoid lupus erythematosus. They begin as scaly, erythematous patches that are frequently distributed on sun exposed skin, especially in the head and neck area . Patients may indicate that the lesions are exacerbated by sun exposure. With time, the lesions may heal spontaneously in one area, only to appear in another area. The healing process usually results in cutaneous atrophy with scarring and hypopigmentation or hyperpigmentation of the resolving lesion. In most cases the oral manifestations of CCLE essentially appear clinically identical to the lesions of erosive lichen planus. Unlike the oral lesions of lichen planus, however, the oral lesions of CCLE seldom occur in the absence of skin lesions. An ulcerated or atrophic, erythematous central zone, surrounded by white, fine, radiating striae, characterizes the oral lesion of CCLE . Sometimes the erythematous, atrophic central region of a lesion may show a fine stippling of white dots. As with erosive lichen planus , the ulcerative and atrophic oral lesions of CCLE may be painful, especially when exposed to acidic or salty foods.



3. Subacute Cutaneous Lupus Erythematosus

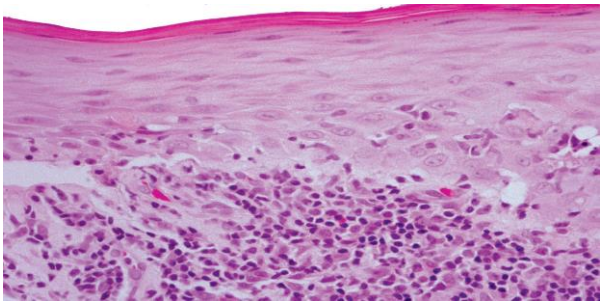
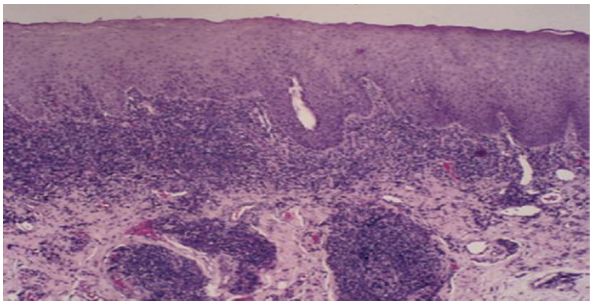
Patients with SCLE have clinical manifestations intermediate between those of SLE and CCLE. The skin lesions are the most prominent feature of this variation. They are characterized by

photosensitivity and are, therefore, generally present in sun-exposed areas. These lesions do not show the induration and scarring seen with the skin lesions of CCLE. Oral lesions similar to those of CCLE have been described in this variant of lupus as well , most patients will have arthritis or musculoskeletal problems.

Histopathology; The histopathologic features of the skin and oral lesions of the various forms of LE show some features in common but are different enough to warrant separate discussions. The skin lesions of CCLE are characterized by hyperkeratosis, often displaying keratin packed into the openings of hair follicles ("follicular plugging"). In all forms of LE, degeneration of the basal cell layer is frequently observed, and the underlying connective tissue supports patchy to dense aggregates of chronic inflammatory cells .In the deeper connective tissue, the inflammatory infiltrate often surrounds the small blood vessels.

The oral lesions demonstrate hyperkeratosis, alternating atrophy and thickening of the spinous cell layer, degeneration of the basal cell layer, and subepithelial lymphocytic infiltration. These features may also be seen in oral lichen planus; however, the two conditions can usually distinguished by the presence in LE of patchy deposits of a periodic acid-Schiff (PAS)-positive material in the basement membrane zone, subepithelial edema (sometimes to the point of vesicle formation), and a more diffuse, deep inflammatory infiltrate, often in a perivascular orientation. Some authorities, however, feel that differentiating lichen planus from LE is best done by direct immunofluorescence studies or histopathologic examination of the cutaneous lesions.

Diagnosis: In addition to the clinical and microscopic features, a number of additional immunologic studies may be helpful in making the diagnosis of LE.

1. Direct immunofluorescence testing of lesional tissue shows deposition of one or more immunoreactants (usually IgM, IgG, or C3) in a shaggy or granular band at the basement membrane zone.
2. Direct immunofluorescence testing of clinically normal skin of SLE patients often shows a similar deposition of IgG, IgM, or complement components. This finding is known as a **positive lupus band test**.
3. Evaluation of serum obtained from a patient with SLE shows various immunologic abnormalities. Approximately 95% of these patients have antibodies directed against multiple nuclear antigens (i.e., antinuclear antibodies [ANAs]).
4. Antibodies directed against double stranded DNA are noted in 70% of patients with SLE, and these are more specific for the disease.
5. Another 30% of patients show antibodies directed against Sm , a protein that is complexed with small nuclear RNA. This finding is very specific for SLE.

Treatment : Patients with SLE should avoid excessive exposure to sunlight because UV light may precipitate disease activity. Mild active disease may be effectively managed using NSAIDs combined with antimalarial drugs, such as hydroxychloroquine.

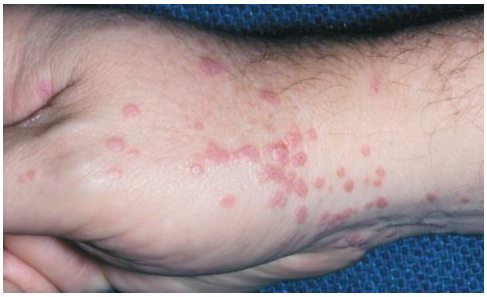
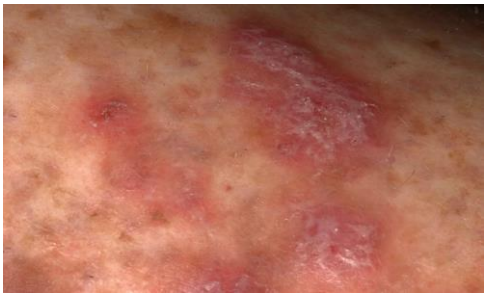
For more severe, acute episodes that involve arthritis, pericarditis, thrombocytopenia, or nephritis, systemic corticosteroids are generally indicated; these may be combined with other immunosuppressive and immunomodulating agents. If oral lesions are present, they typically respond to the systemic therapy.

As with SLE patients, patients with CCLE should avoid excessive sunlight exposure. Because most of the manifestations of CCLE are cutaneous, topical corticosteroids are often reasonably effective. For cases that are resistant to topical therapy, systemic antimalarial drugs, immunosuppressive drugs, immunomodulating drugs, or low-dose thalidomide may produce a response. Topical corticosteroids are also helpful in treating the oral lesions of CCLE.

❖ Lichen Planus (LP):

Lichen planus is a relatively common, an immunologically mediated mucocutaneous disorder. The etiologic agent initiating lichen planus is unknown ,but it appear to be a T-Lymphocyte mediated disorder ,where cytotoxic T-lymphocytes stimulated by antigen presenting cells (intraepithelial langerhans cells) producing tumor necrotic factor (TNF) that contribute to epithelial degeneration .Hepatitis –C- infection, genetic influences, and stress or anxiety are some of suggestive possible factors.Affect middle-aged adults patients . Women predominate in most series of cases. Approximately 1% of the population may have cutaneous lichen planus. The prevalence of oral lichen planus is between 0.1% and 2.2%.

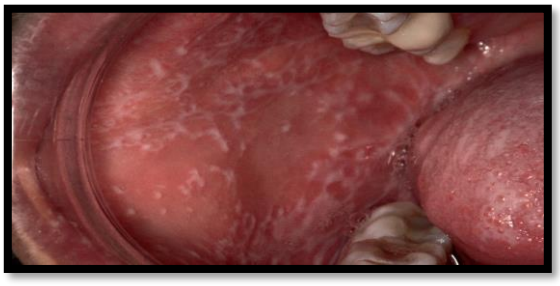
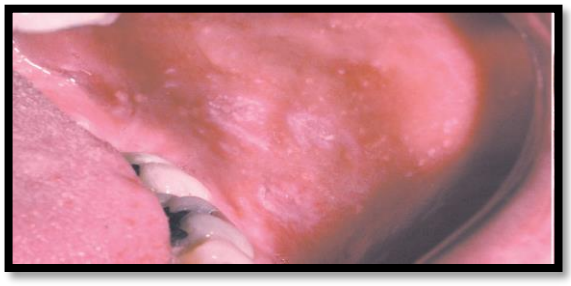
The skin lesions have been classically described as purple, pruritic, polygonal papules. These usually affect the flexor surfaces of the extremities.. Careful examination of the surface of the skin papules reveals a fine, lacelike network of white lines (Wickham striae) .

Essentially there are two forms of oral lesions:

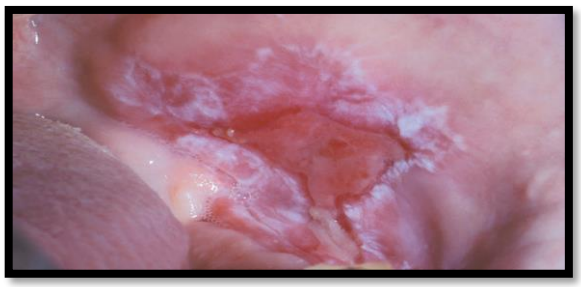
1. Reticular L.P.
2. Erosive L.P.

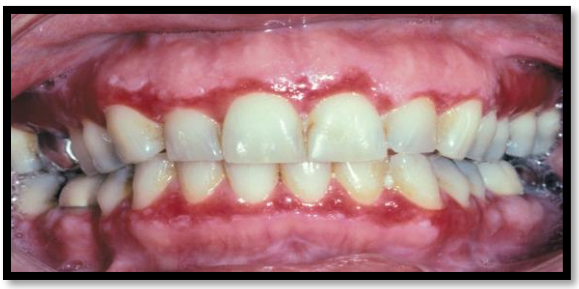
Reticular lichen planus : is much more common than the erosive form. The reticular form usually causes no symptoms and involves the posterior buccal mucosa bilaterally . Other oral mucosal surfaces may also be involved concurrently, such as the lateral and dorsal tongue, the gingivae, the palate, and vermilion border . Reticular lichen planus is thus named because of its characteristic pattern of interlacing white lines (also referred to as Wickham striae). These lesions are typically not static but wax and wane over weeks or months. The reticular pattern may not be as evident in some sites, such as the dorsal tongue, where the lesions appear more as keratotic plaques with atrophy of the papillae ,this variant also called Plaque LP.

Erosive Lichen Planus

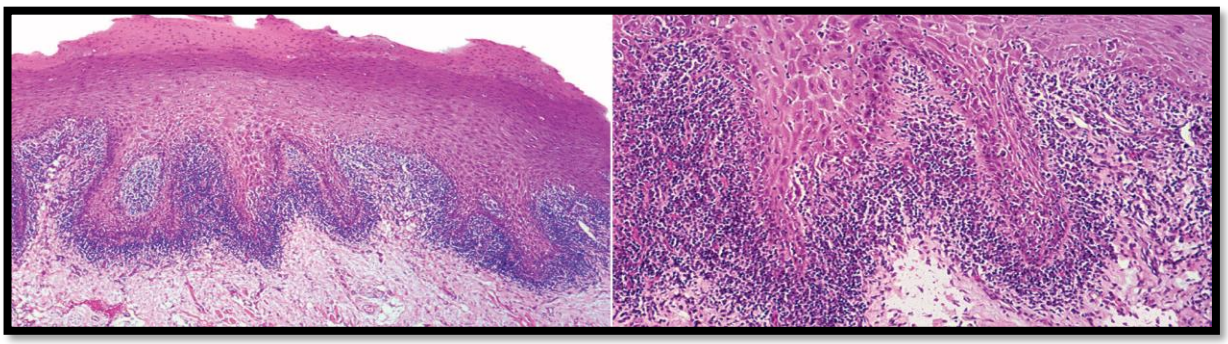
Erosive lichen planus, although not as common as the reticular form, is more significant for the patient because the lesions are usually symptomatic. Clinically, there are atrophic, erythematous areas with central ulceration of varying degrees. The periphery of the atrophic regions is usually bordered by fine, white radiating striae. Sometimes the atrophy and ulceration are confined to the gingival mucosa, producing the reaction pattern called desquamative gingivitis .





Histopathology:

Varying degrees of orthokeratosis and parakeratosis may be present on the surface of the epithelium. The thickness of the spinous layer can also vary(acanthosis). The rete ridges may be absent or hyperplastic, but they classically have a pointed or “saw-toothed” shape. Destruction of the basal cell layer of the epithelium (hydropic degeneration) is also evident. This is accompanied by an intense, bandlike infiltrate of predominantly T lymphocytes immediately subjacent to the epithelium. Degenerating keratinocytes may be seen in the area of the epithelium and connective tissue interface and have been termed colloid, cytoid, hyaline, or Civatte bodies. The immunopathologic features of lichen planus are nonspecific. Most lesions show the deposition of a shaggy band of fibrinogen at the basement membrane zone.



Diagnosis: The diagnosis of reticular lichen planus can often be made based on the clinical findings alone. The interlacing white striae appearing bilaterally on the posterior buccal mucosa are virtually pathognomonic.

Erosive lichen planus is sometimes more challenging to diagnose based on clinical features alone. If the typical radiating white striae and erythematous, atrophic mucosa are present at the periphery of well demarcated ulcerations on the posterior buccal mucosa bilaterally, then the diagnosis can sometimes be rendered. However, a biopsy, often with direct immunofluorescence studies, may be necessary to rule out other ulcerative or erosive diseases, such as lupus erythematosus or chronic ulcerative stomatitis.

Treatment :

- Reticular lichen planus typically produces no symptoms and no treatment is needed.
- Antifungal therapy is necessary when it superimposed with candidiasis.
- Erosive lichen planus is treated by corticosteroids (topical or systemic) .

Vesiculobullous Lesions

Several conditions discussed in this lecture are the result of inappropriate production of antibodies by the patient (autoantibodies).

These autoantibodies are directed against various constituents of the molecular apparatus that hold epithelial cells together or that bind the surface epithelium to the underlying connective tissue. The ensuing damage produced by the interaction of these autoantibodies with the host tissue is seen clinically as a disease process, often termed an immunobullous disease. Because each disease is characterized by production of specific types of autoantibodies, identification of the antibodies and the tissues against which they are targeted is important diagnostically. The two techniques that are widely used to investigate the immunobullous diseases are

1- Direct immunofluorescence

2- Indirect immunofluorescence studies.

❖Pemphigus

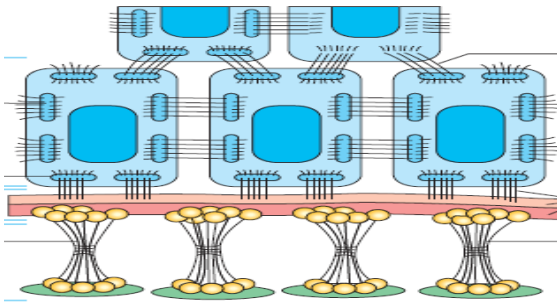
The condition known as pemphigus represents four related diseases of an autoimmune origin:

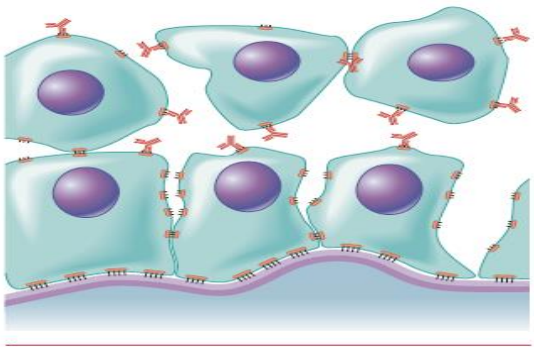
1. Pemphigus vulgaris
2. Pemphigus vegetans
3. Pemphigus erythematosus
4. Pemphigus foliaceus

Only the first two of these affect the oral mucosa, and the discussion is limited to pemphigus vulgaris. Pemphigus vegetans is rare; most authorities now feel it represents simply a variant of pemphigus vulgaris.

Pemphigous Vulgaris

Pemphigus vulgaris (PV) are a group of mucocutaneous diseases characterized by epithelial desquamation caused by abnormal production for unknown reasons of autoantibodies that attack the desmosome of the intercellular cohesive system. The loss of adhesion occurs between the cells located in the zone above the basal cell layer and a result of this immunologic attack on the desmosomes, a split develops within the epithelium, causing a blister (suprabasilar bullous formation) . Destruction of the adhesive factors of the suprabasila spinous cells is referred to as acantholysis.



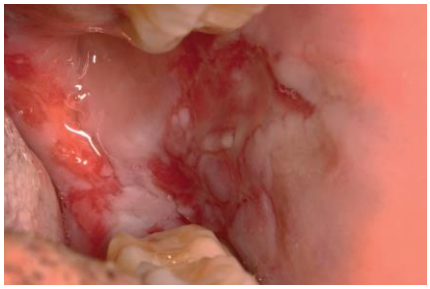
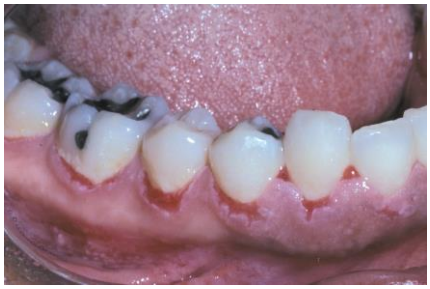
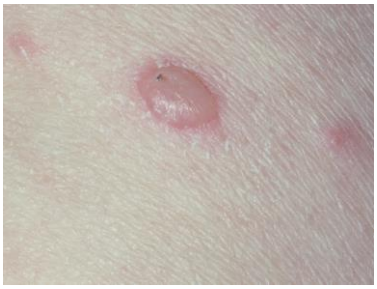


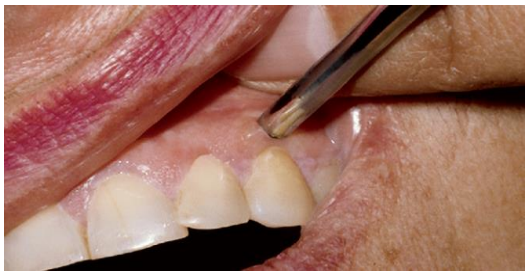
CLINICAL FEATURES:

The initial manifestations of pemphigus vulgaris often involve the oral mucosa, typically in adults. The average age at diagnosis is 50 years. The condition seems to be more common in persons of Mediterranean, South Asian, or Jewish heritage. Patients usually complain of oral soreness, and examination shows superficial, ragged erosions and ulcerations distributed haphazardly on the oral mucosa . Such lesions may affect virtually any oral mucosal location, although the palate, labial mucosa, buccal mucosa, ventral tongue, and gingivae are often involved. Patients rarely report vesicle or bulla formation intraorally, and such lesions can seldom be identified by the examining clinician,probably because of early rupture of the thin, friable roof of the blisters. More than 50% of the patients have oral mucosal lesions before the onset of cutaneous lesions, sometimes by as much as 1 year or more. Eventually, however, nearly all patients have intraoral involvement. The skin lesions appear as flaccid vesicles and bullae that rupture quickly, usually within hours to a few days, leaving an erythematous, denuded surface. Infrequently ocular involvement may be seen, usually

appearing as bilateral conjunctivitis. Unlike cicatricial pemphigoid, the ocular lesions of pemphigus typically do not cause scarring and symblepharon formation .

A characteristic feature of pemphigus vulgaris is that a bulla can be induced on normal-appearing skin if firm lateral pressure is exerted. This is called a positive Nikolsky sign.

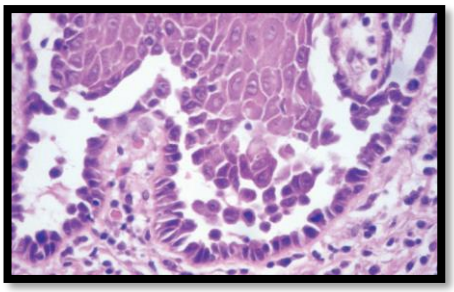




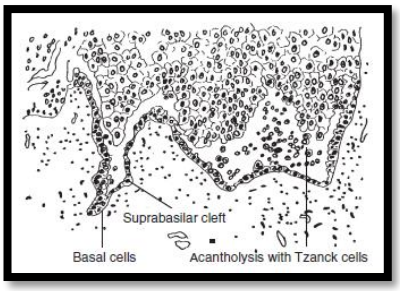

Nikolsky's sign

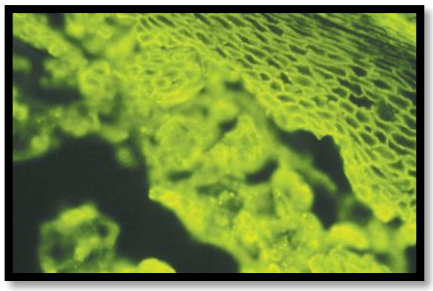
Histopathologic Features:

Biopsy specimens of perilesional tissue show characteristic intraepithelial separation, which occurs just above the basal cell layer of the epithelium . Sometimes the entire superficial layers of the epithelium are stripped away, leaving only the basal cells, which have been described as resembling a “row of tombstones.”The cells of the spinous layer of the surface epithelium typically appear to fall apart, a feature that has been termed acantholysis, and the loose cells tend to assume a rounded shape . This feature of pemphigus vulgaris can be used in making a diagnosis based on the identification of these rounded cells (Tzanck cells) in an exfoliative cytologic preparation. A mild-to-moderate chronic inflammatory cell infiltrate is usually seen in the underlying connective tissue.

The diagnosis of pemphigus vulgaris should be confirmed by direct immunofluorescence examination of fresh perilesional tissue or tissue submitted in Michel’s solution. With this procedure, antibodies (usually IgG or IgM) and complement components (usually C3) can be demonstrated in the intercellular spaces between the epithelial cells in almost all patients with this disease. Indirect immunofluorescence is also typically positive in 80% to 90% of cases, demonstrating the presence of circulating autoantibodies in the patient’s serum.







Treatment:

Pemphigus is a systemic disease; therefore, treatment consists primarily of systemic corticosteroids (usually prednisone), often in combination with other immunosuppressive drugs (so-called steroid-sparing agents) such as azathioprine. The most common approach is to use relatively high doses of systemic corticosteroids initially to clear the lesions, and then attempt to maintain the patient on as low a dose of corticosteroids as is necessary to control the condition. The use of topical corticosteroids in the management of oral lesions is also common with low dose of systemic corticosteroid .

❖ Mucous Membrane Pemphigoid (Cicatricial pemphigoid; benign mucous membrane pemphigoid)

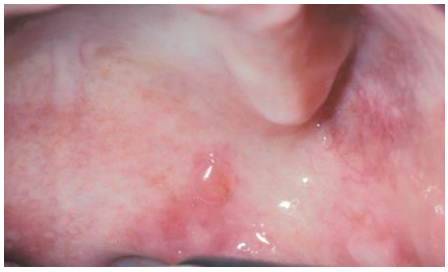
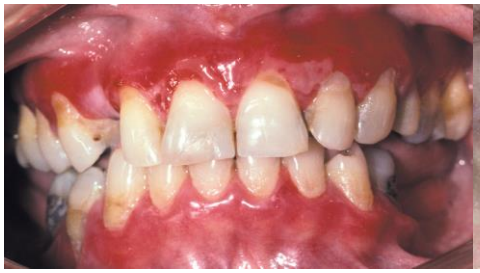
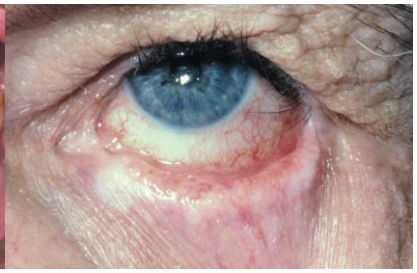
Mucous membrane pemphigoid represents a group of chronic, blistering, mucocutaneous autoimmune diseases in which tissue-bound autoantibodies are directed against one or more components of the basement membrane.

❖ Clinical Features:

Mucous membrane pemphigoid usually affects older adults, with an average age of 50 to 60 years at the onset of disease. Females are affected more frequently than males. Oral lesions are seen in most patients, but other sites, such as conjunctival, nasal, esophageal, laryngeal, and vaginal mucosa, as well as the skin may be involved.

The oral lesions of pemphigoid begin as either vesicles or bullae that may occasionally be identified clinically. In contrast, patients with pemphigus rarely display such blisters. Eventually, the oral blisters rupture, leaving large, superficial, ulcerated, and denuded areas of mucosa . The ulcerated lesions are usually painful and persist for weeks to months if untreated .Often this process is seen diffusely throughout the mouth, but it may be limited to certain areas, especially the gingiva . Gingival involvement produces a clinical reaction pattern termed desquamative gingivitis. The most significant complication of mucous

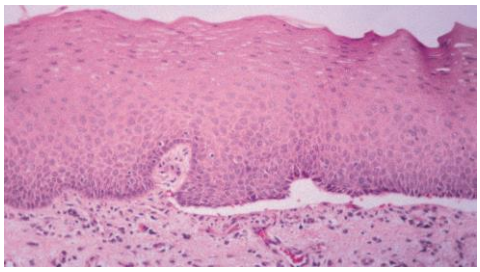
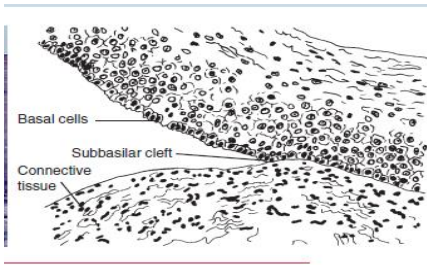
membrane pemphigoid, however, is ocular involvement. The earliest change is subconjunctival fibrosis. As the disease progresses, the conjunctiva becomes inflamed and eroded. Attempts at healing lead to scarring . Other mucosal sites may also be involved and cause considerable difficulty for the patient.

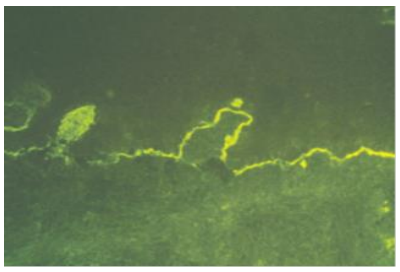




Histopathologic Features:

Biopsy of perilesional mucosa shows a split between the surface epithelium and the underlying connective tissue in the region of the basement membrane . A mild chronic inflammatory cell infiltrate is present in the superficial submucosa.

Direct immunofluorescence studies show a continuous linear band of immunoreactants at the basement membrane zone in nearly 90% of affected patients . The immune deposits consist primarily of IgG and C3 .



Treatment:

In fact, there is no single good therapy for every patient; treatment must be individualized, depending on lesional distribution, disease activity, and therapeutic response. Topical Agents use If only oral lesions are present, such as topical corticosteroids . Once control is achieved, the applications can be discontinued.Patients with only gingival lesions often benefit from good oral hygiene measures. As an additional aid in treating gingival lesions, a flexible mouth guard may be fabricated to use as a carrier for the corticosteroid medication.

Systemic Agents used If topical corticosteroids are unsuccessful. Dapsone, can be used to treat patients with mild-to-moderate involvement by mucous membrane pemphigoid. Another alternative systemic therapy that may be used for patients with less severe disease

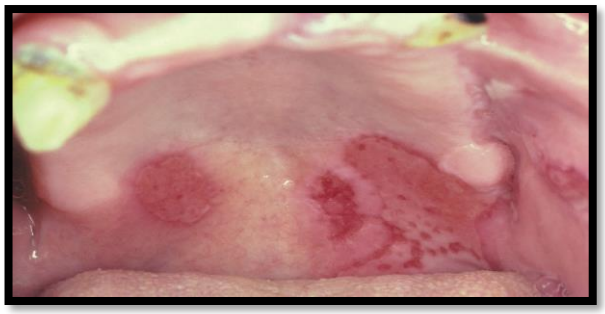
is tetracycline or minocycline and niacinamide (nicotinamide). Some studies have suggested that treatment with intravenous (IV) human immunoglobulin.

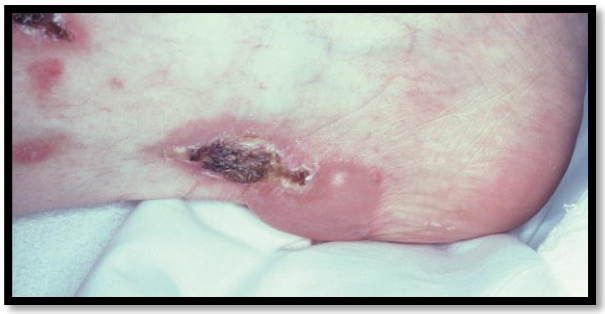
❖ BULLOUS PEMPHIGOID

Bullous pemphigoid is the most common of the autoimmune blistering conditions. The disease is characterized by the production of autoantibodies directed against components of the basement membrane. In many respects, bullous pemphigoid resembles mucous membrane pemphigoid, but most investigators note that there are enough differences to consider these diseases as distinct but related entities. One significant difference is that the clinical course in patients with bullous pemphigoid is usually characterized by periods of remission followed by relapse, whereas the course in patients with mucous membrane pemphigoid is usually protracted and progressive.

Clinical Features:

Bullous pemphigoid typically develops in older people; most patients are between 75 and 80 years of age. No sex or racial predilection is generally reported. Pruritus is often an early symptom. This is followed by the development of multiple, tense bullae on either normal or erythematous skin . These lesions eventually rupture after several days, causing a superficial crust to form. Eventually, healing takes place without scarring.Oral mucosal involvement is uncommon, with approximately 10% to 20% of patients being affected. The oral lesions, like the skin lesions, begin as bullae, but they tend to rupture sooner, probably as a result of the constant low grade trauma to which the oral mucosa is subjected. Large, shallow ulcerations with smooth, distinct margins are present after the bullae rupture .





Histopathologic Features:

Microscopic examination of tissue obtained from the perilesional margin of a bulla shows separation of the epithelium from the connective tissue at the basement membrane zone, resulting in a subepithelial separation. Modest numbers of both acute and chronic inflammatory cells are typically seen in the lesional area, and the presence of eosinophils within the bulla itself is characteristic.Direct immunofluorescence studies show a continuous

linear band of immunoreactants, usually IgG and C3, localized to the basement membrane zone in 90% to 100% of affected patients. These antibodies bind to proteins associated with hemidesmosomes, structures that bind the basal cell layer of the epithelium to the basement membrane and the underlying connective tissue. In addition to the tissue-bound autoantibodies, 50% to 90% of the patients also have circulating autoantibodies in the serum, producing an indirect immunofluorescent pattern that is identical to that of the direct immunofluorescence.

Treatment :

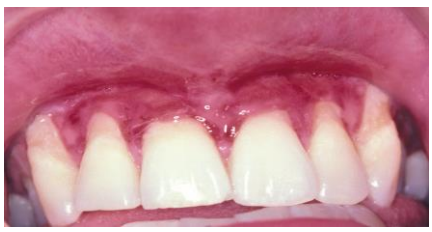
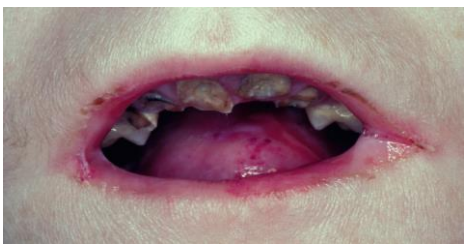
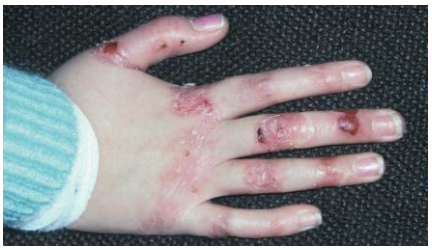
Treatment of patients with mild or localized bullous pemphigoid consists of application of one of the stronger topical corticosteroid preparations. Management of the patient with moderate-to-severe, widespread bullous pemphigoid daily doses of systemic prednisone. If the lesions do not respond to prednisone alone, then another immunosuppressive agent (such as, azathioprine, methotrexate, or mycophenolate mofetil) may be added to the regimen. Dapsone, a sulfa derivative, may be used as an alternative therapeutic agent, and tetracycline and niacinamide therapy is reported to be effective for some patients.

❖ EPIDERMOLYSIS BULLOSA

Epidermolysis bullosa is a general term that encompasses one acquired and as many as 20 genetic or hereditary varieties (dystrophic,junctional, simplex) of diseases that basically are characterized by the formation of blisters at sites of minor trauma.

Clinical features: The initial lesions in all subtypes of epidermolysis bullosa are vesicles or bullae, which are seen early in life and develop on areas exposed to low-grade, chronic trauma, such as the knuckles or knees . The bullae rupture, resulting in erosions or ulcerations that ultimately heal with scarring. In the process, appendages such as fingernails may be lost.

The oral manifestations are typically mild in Dominant Dystrophic Types , with some gingival erythema and tenderness. Gingival recession and reduction in the depth of the buccal vestibule may be observed . In Recessive Dystrophic the oral problems are no less severe. Bulla and vesicle formation is induced by virtually any food having some degree of texture. Even with a soft diet, the repeated cycles of scarring often result in microstomia .

Treatment :

Treatment of epidermolysis bullosa varies with the type. For milder cases, no treatment just avoidance of trauma . Sterile drainage of larger blisters and the use of topical antibiotics are often indicated in these situations.For the more severe cases, intensive management with oral antibiotics may be necessary if cellulitis develops .Treatment also include supportive measures and chemotherapeutic agents, corticosteroids ,vitamin E phenytoin and immunosuppressive agents.

Oral pathology

Vesiculobullous Lesions

Several conditions discussed in this lecture are the result of inappropriate production of antibodies by the patient (autoantibodies).

These autoantibodies are directed against various constituents of the molecular apparatus that hold epithelial cells together or that bind the surface epithelium to the underlying connective tissue. The ensuing damage produced by the interaction of these autoantibodies with the host tissue is seen clinically as a disease process, often termed an immunobullous disease. Because each disease is characterized by production of specific types of autoantibodies, identification of the antibodies and the tissues against which they are targeted is important diagnostically. The two techniques that are widely used to investigate the immunobullous diseases are

1- Direct immunofluorescence

2- Indirect immunofluorescence studies.

❖Pemphigus

The condition known as pemphigus represents four related diseases of an autoimmune origin:

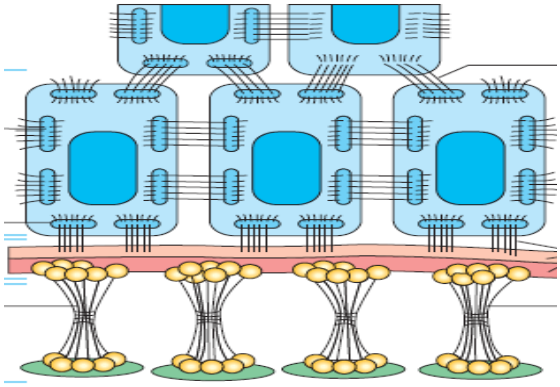
1. Pemphigus vulgaris
2. Pemphigus vegetans
3. Pemphigus erythematosus
4. Pemphigus foliaceus

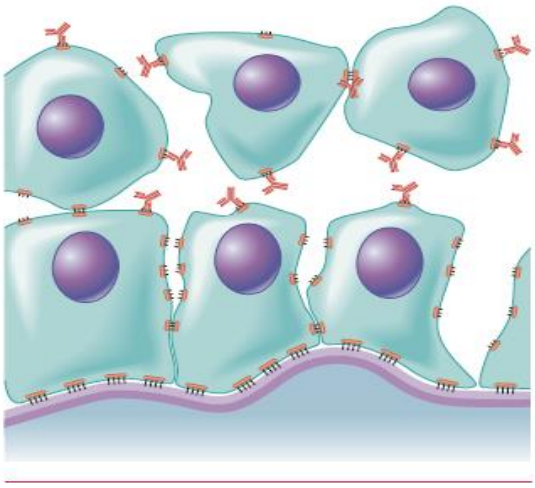
Only the first two of these affect the oral mucosa, and the discussion is limited to pemphigus vulgaris. Pemphigus vegetans is rare; most authorities now feel it represents simply a variant of pemphigus vulgaris.

Pemphigous Vulgaris

Pemphigus vulgaris (PV) are a group of mucocutaneous diseases characterized by epithelial desquamation caused by abnormal production for unknown reasons of autoantibodies that attack the desmosome of the intercellular cohesive system. The loss of adhesion occurs between the cells located in the zone above the basal cell layer and a result of this immunologic attack on the desmosomes, a split develops within the epithelium, causing a

blister (suprabasilar bullous formation) . Destruction of the adhesive factors of the suprabasila spinous cells is referred to as acantholysis.

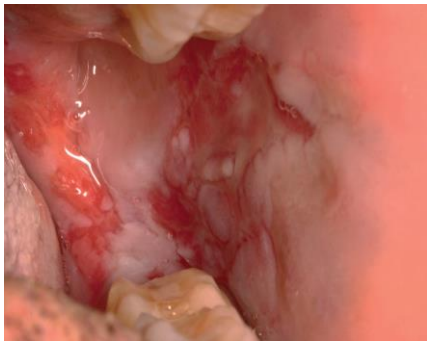
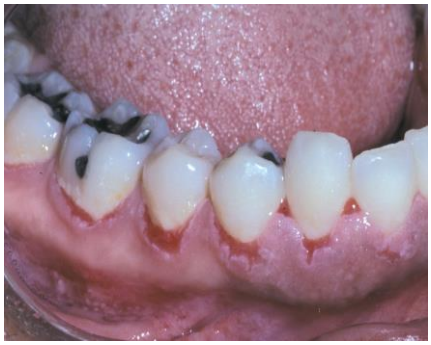
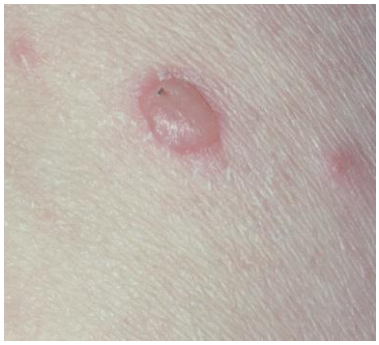


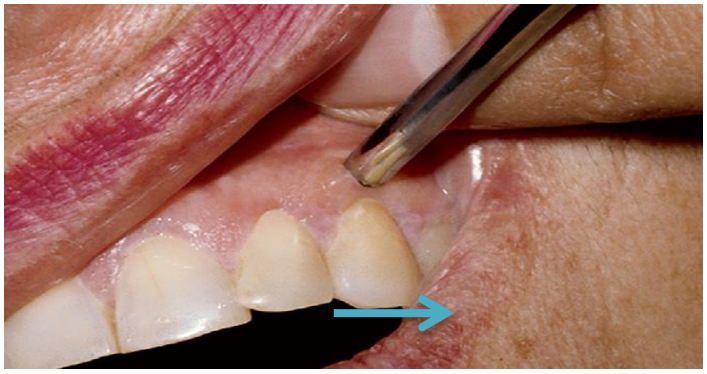


CLINICAL FEATURES:

The initial manifestations of pemphigus vulgaris often involve the oral mucosa, typically in adults. The average age at diagnosis is 50 years. The condition seems to be more common in persons of Mediterranean, South Asian, or Jewish heritage. Patients usually complain of oral soreness, and examination shows superficial, ragged erosions and ulcerations distributed haphazardly on the oral mucosa . Such lesions may affect virtually any oral mucosal location, although the palate, labial mucosa, buccal mucosa, ventral tongue, and gingivae are often involved. Patients rarely report vesicle or bulla formation intraorally, and such lesions can seldom be identified by the examining clinician,probably because of early rupture of the thin, friable roof of the blisters. More than 50% of the patients have oral mucosal lesions before the onset of cutaneous lesions, sometimes by as much as 1 year or more. Eventually, however, nearly all patients have intraoral involvement. The skin lesions appear as flaccid vesicles and bullae that rupture quickly, usually within hours to a few days, leaving an erythematous, denuded surface. Infrequently ocular involvement may be seen, usually appearing as bilateral conjunctivitis. Unlike cicatricial pemphigoid, the ocular lesions of pemphigus typically do not cause scarring and symblepharon formation .

A characteristic feature of pemphigus vulgaris is that a bulla can be induced on normal-appearing skin if firm lateral pressure is exerted. This is called a positive Nikolsky sign.



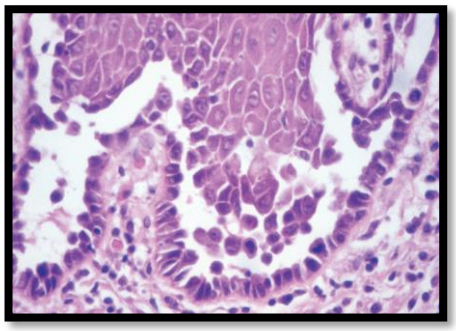
Nikolsky's sign

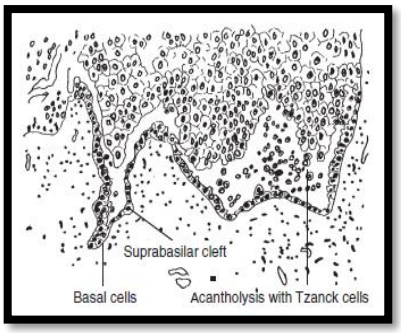
Histopathologic Features:

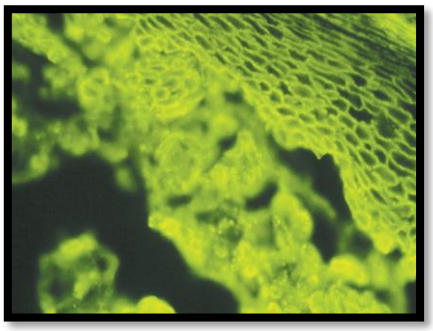
Biopsy specimens of perilesional tissue show characteristic intraepithelial separation, which occurs just above the basal cell layer of the epithelium . Sometimes the entire superficial layers of the epithelium are stripped away, leaving only the basal cells, which have been described as resembling a “row of tombstones.”

The cells of the spinous layer of the surface epithelium typically appear to fall apart, a feature that has been termed acantholysis, and the loose cells tend to assume a rounded shape . This feature of pemphigus vulgaris can be used in making a diagnosis based on the identification of these rounded cells (Tzanck cells) in an exfoliative cytologic preparation. A mild-to-moderate chronic inflammatory cell infiltrate is usually seen in the underlying connective tissue.

The diagnosis of pemphigus vulgaris should be confirmed by direct immunofluorescence examination of fresh perilesional tissue or tissue submitted in Michel’s solution. With this procedure, antibodies (usually IgG or IgM) and complement components (usually C3) can be demonstrated in the intercellular spaces between the epithelial cells in almost all patients with this disease. Indirect immunofluorescence is also typically positive in 80% to 90% of cases, demonstrating the presence of circulating autoantibodies in the patient’s serum.







Treatment:

Pemphigus is a systemic disease; therefore, treatment consists primarily of systemic corticosteroids (usually prednisone), often in combination with other immunosuppressive drugs (so-called steroid-sparing agents) such as azathioprine.

The most common approach is to use relatively high doses of systemic corticosteroids initially to clear the lesions, and then attempt to maintain the patient on as low a dose of corticosteroids as is necessary to control the condition. The use of topical corticosteroids in the management of oral lesions is also common with low dose of systemic corticosteroid .

❖ Mucous Membrane Pemphigoid (Cicatricial pemphigoid; benign mucous membrane pemphigoid)

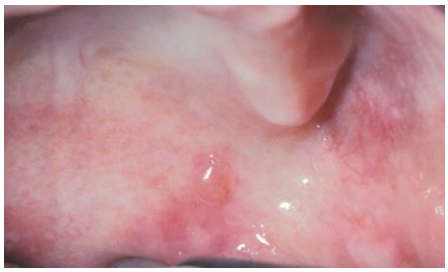
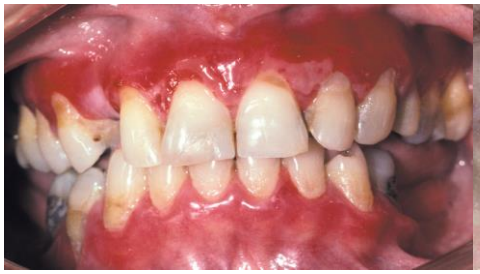
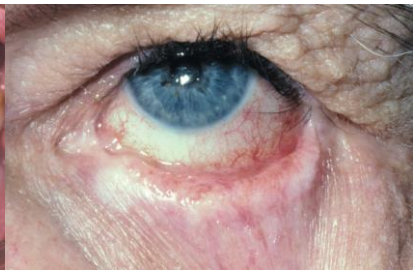
Mucous membrane pemphigoid represents a group of chronic, blistering, mucocutaneous autoimmune diseases in which tissue-bound autoantibodies are directed against one or more components of the basement membrane.

❖ Clinical Features:

Mucous membrane pemphigoid usually affects older adults, with an average age of 50 to 60 years at the onset of disease. Females are affected more frequently than males. Oral lesions are seen in most patients, but other sites, such as conjunctival, nasal, esophageal, laryngeal, and vaginal mucosa, as well as the skin may be involved.

The oral lesions of pemphigoid begin as either vesicles or bullae that may occasionally be identified clinically. In contrast, patients with pemphigus rarely display such blisters. Eventually, the oral blisters rupture, leaving large, superficial, ulcerated, and denuded areas of mucosa . The ulcerated lesions are usually painful and persist for weeks to months if untreated .Often this process is seen diffusely throughout the mouth, but it may be limited to certain areas, especially the gingiva . Gingival involvement produces a clinical reaction

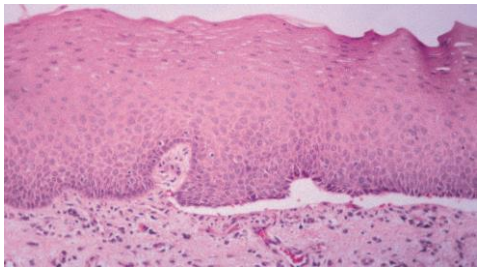
pattern termed desquamative gingivitis. The most significant complication of mucous membrane pemphigoid, however, is ocular involvement. The earliest change is subconjunctival fibrosis. As the disease progresses, the conjunctiva becomes inflamed and eroded. Attempts at healing lead to scarring . Other mucosal sites may also be involved and cause considerable difficulty for the patient.

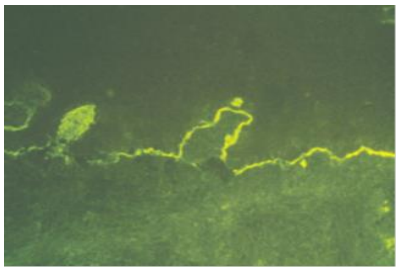




Histopathologic Features:

Biopsy of perilesional mucosa shows a split between the surface epithelium and the underlying connective tissue in the region of the basement membrane . A mild chronic inflammatory cell infiltrate is present in the superficial submucosa.

Direct immunofluorescence studies show a continuous linear band of immunoreactants at the basement membrane zone in nearly 90% of affected patients . The immune deposits consist primarily of IgG and C3 .



Treatment:

In fact, there is no single good therapy for every patient; treatment must be individualized, depending on lesional distribution, disease activity, and therapeutic response. Topical Agents use If only oral lesions are present, such as topical corticosteroids . Once control is achieved, the applications can be discontinued.

Patients with only gingival lesions often benefit from good oral hygiene measures. As an additional aid in treating gingival lesions, a flexible mouth guard may be fabricated to use as a carrier for the corticosteroid medication.

Systemic Agents used If topical corticosteroids are unsuccessful. Dapsone, can be used to treat patients with mild-to-moderate involvement by mucous membrane pemphigoid.

Another alternative systemic therapy that may be used for patients with less severe disease is tetracycline or minocycline and niacinamide (nicotinamide). Some studies have suggested that treatment with intravenous (IV) human immunoglobulin.

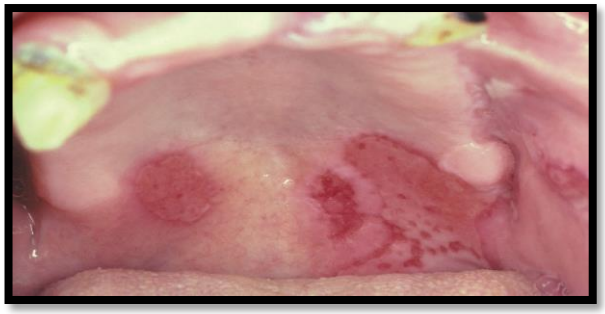
❖ BULLOUS PEMPHIGOID

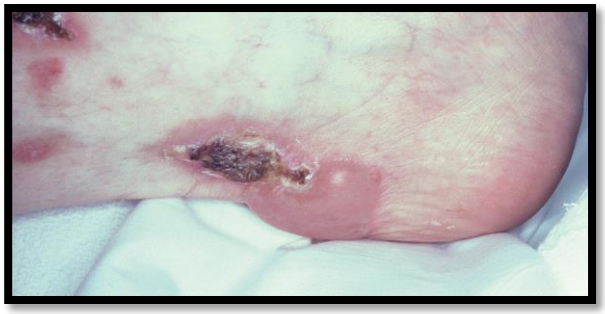
Bullous pemphigoid is the most common of the autoimmune blistering conditions. The disease is characterized by the production of autoantibodies directed against components of the basement membrane. In many respects, bullous pemphigoid resembles mucous membrane pemphigoid, but most investigators note that there are enough differences to consider these diseases as distinct but related entities. One significant difference is that the clinical course in patients with bullous pemphigoid is usually characterized by periods of remission followed by relapse, whereas the course in patients with mucous membrane pemphigoid is usually protracted and progressive.

Clinical Features:

Bullous pemphigoid typically develops in older people; most patients are between 75 and 80 years of age. No sex or racial predilection is generally reported. Pruritus is often an early symptom. This is followed by the development of multiple, tense bullae on either normal or erythematous skin . These lesions eventually rupture after several days, causing a superficial crust to form. Eventually, healing takes place without scarring.

Oral mucosal involvement is uncommon, with approximately 10% to 20% of patients being affected. The oral lesions, like the skin lesions, begin as bullae, but they tend to rupture sooner, probably as a result of the constant low grade trauma to which the oral mucosa is subjected. Large, shallow ulcerations with smooth, distinct margins are present after the bullae rupture .





Histopathologic Features:

Microscopic examination of tissue obtained from the perilesional margin of a bulla shows separation of the epithelium from the connective tissue at the basement membrane zone, resulting in a subepithelial separation. Modest numbers of both acute and chronic

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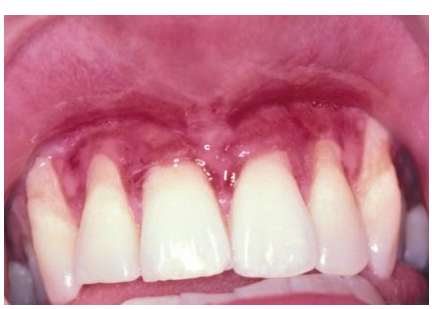
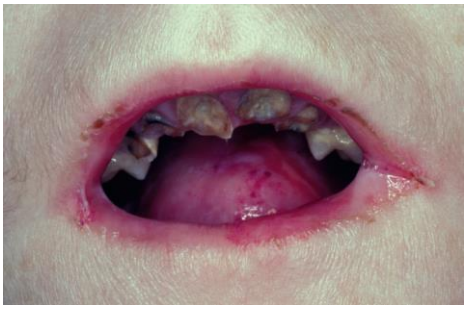
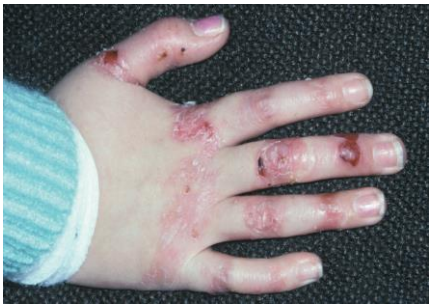

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Oral Pathology

Salivary gland lesions and tumors

Salivary glands are tubulo-acinar exocrine organs responsible for the production and secretion of saliva. They comprise the three-paired major glands, the parotid, submandibular, and sublingual. There are also several hundred minor glands, which are widely distributed throughout the oral and oropharyngeal submucosa and, in some cases, the underlying muscle.

Similar seromucous glands are present in the upper respiratory and sinonasal tracts, The functional unit of salivary glands is the secretory acinus and related ducts and myoepithelial cells. Acini may be serous, mucous, or mixed.

Normal function & health of the mouth depend on normal secretion of the saliva by the major & minor salivary glands. Failure of salivary secretion causes a dry mouth which promotes oral infections.

Both the major & minor glands are composed of parenchymal elements which are supported by C.T. The parenchyma derived from the oral epithelium consists of terminal secretary units leading into ducts that open into the oral cavity.

The C.T. forms a capsule around the gland & extends into it. The blood & lymph vessels & nerves that supply the gland are contained within the C.T.

The most important function of S.G. is the production of saliva which contains various organic & inorganic substances & help in the mastication, deglutition & digestion of food.

Mucocele (mucus extravasation phenomenon; mucus escape reaction)

The mucocele is a common lesion of the oral mucosa that results from rupture of a salivary gland duct and spillage of mucin into the surrounding soft tissues. This spillage is often the result of local trauma, although there is no known history of trauma in many cases.

Clinical Features

Mucoceles typically appear as dome-shaped mucosal swellings that can range from 1 or 2 mm to several centimeters in size . They are most common in children and young adults, perhaps because younger people are more likely to experience trauma that induces mucin spillage. However, mucoceles have been reported in patients of all ages, including infants and older adults. The spilled mucin below the mucosal surface often imparts a bluish translucent hue to the swelling, although deeper mucoceles may be normal in color. The lesion characteristically is fluctuant, but some mucoceles feel firmer to palpation. The reported duration of the lesion can vary from a few days to several years; most patients report that the lesion has been present for several weeks. Many patients relate a history of a recurrent swelling that periodically may rupture and release its fluid contents. The lower lip is by far the most common site for the mucocele.

Treatment and Prognosis

Some mucoceles are short-lived lesions that rupture and heal by themselves. Many lesions, however, are chronic in nature, and local surgical excision is necessary. The excised tissue

should be submitted for microscopic examination to confirm the diagnosis and rule out the possibility of a salivary gland tumor. The prognosis is excellent, although occasional mucoceles will recur, necessitating re-excision, especially if the feeding glands are not removed.

RANULA

Ranula is a term used for mucoceles that occur in the floor of the mouth, arising from the sublingual gland. The name is derived from the Latin word rana, which means “frog”, because the swelling may resemble a frog’s translucent underbelly.

Clinical Features

The ranula usually appears as a blue, dome-shaped, fluctuant swelling in the floor of the mouth , but deeper lesions may be normal in color. Ranulas are seen most frequently in children and young adults. They tend to be larger than mucoceles in other oral locations, often developing into large masses that fill the floor of the mouth and elevate the tongue. Like other mucoceles, ranulas may rupture and release their mucin contents, only to re-form. An unusual clinical variant, the plunging or cervical ranula, occurs when the spilled mucin dissects through the mylohyoid muscle and produces swelling within the neck.

Treatment and Prognosis

Treatment of the ranula consists of removal of the feeding sublingual gland and/or marsupialization.

Sialadenitis

Inflammation of the salivary glands **(sialadenitis)** can arise from various infectious and non-infectious causes. The most common viral infection is mumps, although a number of other viruses also can involve the salivary glands, including Coxsackie A, ECHO, choriomeningitis, parainfluenza, and cytomegalovirus (CMV) (in neonates). Most bacterial infections arise as a result of ductal obstruction or decreased salivary flow, allowing retrograde spread of bacteria throughout the ductal system. Blockage of the duct can be caused by sialolithiasis, congenital strictures, or compression by an adjacent tumor. Decreased flow can result from dehydration, debilitation, or medications that inhibit secretions.

Clinical and radiographic features

Acute bacterial sialadenitis is most common in the parotid gland and is bilateral in 10% to 25% of cases. The affected gland is swollen and painful, and the overlying skin may be warm and erythematous. An associated low-grade fever and trismus may be present. A purulent discharge often is observed from the duct orifice when the gland is massaged the main organisms involved being Streptococcus pyogenes and staphylococcus aureus, less commonly Haemophilus species. Recurrent or persistent ductal obstruction (most commonly caused by sialoliths) can lead to a chronic sialadenitis. Periodic swelling and pain occur within the affected gland, usually developing at mealtime when salivary flow is stimulated. In the submandibular gland, persistent enlargement may develop **(Küttner tumor),** which is difficult to distinguish from a true neoplasm. Sialography often demonstrates sialectasia (ductal dilatation) proximal to the area of obstruction In chronic parotitis, Stensen’s duct may

show a characteristic sialographic pattern known as "sausaging," which reflects a combination of dilatation plus ductal strictures from scar formation. Chronic sialadenitis also can occur in the minor glands, possibly as a result of blockage of ductal flow or local trauma.

Histopathologic features In patients with acute sialadenitis, accumulation of neutrophils is observed within the ductal system and acini. Chronic sialadenitis is characterized by scattered or patchy infiltration of the salivary parenchyma by lymphocytes and plasma cells. Atrophy of the acini is common, as is ductal dilatation. If associated fibrosis is present, then the term **chronic sclerosing sialadenitis** is used.

treatment and prognosis

The treatment of acute sialadenitis includes appropriate antibiotic therapy and rehydration of the patient to stimulate salivary flow. Surgical drainage may be needed if there is abscess formation. Although this regimen is usually sufficient, a 20% to 50% mortality rate has been reported in debilitated patients because of the spread of the infection and sepsis. The management of chronic sialadenitis depends on the severity of the condition and ranges from conservative therapy to surgical intervention.

MUMPS (EPIDEMIC PAROTITIS)

Mumps : Is a glandular viral disease usually affecting the parotid gland. The sub mandibualr & sub lingual gland may also be affected. Mumps is due to paramyxo virus (mumps virus), children are mainly affected, the incubation period of about 21 days, the infection start with high fever followed by a painful swelling behind the ear, the papilla of parotid (stensen's) duct may be swollen & secretion of the parotid are less so the mouth may be dry. The pain subsides but the swelling persist for 5 days &then decrease. Permanent nerve deafness & meningitis are possible complication. In adult complications of mumps may develop orchitis.

After an attack immunity is long lasting, with wide use of immunization childhood mumps is becoming infrequent & mumps in adult may take a typical form.

Treatment and prognosis

The treatment of mumps is palliative in nature. Frequently, non-aspirin
analgesics and antipyretics are administered. In an attempt to minimize orchitis, bed rest is recommended for males until the fever breaks. Avoidance of sour foods and drinks helps to decrease the salivary gland discomfort. As with measles and rubella, the best results come from prior vaccination, thereby preventing the infection.

Other causes of viral sialadenitis

1- Cytomegalic inclusion disease (salivary gland inclusion disease) Infection with cytomegalovirus, a member of herpesvirus group, is common in human and endemic worldwide. Most primary infections are asymptomatic, but the virus can cause severe disseminated disease in neonates and in immunocompromised hosts such as transplant patients and HIV infected persons
2- Postirradiation sialadenitis: Radiation sialadenitis is a common complication of radiotherapy and there is a direct correlation between the dose of radiation and the severity of the damage

3- Sarcoidosis : Sarcoidosis may affect the parotid and minor salivar gland, parotid involvement presents as a persistent, often painless, enlargement and may be associated with involvement of the lacrimal glands in Heerfordt syndrome

Salivary calculi (sialoliths)

Sialoliths are calcified structures that develop within the salivary ductal system. Researchers believe that they arise from deposition of calcium salts around a nidus of debris within the duct lumen. This debris may include inspissated mucus, bacteria, ductal epithelial cells, or foreign bodies. The cause of sialoliths is unclear, but their formation can be promoted by chronic sialadenitis and partial obstruction. Their development is not related to any systemic derangement in calcium and phosphorus metabolism.

Clinical and radiographic features

Sialoliths most often develop within the ductal system of the submandibular gland; the formation of stones within the parotid gland system is distinctly less frequent. The long, tortuous, upward path of the submandibular (Wharton's) duct and the thicker, mucoid secretions of this gland may be responsible for its greater tendency to form salivary calculi. Sialoliths also can form within the minor salivary glands, most often within the glands of the upper lip or buccal mucosa. Salivary stones can occur at almost any age, but they are most common in young and middle-aged adults. Major gland sialoliths most frequently cause episodic pain or swelling of the affected gland, especially at mealtime. The severity of the symptoms varies, depending on the degree of obstruction and the amount of resultant backpressure produced within the gland. Sialoliths typically appear as radiopaque masses on radiographic examination. However, not all stones are visible on standard radiographs (perhaps because of the degree of calcification of some lesions). They may be discovered anywhere along the length of the duct or within the gland itself Minor gland sialoliths often are asymptomatic but may produce local swelling or tenderness of the affected gland. A small radiopacity often can be demonstrated with a soft tissue radiograph.

Sjogren's syndrome:

This is a condition characterized by a triad of keratoconjuctivitis sicca (dry eye), xerostomia (dry mouth) & rheumatoid arthritis. Sjogren's syndrome is divided into:

1. Primary Sjogren's syndrome: also called sicca syndrome which consist of xerostomia & xerophthalmia.
2. secondary sjogren's syndrome: there is an associated rheumatoid arthritis or other connective tissue disease cyst (lupus erythromatosis, scleroderma)

The etiology is thought to be auto immune.

Clinical features:

1. Occur predominantly in middle-aged women.
2. Dryness of the mouth & eyes as a result of the hypo function of the salivary & lacrimal glands.

The oral mucosa is obviously dry, red, shiny & wrinkled & sticks to the fingers or mirror during examination. The tongue appears red, atrophy of the papillae & the dorsum becomes lobulated. With diminished saliva secretion the oral flora changes & candida infection are common.

Histopathology: A labial biopsy is characterized by atrophy of the acini & replacement by lymphocytes mainly T-lymphocytes.

Diagnostic aspect: Normal salivary flow is between 1&2 ml/min:

1. Diminished mixed salivary flow rate May be reduced to 0.5 ml/min or less.
2. Labial salivary gland biopsy showing periductal lymphocytic infiltrate.
3. Antibody screen especially rheumatoid factor.
4. Sialectasis on sialography (iodine-containing contrast medium)

Poor elimination of the contrast medium is noted with retention of the material for over a mouth, because of the reduced salivary flow. Snow storm appearance of blobs of contrast.

Treatment:

The treatment of patient with Sjogren's syndrome is mostly supportive.

1. Periodic use of artificial tears for the dry eye.
2. Artificial saliva for xerostomia & because of increased risk of dental caries.
3. Daily fluoride application may be indicated in edentulous patients; also antifungal therapy is often needed to treat secondary candidiasis.

Malignant lymphoma can develop in Sjogren's syndrome.

Salivary Gland Tumors

Tumors of the salivary glands constitute an important area in the field of oral and maxillofacial pathology. Although such tumors are uncommon, they are by no means rare. The annual incidence of salivary gland tumors around the world ranges from about 1.0 to 6.5 cases per 100,000 people. Although soft tissue neoplasms (e.g., hemangioma), lymphoma, and metastatic tumors can occur within the salivary glands

Pleomorphic adenoma (benign mixed tumor)

Is a benign tumor which is the commonest of all salivary gland tumors, it account for about 75% of parotid gland tumors. The origin of this tumor is thought to arise from the myoepithelial cell or duct epithelium.

Clinically: The most common site is the parotid gland, typically present as a painless size slowly reaching to several cm, there is no fixation to the deeper tissue or to the overlying skin, the skin rarely ulcerated. Pleomorphic adenoma is also the most common intraoral salivary gland tumor, its usual location is the palate, when it presents as a smooth surface swelling resemble a fibroma, the upper lip is the next common site. The lesion can occur at any age but is most common in young adults between the age of 30&50 years. There is a slight female predilection.

Histopathological features:

A pleomorphic adenoma is a circumscribed encapsulated tumor characterized by its pleomorphic or mixed appearance. The capsule may be incomplete or show infiltration by tumor cells. The lesion shows a great variation in appearance, some area show:

1. Cuboidal cells arranged in tubes or duct like structure which may contain an eosinophilic coagulum.

2. The tumor epithelial cells may be arranged in sheets or strands about these tubular structures. Sometime the cells may assume a stellate, polyhydrate or spindle form.
3. Squamous epithelial cells are relatively common & there may be keratin pearls form.
4. Loose myxoid material can be seen.
5. The hyaline, mucoid, cartilage or even bone is a common finding.

Treatment:

Is by wide excision, in the parotid gland, the tumor & the involved lobe should be removed, recurrent rate in this position is high because of difficult surgical complete removal of tumors from the parotid, where the facial nerve is present. The recurrence rate is low in skilled hands. In the submandibular gland, tumor is removed with the whole gland because of malignancy. Lesion of the minor salivary gland of the palate should be excised with the overlying mucosa, while those in the lip, soft palate & buccal mucosa treated successfully by encapsulation. The tumors are radio resistant. Recurrence may occur due to incomplete resection or incomplete encapsulation. Benign pleomorphic adenoma may undergo malignant changes either to a carcinoma, adenocarcinoma or cylindroma.

Warthins tumor: (Adenolymphoma, papillary cystadenoma lymphomatosum).

Is a benign neoplasm of the parotid gland. It accounts 9% of all parotid tumors. The pathogenesis of these tumors is uncertain, it is thought that they arise from heterotopic salivary gland tissue found within parotid lymph nodes. It has also been suggested that these tumors may develop from a proliferation of SG ductal epithelium that is associated with secondary formation of lymphoid tissue, besides these several studies demonstrated a strong association between the development of this tumor and smoking.

Clinically: This tumor present as slowly growing, painless, nodular mass of the parotid gland. It is most frequently occur in the tail of parotid near the angle of the mandible.
This tumor has a tendency to occur bilaterally but most of these bilateral tumors do not occur simultaneously but are occurring at different times, most common in man usually middle aged.

Histopathological features: The tumor is composed of a mixture of ductal epithelium & lymphoid stroma. The epithelium is oncocytic in nature, forming uniform rows of cells surrounding cystic spaces. The cells have abundant, finely granules, eosinophilic cytoplasm & are arranged in two layers. The inner terminal layer consists of tall columnar cells with centrally placed pyknotic nuclei. Beneath this, is a second layer of cuboidal or polygonal cells with more vesicular nuclei. The lining epithelium demonstrates multiple papillary projections into the cystic spaces. The epithelium is supported by a lymphoid stroma.

Treatment: Surgical removal, these tumors are well encapsulated & seldom reoccur after removal.

BASAL CELL ADENOMA

The basal cell adenoma is a benign salivary tumor that derives its name from the basaloid appearance of the tumor cells. It is an uncommon neoplasm that represents only 1% to 2% of all salivary tumors. Because of its uniform histopathologic appearance, it often has been classified as one of the monomorphic adenomas

Oncocytoma

The is a benign salivary gland tumor Surrounded by a thin capsule and consisted of large epithelial cells known as **oncocytes**. The prefix *onco-* is derived from the Greek word *onkoustai*, which means *to swell*. The swollen granular cytoplasm of oncocytes is due to excessive accumulation of mitochondria.

A canalicular adenoma

The **canalicular adenoma** is an uncommon tumor that occurs almost exclusively in the minor salivary glands. Because of its uniform microscopic pattern, the canalicular adenoma also has been called a *monomorphic adenoma*.

Malignant tumors of salivary gland

Malignant tumors of salivary gland are relatively uncommon, accounting for about 1 per cent or less of all malignancies and about 5 percent of malignant tumors in the head and neck region. Although carcinomas of salivary gland arise most frequently in major glands especially parotid gland.

Mucoepidermoid carcinoma

The **mucoepidermoid carcinoma** is one of the most common salivary gland malignancies. Because of its highly variable biologic potential, it was originally called **mucoepidermoid tumor.** The term recognized one subset that acted in a malignant fashion and a second group that appeared to behave in a benign fashion with favorable prognosis. However, researchers later recognized that even low-grade tumors occasionally could exhibit malignant behavior; therefore, the term *mucoepidermoid carcinoma* is the preferred designation.

Clinical features The tumor occurs fairly evenly over a wide age range, extending from the second to seventh decades of life. Rarely is it seen in the first decade of life, The mucoepidermoid carcinoma is most common in the parotid gland and usually appears as an asymptomatic swelling. Most patients are aware of the lesion for 1 year or less, although some report a mass of many years' duration. Pain or facial nerve palsy may develop, usually in association with high-grade tumors Minor gland tumors also typically appear as asymptomatic swellings, which are sometimes fluctuant and have a blue or red color that can be mistaken clinically for a mucocele. Although the lower lip, floor of mouth, tongue, and retromolar pad areas are uncommon locations for salivary gland neoplasia

Histopathological features : From its name the mucoepidermoid CA is composed of a mixture of mucous –producing cells and epidermoid or squamous cells . If the mucous – secreating cells are mainly predominant then the tumor tend to be cystic, if mainly epidermoid the tumor is solid and then more aggressive. There is no well-defined capsule, and is invasive and occasionally metastasise. Traditionally, mucoepidermoid carcinomas have been categorized into one of three histopathologic grades based on the following:

1. Amount of cyst formation
2. Degree of cytologic atypia
3. Relative numbers of mucous, epidermoid, and intermediate cells

Low-grade tumors show prominent cyst formation, minimal cellular atypia, and a relatively high proportion of mucous cells.

High-grade tumors consist of solid islands of squamous and intermediate cells, which can demonstrate considerable pleomorphism and mitotic activity. Mucus-producing cells may be infrequent, and the tumor sometimes can be difficult to distinguish from squamous cell carcinoma

Intermediate-grade tumors show features that fall between those of the low-grade and high-grade neoplasms. Cyst formation occurs but is less prominent than that observed in low-grade tumors. All three major cell types are present, but the intermediate cells usually predominate. Cellular atypia may or may not be observed.

Treatment: is by wide excision but the tumor may recur.

ADENOID CYSTIC CARCINOMA

The adenoid cystic carcinoma is one of the more common and best-recognized salivary malignancies. Because of its distinctive histopathological features, it was originally called a **cylindroma,** and this term still is used sometimes as a synonym for this neoplasm. However, use of the term **cylindroma** should be avoided because it does not convey the malignant nature of the tumor, and also because this same term is used for a skin adnexal tumor that has a markedly different clinical
presentation and prognosis.

Adenoid cystic carcinoma usually grows slowly but usually shows distinct infiltrative spread. The tumor cells are of two types, duct lining cells and cells of myoepithelial type. It occurs most frequently in the minor salivary gland of the palate, the parotid, submandibular and accessory gland in the tongue is also involved. The lesion is most common in middle – aged adult equal sex distribution. It present as slowly growing mass, there is early local pain, facial paralysis may develop with parotid tumors; palatal tumors can be smooth- surfaced or ulceration and may show radiographic evidence of bone destruction.

Histopathology:

1. Composed of small, deeply staining uniform cells resemble basal cells, which are commonly arranged in anastomosing cords or duct like pattern with mucoid material in the center. This produce a typical cribriform (honey comb or Swiss cheese appearance). Pattern
2. In the tubular pattern, the tumor cells are similar but occur as multiple small ducts or tubules within a hyalinized stroma.
3. The solid form consist of larger islands or sheets of tumor cells which show little tendency toward duct or cyst formation. Spread of the tumor cells along the perineural sheaths is a common feature of the disease.

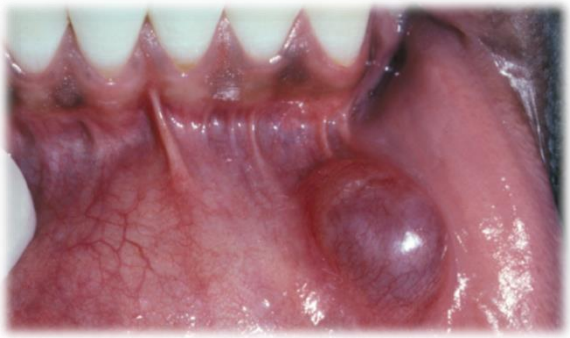
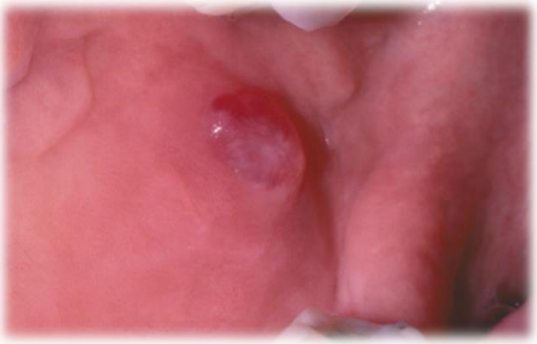
Treatment: Surgical removal with radiation. Metastasis occurs late in the course of the disease.

Carcinoma in pleomorphic adenoma (Malignant pleomorphic adenoma)

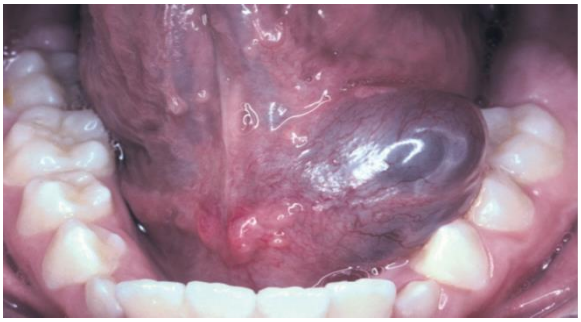
Pleomorphic adenoma can undergo malignant change; this is seen in a slowly growing lesion which rapidly starts to increase in size, or sudden development of pain or facial palsy. The diagnosis require evidences evidence of a pre-existing pleomorphic adenoma

Histologically:

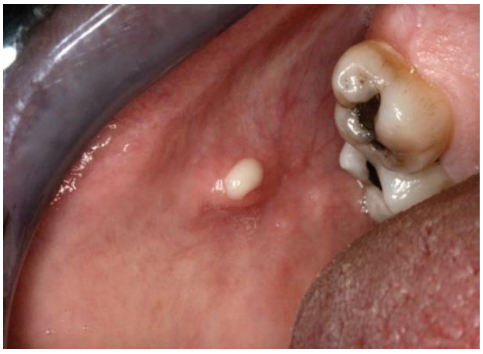
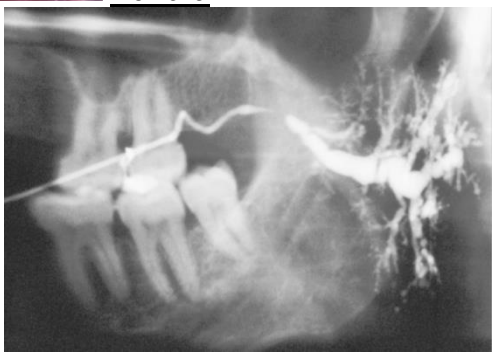
There may be only a few foci of malignant change or the lesion may be entirely malignant. The malignant transformation is either into:
1. Epidermoid carcinoma.
2. Adenocarcinoma.
3. Sometime into both types.
The treatment is by surgery, although the lesion shows a high tendency to reoccur as well as a high incidence of regional lymph node involvement & some time distant metastasis CT carcinoma)
The **polymorphous low-grade adenocarcinoma** is a more recently recognized type of salivary malignancy that was first described in 1983. Before its identification as a distinct entity, examples of this tumor were categorized as pleomorphic adenoma, an unspecified form of adenocarcinoma, or sometimes as adenoid cystic carcinoma. Once recognized as a specific entity, however, it was realized that this tumor possesses distinct clinicopathologic features and is one of the more common minor salivary gland malignancies.

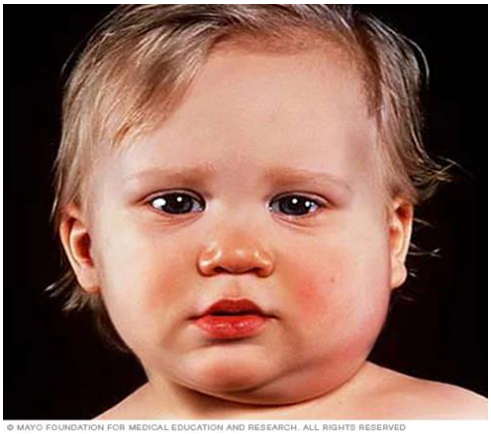
Mucocele



Ranula

Sialadenitis



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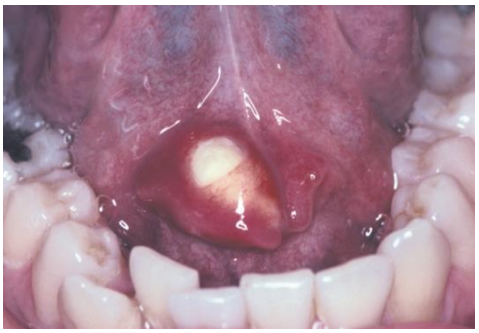
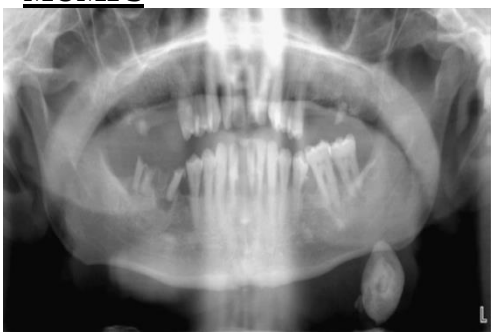
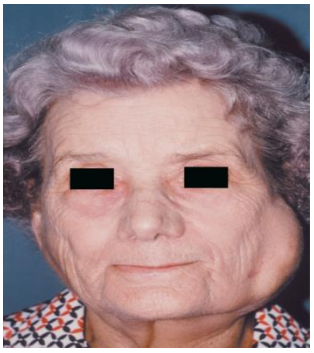
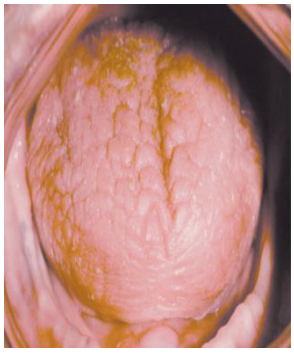
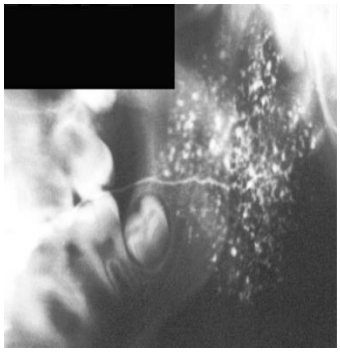
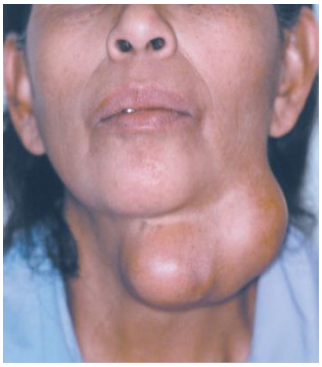
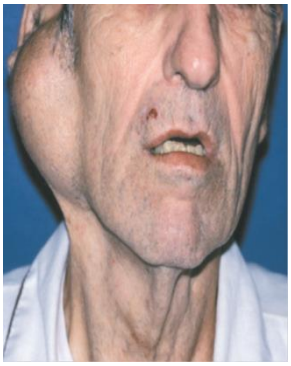
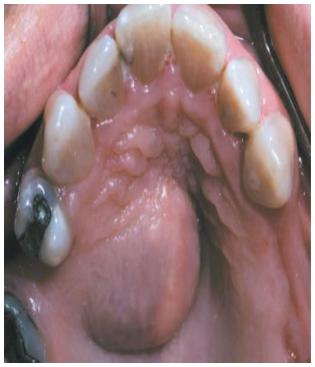



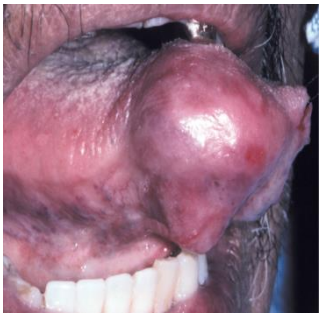
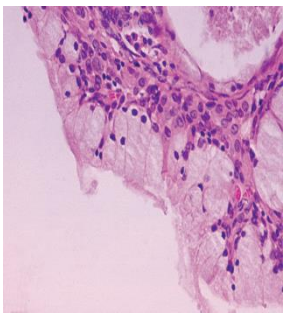
sialoliths

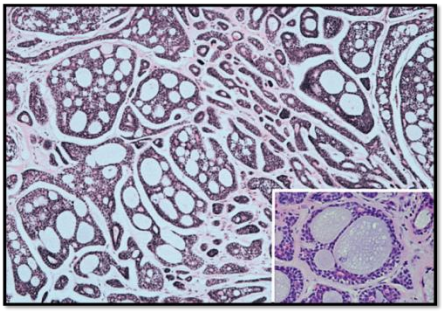
Sjogren's syndrome

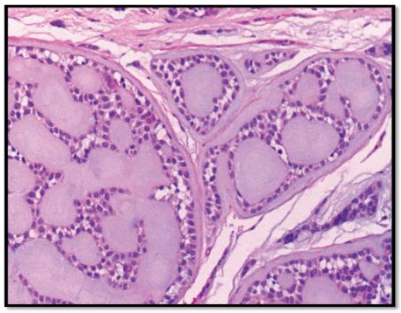




Pleomorphic adenoma

Mucoepidermoid carcinoma





ADENOID CYSTIC CARCINOMA