Oral Pathology/4th level

Introduction

Biopsy(Principles and techniques)

Lecture1 Refrences

1- Oral and Maxillofacial Pathology, Brad W. Neville, 3rd edition 2009

2- Contemporary Oral and Maxillofacial Pathology, G. Philip Sapp, 2nd edition 2004

3- Regzi oral pathology Joseph A. Regzi. Et al 5th edition 2008

4- Ackerman Rosai and Ackerman's Surgical Pathology,10th edition 2011

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 and its indication :-

- **1- Incisional** biopsies, only a portion of the lesion are sampled, and.made for large lesion particularly those of deep soft tissues, 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 made for small lesion and therefore the procedure serves both a diagnostic and a therapeutic function.

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

- **Cone biopsy** *** Punch biopsy**
- **Core needle biopsy** *** Surface biopsy**
- **Vaccum assisted biops** *** Endoscopic biopsy**
- **Cautery biopsy**

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

2-Endoscope an endoscope is used to take a tissue sample, such as from the stomach during a gastroscopy (a diagnostic procedure of the stomach or upper gastrointestinal tract)

3-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.

4-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.

6-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

7-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.

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

9-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).

Some 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 render a biopsy impossible to interpret.

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 and avoid mutilation of the tissues when grasping with forceps.
4- Remove a border of normal tissue if possible
5- Fix immediately with 10% buffered formalin or 70% alcohol
6- Put a land marks on tissue to indicate direction (e.g. sutures)
7- 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
- Inflammatory changes of unknown cause that persist for long peroids
- 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 un ulcer
- 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

Diagnostic cytology

Diagnostic cytology, when performed by well-trained, experienced individuals, offers an extremely high degree of reliability. A positive cytologic 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) 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.

Abrasive cytology

1. Abrasive cytology – cell or specimen that obtained from superficial scraping of lesion cervical scraping pap smear ,buccal mucosal smear ,skin scraping for various lesion .

2. Exfoliative cytology is a branch of cytology in which the cells that a pathologist examines are either "shed" by your body naturally or are manually scraped or brushed (exfoliated) from the surface of your tissue

Laboratory techniques

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 immunohistochemical techniques, as long as the tissue is placed in fixative shortly (<30 min) after surgical removal, and overfixation (>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 is very poor

Carnoy fixative is a mixture of ethanol, chloroform, and glacial acetic acid. Thus at the same time that it fixes the tissues, it dissolves most of the fat. This property has been found useful for the identification of lymph nodes in radical resection specimens

70% ethanol which – in contrast to formalin – is a noncross-linking agent and brings very little chemical change to the DNA except for a reversible collapseAnother proposed fixative is *methacarn,* which is a Carnoy solution in which methanol is used in place of ethanol

2-Laboratory tissue processing
This reffer to any treatment of tissues necessary to impregnate them with a solid medium to facillitae the producton 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 processign
6-microtomy-is the sectioning of tissue blocks by microtome
7-staining either by ordinary stains (hematoxylin and eosin) or special stains

Special stains

. 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 and that it is also useful for the demonstration of the intracytoplasmic crystals in alveolar soft part sarcoma.

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

Immunohistochemistry (IHC) combines anatomical, immunological and biochemical techniques to image discrete components in tissues by using appropriately-labeled antibodies to bind specifically to their target antigens in situ. IHC makes it possible to visualize and document the high-resolution distribution and localization of specific cellular components within cells and within their proper histological context.

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 (Q BEND 10). This marker stains normal and neoplastic endothelial cells, as well as a variety of soft tissue neoplasms, including dermatofibrosarcoma protuberans, solitary fibrous tumor

Epidermal growth factor receptor (EGFR). This is a tyrosine kinase anchored on the cell membrane, thought to be important for tumor progression. It is present in various types of epithelial tumor, notably breast carcinoma

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.

Bone Neoplasms
benign and malignant tumor of the bone

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. According to the type of differentiation of the tumor cells

No.	Tumor origin	Benign	Malignant
1	**Primary bone tumors**		
	a-of bone origin	**Osteoma** **Osteoid osteoma**	**Osteosarcoma**
	b-of chondroid origin	**Chondroma**	**Chondrosarcoma**
	c-of marrow origin		**Ewings sarcoma** **Lymphoma** **Multiple myeloma** **Leukemia**
	d-of 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. The incidence varies, ranging from 0.0029 % to 3 %, the true incidence is unknown.

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 endosteal osteomas 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 obstruction, a painful or painless mass, exophthalmus, focal facial asymmetry, difficulty in mouth opening, meningitis, and hearing loss.

Radiologically, 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.

Pathologic 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. Because of the variable degree of penetrance, only one of the extracolonic manifestations may be present such as fibromatosis. 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 prevalence is variable from 1:8300 to 1:16000 live births. 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 pin is the most prominent symptom, this is often sharply localized and accompanied by clinical or lab. Evidence of infection.

Oseoid 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 larger 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. 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.

Treatment

Complete en block 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.

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 bodyramus 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. Radiographically, 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 intrabony hemangiomas 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 multilocular hemangioma of bone includes ameloblastoma, odontogenic myxoma, odontogenic keratocyst, 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.

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 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 and Radiographic 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, 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. From the origin the tumor may:

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 for bone (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 spindle-shaped 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

Cartilage Forming Tumors

Chondroma

Chondromas are benign tumors composed of mature hyaline cartilage. It is one of the more common bone tumors and is located most often in the short tubular bones of the hand and feet. A diagnosis of chondroma in the jaw, facial bones, and the base of the skull should be viewed with great skepticism, because many of these are actually low-grade chondrosarcoma.

Clinically:

usually arise in the 3rd to 4th decade of life. Mostly seen in the condyle or anterior maxilla of adult patient. They are painless slow growing lesions.

Radiographically:

chondroma appears radiolucent with central radio-opacity.

Histologically

Chondroma appears as a circumscribed mass of mature hyaline cartilage, with well formed lacunae containing small chondrocytes with pale cytoplasm and small round nuclei.

Treatment and Prognosis

It is wise to consider any lesion diagnosed as chondroma of the jaw to represent a potential chondrosarcoma and treated with radical resection.

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 and Radiographic 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.

<u>Radiographically,</u> 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 oro-antral 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. 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 and Radiographic 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.

Plasmacytoma

Is a unifocal, monoclonal, neoplastic proliferation of plasma cells that usually arises within bone, although extramedullary type is present.

Clinical and Radiographic Features

Affects adult males with average age at diagnosis of 55 years. Most of the lesions are central within a bone. The spine is the most common site.

The presenting features are pain and swelling although some cases are asymptomatic.

X-Ray ► well defined unilocular radiolucency.

Histopathology

The same as MM.

Differentiation from MM.

All the findings mentioned in the diagnosis of MM. are negative in Plasmacytoma.

Treatment

Radiation or surgery, It may evolve to MM. in 30 to 50% of cases.

Langerhans Cell Histiocytosis

The old term Histiocytosis-X was introduced to describe a spectrum of disorders which characterized by proliferation of histiocyte-like cells, that are accompanied by varying numbers of eosinophils, lymphocytes, plasma cells, and multinucleated giant cells. The neoplastic cells are the Langerhns cell, which are dendritic mononuclear cells normally found in the epidermis, mucosa, lymph nodes, and bone marrow.

Clinical and Radiographic Findings

1. Monostotic or polyostotic epsinophilic granuloma of bone without visceral involvement.
2. Chronic disseminated histiocytosis- disease involving bone, skin, and viscera ► Hand-scűler-christian disease.
3. Acute disseminated histiocytosis, prominent cutaneous, visceral, and bone marrow involvement ► Letterer-Siwe disease.

The lesion may affect any bone, but skull, ribs, vertebrae, and mandible are mostly affected.

50% of patients are under the age of 10 years.the jaws are affected in 10-20% of all cases, with dull pain and tenderness.

Radiographically, punched out radiolucent lesions.

- Mandibular bone involvement ► posterior region, ► destruction of alveolar bone ► scooped appearance.
- bone destruction and loosening of teeth ► floating in air appearance.

Histopathology

Diffuse infiltration of large pale-staining mononuclear cells that resemble histiocytes. The cells have indistinct cytoplasmic borders with rounded or indented vesicular nuclei. Varying numbers of eosinophils are seen.

Treatment

Maxillary and mandibular lesions ► curettage.

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.

Oral Pathology

Connective tissue neoplasms and allied conditions

► 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- Solitary fibrous tumor.

2- Myxoma.

3- Nasopharyngeal angiofibroma.

4- Giant cell fibroma.

5- Myofibroblastic tumors.

6- Fibromatosis.

7- 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 (Gingiva):-

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) **Fibroma (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. Unlike the traumatic fibroma, it is not associated with trauma. Its asymptomatic sessile or pedunculated with papillary surface. Gingiva affected in 50% , Tongue and palate are also can be involved (non traumatized sites). 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

No gender or racial predilection for the development of this intraoral lesion. 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 ill-fitting 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. The cause of their proliferation is unknown. 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 ill-defined.

Treatment

Wide surgical excision, with high recurrence rate.

3-Fibrohistiocytic tumors

The original concept of these tumors is that some show dual population of fibroblasts and histiocytes (macrophages). Now it's known that this concept is incorrect and that the tumors show no histocytic differentiation and are of fibroblastic origin.

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:-

Pyogenic granuloma, vascular lesions, Kaposi's sarcoma and angiosarcoma

↓

↓

Hemanigoma ↔ Vascular malformation

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. Admixed inflammatory 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.

► Vascular lesions:-

- **Pyogenic granuloma.**
- **Intravascular lesions**

Congenital hemangioma & congenital vascular malformations.

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 seperate one from another:-

	Criteria	Congenita hemangioma	Vascular malformation
1	Description	Benign congenital neoplasms of proliferating 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 bone	Poorly circumscribed, may affects bone
5	Thrill & bruit	No associated thrill or bruit	Maybe produced
6	Involution	Spontaneously involutes	Does not
7	Resection	Persistent lesion resection	Difficult to be resect
8	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.

► 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	Schwann cells	Schwann cells and perineural fibroblasts
2	Site	Any, especially tongue	Any, especially tongue, buccal mucosa or bone
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 de novo.

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

↕ ↕

Children Adults

◊ Embryonal type consists of primitive round cells, spindle cells. Botryoid types

◊ Alveolar variant consists of round cells, but in compartments.

◊ Pleomorphic type consists of sharp or spindle cells. When it occurs in the head and neck region, Rhabdomyosarcoma is mainly found in children outside the head and neck, it is mainly found in adults.

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 differntiated

● 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.

ORAL pathology

Lec :2

Dental Caries

Dental caries :-

Its bacterial disease of a calcified tissue of the teeth, which characterized by demineralization of the inorganic and destruction of the organic substance of the tooth.

So the loss of tooth substance due to :-

a- **Bacterial** cause which result with dental caries

b-**Non bacterial** cause : there are 3 types which are:-

1-**Mechanical** cause like, abrasion and attrition.

2-**Chemical** cause like, erosion.

3-**Pathological** cause like, resorption

-**Abrasion** :- wearing of the teeth particularly at gingival 1/3 by incorrect brushing. Characteristically appear as cervical notches.

-**Attrition:**-wearing of tooth surface by the action of opposing teeth [on occlusal surface].

*Usually small amount of attrition [mild attrition] seen with progressing of age.

*Accelerated wear result when it combined with a bruxism and certain diet.

-**Erosion** :-loss of tooth substance due to repeated application of acid lead to softening of enamel.

Dental caries is a common disease in human and major cause of tooth loss.

*Interaction of 4 factors lead to dental caries development:-

1-Tooth (host)

2-Diet (food)

3-Microorganism (bacterial flora) cariogenic or acidogenic bacteria.

*mostly the cariogenic bacteria is streptococcus mutans (responsible for initiation of dental caries) and lactobacilli (responsible for progression)

4-Time

Diet with presence of Bacterial flora will produces acid which may act on tooth surface with time result in production of dental caries.

So dental caries controlled by controlling these 4 factors:-

1-Host :-by using :-

a-**systemic application** of fluoride (in water) and **topical application** of fluoride.

*fluoride displace the Ca^{+} and convert the hydroxyapatite to fluoroapitite which will increase enamel strength.

b-**Fissure sealant** [in children], like a composite apply in the groove of tooth and decrease the dental caries by 60-70%.

* impaction of food debris in pits and fissure with presence of bacteria lead to production of acid which result with dental caries.

c-**Well contour filling** [no leakage, no rough margins to prevent food stagnation]

2-Microorganism :-It's action removed by :-

a- Active and passive immunization.

b- Reduce sugar intake.

3-Diet :-

a- caries prevalence increase with sucrose rich diet.

-frequency of sugar intake more important than the amount consumed.

-Extrinsic sugar more damaging than intrinsic sugar.

*Sucrose is easily fermented by bacteria and converted to extra cellular substance called **glucan** act as glucose [adhere M.O to the tooth surface]

4-Tim:-

Frequent sugar intake with stopping brushing (for 12 hours) lead to formation dental plaque which resulted in dental caries production.

Etiological variables for dental caries development:-

Indirect factors:-

A-Factors **intrinsic to tooth** :-regarding its:-

1-Enamel composition :-an inverse relationship between enamel solubility and enamel fluoride concentration.

2-Tooth morphology :- deep narrow pits and fissures lead to retention of food and plaque.

3-Tooth position :-mal posed (=mal aligned) tooth lead to retention of food and plaque.

B-Factors **extrinsic to tooth**:-

1-Saliva:- regarding it's:-

a- composition :- inorganic constituent beneficial for mineralization .

b-pH :- higher pH less action of bacteria

c-Quantity :- (= flow rate) the more flow lead to best washing action for plaque removal

d-Viscosity :- more watery, the best for plaque removal.

e-Salivary antibacterial agent (immunoglobulin IgA):- prevent bacterial proliferation lead to decrease occurrence of dental caries.

2-Diet :regarding it's :-

a-quantity of diet

b-state of diet (=soft, sticky, cellulose)

C-Systemic factors:-

a-Hereditary

b-Pregnancy [poor oral hygiene, vomiting, changing the dietary habits]

c-Certain systemic diseases ex:-diabetes mellitus is a modified factor (cofactor for dental caries development).

Tooth composed of :-

1-Pulp:- fibrous C.T, B.V, lymphatic's and nerve (soft tissue)

2-Dentin :- hard tissue forming bulk of tooth structure.

30% organic, 70% inorganic

a-Dentinal tubules (inside it odontoblast process)

b-Intratubular substance.

3-Enamel :-hard tissue (protection to crown)

4%organic, 96%inorganic

a-Enamel rods (prism)

b-Rod sheath, interprismatic substance.

4-Cementum :- hard tissue (protection to the root)

50-55% organic , 40-45% inorganic .

Two way to examine dental caries under Microscope:-

-Ground section :studying enamel [=inorganic part]

-Decalcified section :pulp and other structure [=organic part]

Etiology of dental caries :-

The **theories** explaining development of dental caries are :-

1/Acidogenic theory (Miller's theory 1890)

The more accepted and supported one.(supported by experiments)

Dental caries developed in 2 phases :-

1- **1st phase** decalcification of enamel and dentin

Microflora attack the **inorganic structure** where decalcification of enamel and dentin is carried out by acid produced as a result of fermented sugar accumulating in the retaining spots on the tooth surface.

2- **2nd phase :-** dissolution or disintegration of **soft organic part** is carried out.

microflora act on inorganic substance produces acid which lead to organic dissolution.

2/Proteolytic theory :-

microflora act on organic sub. produces acid which Lead to inorganic decalcification dissolution.

Microorganisms attack the organic portion of enamel and generate acid responsible for further decalcification of inorganic part, the bacteria penetrate into enamel through enamel lamella and interprismatic substance.

3/Proteolysis- chelation theory :-

Organic part of enamel attacked, M.O. forming **chelation agent** which remove calcium from enamel and dentin [decalcification].

*The last 2 theories disregarded because they are not supported by experiments.

Clinical aspects of dental caries :-

dental caries classified as

1-location of lesion (=site of attack)

2-Rate of attack

A-Classification by site of attack:-

1-Pits and fissure caries :-

-occlusal surface of molars and premolars, lingual surface and buccal surface of molars and lingual surface of maxillary incisors gingival pit).

-Early caries appear as brown or black discoloration of fissure in which probe stick.

-Enamel may appear opaque, bluish-white which undermined by caries (=strengthening of enamel by fluorapatite formation).

2-Smooth surface caries:-

Occur on the proximal surface and gingival third of buccal and lingual surface occur below contact point, as well-demarcated chalky white opacity without continuity loss, not detected by a probe or on radiograph (initial lesion).

In progressive lesion, detected by probe, and on radiograph as a radiolucent area.

3-cervical caries

appear as proximal one, but with a wide open cavity.

4-Cemental caries :-

occur due to root exposed as a result of periodontal disease (=gum recession).

Appear as a shallow, saucer-shaped with ill defined boundaries.

5-Recurrent caries :-

occurs around margins , or at base of an existing restoration.

B-Classification by rate of attack :-

1-Rampant (acute) caries:-

Rapidly progressing caries affecting many teeth (primary and /or permanent, bottle feeding).

An early pulpal involvement (no pulpo-dentinal complex formation because there's no time for development of reparative dentin).

2-Slowy progressing (chronic) caries :- slowly progressing

- Later pulpal involvement - common in adult
- Pulp-dentinal complex develop.

3-Arrested caries :-

-occurs in self- cleansing area (remineralization of dentin by fluoride in saliva)

-Caries become static, no tendency for progression.

ORAL PATHOLOGY

DEVELOPMENTAL DEFECTS OF THE ORAL AND MAXILLOFACIAL REGION

1- DEVELOPMENTAL DISORDERS OF TEETH.
2- DEVELOPMENTAL DEFECT OF THE ORAL MUCOSA.
3- DEVELOPMENTAL DEFECT OF THE TONGUE.
4- DEVELOPMENTAL DEFECT OF THE LIPS AND PALATE.
5- DEVELOPMENTAL DEFECT OF THE JAW BONES.
6- DEVELOPMENTAL CYST.

1- Developmental Disorders 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.

Developmental Alterations of Teeth

1- Developmental alteration in the *size* of teeth.
2- Developmental alteration in the *number* of teeth.
3- Developmental alteration in the *shape* of teeth.
4- Developmental alteration in the *eruption* of teeth.
5- Developmental alteration in the *structure* of teeth.

1- Alteration in size of teeth

Microdontia

Generalized microdontia: all teeth in the dentition appear smaller than normal, as in ***pituitary dwarfism***, or they may be relatively small in comparison with a large mandible and maxilla.

Focal or localized microdontia: a single tooth is smaller than normal. The shape of these microdonts is also 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, **(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**.

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 condition results in crowding of teeth and possibly an abnormal eruption pattern because of insufficient arch space.

Focal, or localized, macrodontia: is characterized by an abnormally large tooth or group of teeth. This relatively uncommon condition is usually 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.

2- Abnormalities in number of teeth

A -Anodontia

B - Hypodontia

C -Additional teeth (hyperdontia)

Anodontia

Total lack of tooth development, total failure of development of a complete dentition **(anodontia)** is rare. If the permanent dentition fails to form, the deciduous dentition is retained for many years, but when these deciduous teeth become too much damaged by caries then they must be replaced by dentures or implants.

pseudoanodontia, when teeth are absent clinically because of impaction or delayed eruption; or as *false anodontia*, when teeth have been exfoliated or extracted.

Anodontia associated with systemic defects: Hereditary ectodermal dysplasia

In severe cases no teeth form. More often, most of the deciduous teeth form but there are few or no permanent teeth. The teeth are usually peg-shaped or conical. When there is anodontia, the alveolar process fails to develop and has too little bone to support implants because of lack of teeth support.

The profile of such patients then resembles that of an elderly person because of the gross **loss of vertical dimension**. The hair is fine and sparse. The skin is smooth, shiny and dry due to absence of sweat glands. Heat is therefore poorly tolerated. The finger nails are usually also defective.

To improve the patient's appearance and mastication fitting dentures is required, which are usually well tolerated by children.

Hypodontia

Failure of development of **one or two teeth** is relatively common and often hereditary. The teeth most frequently missing are **third molars, second premolars, or maxillary second incisors.**

Absence of these teeth may have little or no noticeable effect except,

1-Absence of third molars can be a disadvantage if first or second molars, or both, have been lost.

2- The absence of lower premolars worsens malocclusion if there is already disparity between an under developed mandible and a normal upper arch.

Other conditions associated with hypodontia:

There are many rare syndromes where hypodontia is a feature, but the only common one is **Down's syndrome.** One or more third molars are absent in over 90% of these patients. Absence of individual teeth scattered about the arch is also common.

Hyperdontia (Additional teeth)

Additional teeth are relatively common. They are usually of simple conical shape **(supernumerary teeth)** but less frequently resemble teeth of the normal series **(supplemental teeth).** These are the results of excessive but organized growth of the dental lamina of unknown cause.

Supernumerary teeth: Conical or malformed additional teeth, most frequently form in the **incisor or molar region** and very occasionally, in the **midline (mesiodens).**

Supplemental teeth:. Occasionally an additional **maxillary incisor, premolar** or, rarely, a **fourth molar** develops.

Effects and treatment:

Additional teeth usually erupt in abnormal positions, labial or buccal to the arch, creating stagnation areas and increasing susceptibility to caries. A supernumerary tooth may prevent a normal tooth from erupting. These additional teeth should usually be extracted.

Syndromes associated with hyperdontia:

The best known are Gardner’s syndrome and cleidocranial dysplasia where many additional teeth develop but fail to erupt.

Natal and neonatal teeth

Natal teeth: Erupted deciduous teeth present at birth.
Neonatal teeth: Deciduous teeth that erupt during the first 30 days of life. This is an artificial distinction, and it appears appropriate to call all of these teeth **natal teeth**, most are representing *premature portions of deciduous dentition.*

TREATMENT

If the teeth are mobile and at risk for aspiration, then removal is indicated. If mobility is not a problem and the teeth are stable, then they should be retained.

3- Developmental alteration in the shape of teeth

Gemination

It is the fusion of two teeth from a **single enamel organ.** The typical result is the appearance of two crowns that share the same root canal. Twinning occasionally occurs, resulting in two teeth from one tooth germ. The cause of gemination is unknown, but trauma has been suggested as a possible cause.

These teeth may be cosmetically unacceptable and may cause crowding.

Fusion

It 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. The cause of this condition is unknown, although trauma has been suggested.

Gemination and Fusion appear similar and may be differentiated by assessing the number of teeth in the dentition.

Concrescence

It is a form of fusion in which the adjacent, already-formed teeth are joined by cementum. This may take place before or after eruption of teeth and is believed to be related to trauma or overcrowding. Concrescence is most commonly seen in **maxillary second and third molars.** This condition is of no significance, unless if one of the teeth involved requires extraction, surgical sectioning may be required to save the other tooth

Dilaceration

It is an *extraordinary curving or angulations of tooth roots.* The cause of this condition has been related to trauma during root development. Hereditary factors are believed to be involved in a small number of cases. Eruption generally continues without problems. However, extraction may be difficult, in addition, if root canal fillings are required in these teeth, the procedure is challenging.

Dens Invaginatus

Also known as ***Dens in Dente*** or ***tooth within a tooth***. It is an uncommon tooth anomaly that *represents an 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. 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.

Dens Evaginatus

It is a relatively common developmental condition affecting predominantly **premolar teeth.**

The defect, which is often bilateral, *is a cusp, located in 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.

Taurodontism

It 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. Taurodontism may be seen as an isolated incident, in families, and in association with syndromes such as Down syndrome and Klinefelter's syndrome. Diagnosis is made from radiographic appearance. **No** treatment is required.

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.

Enamel Pearls

*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 are mandibular molars.

This developmental disturbance of enamel formation may be detected on radiographic examination. It is generally 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.

Accessory cusps

The cuspal morphology of teeth exhibits minor variations among different populations; of these:

(1) Cusp of Carabelli.
(2) Talon cusp.

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

Clinical and Radiographic Features

1-The cusp of Carabelli is an accessory cusp located on the palatal surface of the mesiolingual 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. The cusp is most pronounced on the first molar.

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.

4- Disorders of eruption

Eruption of deciduous teeth starts at about 6 months, usually with the appearance of the lower incisors, and is completed by about 2 years. Mass failure of eruption is very rare. More often eruption of a single tooth is prevented by local obstruction.

Local factors affecting eruption of deciduous teeth

Deciduous teeth usually erupt unobstructed. Occasionally an *eruption cyst* may overlie a tooth but is unlikely to block eruption.

Local factors affecting eruption of permanent teeth

A permanent tooth may be prevented from erupting or misplaced by various causes:

1- Loss of space (too early loss of a deciduous predecessor tends to cause irregularities because movement of adjacent teeth closes the available space)
2- Abnormal position of the crypt
3- Overcrowding
4- Supernumerary and supplemental teeth
5- Displacement in a dentigerous cyst
6- Retention of a deciduous predecessor

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.

Delayed eruption associated with skeletal disorders

1- Cleidocranial dysplasia, in which there are typically many additional teeth but most of them fails to erupt.
2- Severe hereditary gingival fibromatosis, eruption may apparently fail merely because the teeth are buried in the excessive fibrous gingival tissue and only their tips show in the mouth **(pseudoanodontia).**
3-Cherubism: several teeth may be displaced by the proliferating connective tissue masses that containing giant cells and are prevented from erupting.

Treatment depends on the circumstances, but room may be made for the unerupted tooth by orthodontic means or extractions.
A retained deciduous tooth should be extracted if radiographs show a normal permanent successor. If a buried tooth partially erupts and becomes infected, it may have to be removed.

5- Defects of tooth structure

Hypoplasia And Hypocalcification

They are represented by minor structural defects of the teeth, such as pitting or discolouration. Hypoplasia of the teeth is not an important cause of dental caries; indeed, hypoplasia due to fluorosis is associated with enhanced caries resistance. The main clinical requirement is usually cosmetic improvement.

Defects of deciduous teeth:

Calcification of deciduous teeth begins about the fourth month of intrauterine life. Disturbances of metabolism or infections that affect the fetus at this early stage without causing abortion are rare. Defective structure of the deciduous teeth is therefore uncommon, but in a few places such as parts of India, where the fluoride content of the water is excessively high, the deciduous teeth may be mottled.

Defects of permanent teeth:

Single permanent teeth may be malformed as a result of local causes such as periapical infection of a predecessor (Turner teeth) or multiple teeth by systemic diseases as:

*Genetic:

1- Amelogenesis imperfecta
A- Hypoplastic (type 1)
B- Hypomaturation (type 2)
C- Hypocalcified (type 3)
2- Dentinogenesis imperfecta Shell teeth
3- Dentinal dysplasia
4- Regional odontodysplasia
5- Multisystem disorders with associated dental defects
***Infective:** Congenital syphilis
***Metabolic:** Childhood infections, rickets, hypoparathyroidism
***Drugs:** Tetracycline pigmentation, Cytotoxic chemotherapy, Fluorosis

1-Amelogenesis imperfecta

Etiology

Intrinsic enamel defect that affects all teeth of both dentitions
Results from defective *amelogenin genes on X and Y chromosomes and also chromosome 4*
At least 16 variants noted based upon inheritance pattern, enamel qualities, and radiographic features.

Clinical Presentation

One of three basic alterations of enamel may be seen: **hypoplasia, hypomaturation, or hypocalcification**
Enamel hardness varies depending upon type of defect:
normal hardness in hypoplastic form but deficient amounts of enamel; **soft enamel in the hypocalcified variant** but normal amounts of enamel
Color ranges from **normal (hypoplastic)** to **dark yellow-brown (hypocalcified)**
Radiographic changes range from **normal density (hypoplastic)** to **less dense (hypocalcified)**

Diagnosis

1-Clinical and radiographic features
2-Family history (autosomal, X-linked forms)

Treatment

1-Full-crown restorations for esthetics
2-Genetic counseling

2-Dentinogenesis Imperfecta

Etiology

Hereditary disorder of dentin (autosomal dominant) . It may be seen in association with osteogenesis imperfecta. Altered dentin matrix is related to the defective degradation of dentin phosphoprotein during dentinogenesis

Clinical Presentation

Primary and permanent dentition exhibit gray to brownish opalescence
Normal enamel fractures easily from defective underlying Dentin.
Severe tooth abrasion related to exposed dentin following enamel loss

Radiographically: roots are slender to spike with pronounced cervical constriction and obliterative pulpal calcification. Constricted tooth cervix gives molar crowns a "tulip" profile.

Diagnosis

1-Clinical and radiographic appearance
2-Family history

Differential Diagnosis

Osteogenesis imperfecta

Treatment

Functional and esthetic restorations (full crowns)

Shell teeth (dentinogenesis imperfecta type 3)

This rare anomaly is so called because only a thin shell of hard dental tissue surrounds overlarge pulp chambers. Like other types of dentinogenesis imperfecta there is normal, but thin, mantle dentine which covers irregular dentine. The pulp lacks a normal odontoblast layer and consists of coarse connective tissue which becomes incorporated into the deep surface of the dentine.

3-Dentinal dysplasia ('rootless' teeth)

In dentinal dysplasia, the roots are very short and conical. The pulp chambers are obliterated by multiple nodules of poorly organized dentine containing sheaves of tubules; these teeth tend to be lost early in life.

4-Regional odontodysplasia (ghost teeth)

This is a localized disorder of development affecting a group of teeth in which there are severe abnormalities of enamel, dentine, cementum and pulp. The disorder is not hereditary and the etiology is unknown. There is no sex or racial predilection.

Clinically, regional odontodysplasia may be recognizable at the time of eruption of the deciduous teeth (2 to 4 years) or of the permanent teeth (7 to 11 years). **The maxillary teeth** are most frequently affected, two quadrants may be affected. The abnormal teeth frequently fail to erupt, but if they erupt, show yellowish deformed crowns, often with a rough surface. In addition they are susceptible to caries and fracture. Affected teeth have very thin enamel and dentine surrounding a greatly enlarged pulp chamber.

In radiographs, the teeth appear crumpled and abnormally radiolucent or hazy, due to the decrease in mineralization of dental hard tissues, hence they are called **ghost teeth'**.

Treatment

If affected teeth can be preserved and restored, crown and root dentine continue to form and the teeth may survive long enough to allow normal development of the alveolar ridge and occlusion. However, extraction is often required.

Disturbance affecting cementum structure

Cementum is continuously formed with life either with age or to compensate for occlussal wears. Sometimes we may have:

1-Hypercementosis (excess deposition of cementum in root area) lead to increase the thickness of the root and ankylosis and this will lead to difficult extraction , **or we may have**

2- **Hypocementosis** this will lead to loss of attachment to the surrounding bone, mobile teeth and then early loss of teeth.

Post developmental loss of tooth structure (enamel, dentin and cementum)

Enamel can be lost by attrition, abrasion and erosion

- **In addition to these conditions**
  Dentin can be lost due to internal resorption
  Cementum can be lost by external resorption

Environmental discoloration of teeth

A-Exogenous or extrinsic stains: These are the Stains on the surface of teeth that can be removed with abrasives. The color change may be caused by

1- Pigments in dietary substances (e.g., coffee, "betel" areca nut, tobacco).

2- 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.

3- Blood pigments

4- Restorative materials.

5- Medications (iron and iodine containing drugs).

These are generally easily removed.

B-Endogenous or intrinsic staining

Discoloration of teeth resulting from deposits of systemically circulating substances during tooth development

1- **Amelogenesis imperfecta(A.I.).**

2-**Dentinogenesis imperfecta(D.I.).**

3- **Dental flourosis.**

4- **Hyper bilirubnemia**. 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. No treatment is required, because only primary teeth are affected.

5- **Drugs (Tetracycline).** Tetracycline binds calcium and therefore is deposited in developing teeth and bones. The drug's bright yellow color is reflected in the subsequently erupted teeth. Because tetracycline can cross the placenta, it may stain primary teeth if taken during pregnancy. If it is administered after birth and between age 6 or 7 years, permanent teeth may be affected.

ORAL PATHOLOGY

DEVELOPMENTAL DEFECTS OF THE ORAL AND MAXILLOFACIAL REGION

2-Developmental Defects of the Oral Mucosa

1-FORDYCE'S GRANULES

They represent ectopic sebaceous glands which are present in the oral mucosa in at least 80% of adults, particularly in elderly people. They grow in size with age and appear in the oral mucosa as soft, symmetrically distributed, creamy spots a few millimetres in diameter. The **buccal mucosa** is the main site, but sometimes the lips and rarely, even the tongue is involved.

These glands are sometimes mistaken for disease but patients can be reassured that they are of **no significance.** If a biopsy is carried out it shows a normal sebaceous gland with two or three lobules.

2-LEUKOEDEMA

Leukoedema is a bilateral, diffuse, translucent greyish thickening, particularly of the **buccal mucosa**. It is a variation of normal, present in 90% of blacks and variable numbers of whites.

Histologically, there is thickening of the epithelium with intracellular oedema of the spinous layer

Treatment is unnecessary but reassurance may be required.

3-WHITE SPONGE NAEVUS

A developmental anomaly inherited as an autosomal dominant trait.

Clinical features:

The affected mucosa is white, soft and irregularly thickened. The abnormality is **usually bilateral** and sometimes involves the whole oral mucosa. There are no defined borders and the edges fade into normal tissue. The anus and vagina can also be affected.

No treatment is required only reassurance.

3- Developmental defects of the tongue

1- Macroglossia It is an abnormaly large tongue, it could be congenital or acquired.

Congenital macroglossia e.g. Down's syndrome, Congenital haemangioma or lymphangioma .
Acquired macroglossia e.g. Cretinism, Acromegaly, Amyloidosis, Lingual thyroid, Cancer.

2- Microglossia:

It is an abnormally small tongue. It is uncommon, but mostly associated with a group of overlapping conditions known as (oromandibular-limb hypogenesis syndrome) which is characterized by limb abnormalities like absence of digits.

3-Hairy tongue

The **filliform papillae** can become elongated and hair-like forming a thick fur on the dorsum of the tongue. The filaments may be up to half a centimetre long and pale brown to black in colour. Adults are affected but the cause is unknown. Heavy smoking, excessive use of antiseptic mouth washes and defective diet has been blamed, but their effect is questionable. The discoloration is probably caused by pigment-producing bacteria and fungi but **not *Candida albicans***.

Treatment

It is difficult. The measure most likely to succeed is to persuade the patient to scrape off the hyperplastic papillae and vigorously clean the dorsum of the tongue with a firm toothbrush. This removes large numbers of microorganisms mechanically and also, by removing the overgrown papillae, makes conditions less favorable for their proliferation.

4-Black tongue

The dorsum of the tongue may sometimes become black without overgrowth of the papillae. This may be staining due to drugs such as iron compounds used for the treatment of anemia, but is then transient. Occasionally the sucking of antiseptic lozenges causes the tongue to become black, and this may be due to pigment producing organisms, particularly Bacteroides strains.

5-Furred tongue

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

6-**Lingual varicositis**

Dilated tortuous veins may be seen along the ventral surface of the tongue and tend to become more prominent with age. They may be noticed by patients who need to be reassured that they are not abnormal.

7-**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.

Histologically: there is thinning of the epithelium in the centre of the lesion with mild hyperplasia and hyperkeratosis at the periphery, there are chronic inflammatory cells in the underlying connective tissue. Sometimes the changes are the same as those of psoriasis.

The Condition is considered important, because it can be confused with more serious form of **glossitis and even premalignant or malignant lesions**.

8-**Ankyloglossia**

It is characterized by a **short, thick lingual frenum** resulting limitation of tongue movement. The frenum sometime extends forward and attach to the tip of the tongue and there may be a slight clefting of the tongue. Occasionally, high mucogingival attachment of the lingual frenum may lead to local gingival and periodontal diseases in the regional frenal attachment.

9-**Lingual thyroid nodule:**

1- Accessory accumulation of thyroid tissue within the body of posterior tongue.

2- It represents a thyroid remnant in the region of the thyroid gland origin.

3- More common in females apparent during puberty and adolescence.

4- 2-3 cm, smooth, sessile mass on mid –posterior dorsum of the tongue in the region of foramen caecum.

5- Symptoms include dysphagia, dysphonia and hypothyroidism.

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

11- 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

4-DEVELOPMENTAL DEFECTS OF THE LIPS AND PALATE

1-Orofacial clefts:

A- Cleft 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.

Cleft lip: Developing defect usually of the upper lip characterized by a wedge-shaped defect resulting from the failure of two parts of the lips to fuse into single structure. Cleft lip (with or without a palatal cleft) is **more common in males**, while cleft palate alone is approximately twice **as common in females**. The incidence of cleft lip is about 1 per 1000 live births, while that of isolated palatal clefts is about 1 per 2000 live births.

In terms of relative frequencies, cleft lips form about 22%, combined defects of lip and palate form about 58% and isolated palatal clefts form about 20% of this group of defects. **The reason for the variations in the sites of clefts is that the lip and anterior palate (the primary palate) develop before the hard and soft palates (the secondary palate).**

Fusion of the secondary palate is from behind forwards. Isolated cleft lip is therefore the result of an early developmental disorder, while isolated cleft palate results from influences acting later, after the primary palate has closed. By contrast, a prolonged disorder of development can prevent both primary and secondary palates from closing and leaves a severe combined defect.

Classification

The main types of cleft lip and palate are:-

1- Cleft lip

Unilateral (usually on the left side), with or without an anterior alveolar

ridge cleft
Bilateral, with or without alveolar ridge clefts, complete or incomplete
2- Palatal clefts
Bifid uvula, Soft palate only, both hard and soft palate

3- Combined lip and palatal defects
Unilateral, complete or incomplete
Cleft palate with bilateral cleft lip, complete or incomplete

In the worst cases there is complete separation of the anterior palate, which projects forward with the centre section of the lip and is attached only by the nasal septum.

Enveromental factors: - include

1- Physiologic, emotional or traumatic stress.
2- Nutritional deficiency or excess of vitamin A and Riboflavin deficiency.
3- Mechanical obstruction by large tongue.
4- Relative ischemia to the area.
5- Substances like, alcohol, drugs and toxins.
6- Infections.

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.

2- Double lip: - this anomaly characterized by a horizontal fold of redundant mucosal tissue that is usually located on the inner aspect of the upper lip. Most often congenital in nature, but it may be acquired later in life.

3- Congenital lip pits: - developmental defects that may involve the Para median portion of the vermilion of the lower and upper lip **(Para median lip pit),** or the labial commissural area (commissural lip pit).

Para median lip pit: present as bilateral and symmetric fistulas on either side of the midline of the vermilion of the lower lip. It occurs as an isolated condition or may be associated with cleft lip or cleft palate.

Commissural lip pits: A small mucosal invagination that occur at the corner of the mouth on the vermilion border. It may represent a failure of

fusion of the maxillary process and mandibular process. It is either unilateral or bilateral.
Clinically it represents as blind fistula that may extend to a depth of 1-4 mm or it may be present as dilated ectopic salivary gland tissue.

4-DEVELOPMENTAL DEFECTS OF THE JAW BONES

1-BONY OVERGROWTHS(Bony exostosis)

Localised overgrowths of bone that arises from normal cortical plate (exostoses) are more common.
Small exostoses may form irregularly on the surface of the alveolar processes and specific variants are **torus palatinus** and **torus mandibularis**. They differ from other exostoses **only in that they develop in characteristic sites and are symmetrical.**

Torus palatinus commonly forms towards the posterior of the midline of the hard palate. The swelling is rounded and symmetrical, sometimes with a midline groove. It is not usually noticed until middle age and, classified according to their morphology into:

1- Flat torus which have broad base.
2- Spindle torus appears as a midline ridge.
3- Nodular torus appears as multiple protuberances.
4- Lobular torus appears as lobulated mass arises from single base.

It should be removed, if it interferes with the fitting of a denture.

Torus mandibularis form on the lingual aspect of the mandible opposite the mental foramen. They are typically bilateral, forming hard, rounded swellings. The management is the same as that of torus palatinus.

2-Agnathia:- (nathia= jaw, Ag = Agenesis).

It is developmental congenital absence of one of the jaws; it is a rare condition and mostly occurs as part of the mandible is absent.

3-Macrognathia:-

It is abnormally large jaw, some times called prognathism. This defect 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 and Pagets disease of bone.

4-**Micrognathia:- very small jaw**

It is a developmental disturbance affecting one of the jaws and lead to abnormally small jaw. The condition 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 the tongue, lack of support of tongue musculature and airway obstruction).

5-**Coronoid hyperplasia:-**

It is rare developmental anomaly which results in limitation of mandibular movement. The condition 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.

Aquired: - result from disturbance of growth center of the 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 the face as a result of an increased neurovascular supply to the affected side of the face.

Unilateral enlargement of the facial tissues, bones and teeth is usually present resulting in asymmetry of the face with malocclusion and deviation of the affected side of the face to the unaffected side of the face.

10-**Hemifacial atrophy:-**

Uncommon poorly understood degenerative condition, characterized by:

1- Atrophic changes affecting one side of the face.
2- The mouth and nose are deviated toward the defective side.
3- The covering skin often exhibit dark pigmentation.

11-**11.Lingual mandibular salivary gland depression (Stafne defect) (Stafne's mandibular lingual cortical defect) (Stafne cyst)**

Developmental concavity of the cortex of the mandible in the molar area, that forms around an accessory lateral lobe of submandibular gland which has **radiographical(r a d i o l u c e n c y) appearance** of a **well-circumscribed cystic lesion** within the bone usually below the inferior alveolar canal.

In most cases biopsy revealed **histologically normal salivary gland** tissue suggesting that these lesions represent developmental defects containing portion of the submandibular gland. **Treatment** - routine follow up

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**

ORAL PATHOLOGY

Diseases of the pulp

Pulp

Delicate fibrous connective tissue containing blood and lymphatic vessel, nerves and undifferentiated mesenchymal cells.

There are three basic features about the location of the pulp that profoundly affect an inflammatory response to infection:

1- Pulp surrounded by hard dentin which limits the ability of pulp to tolerate oedema.

Inflammation —heat→ swelling → no pulp expansion → sever pain (break pressure on nerve in pulp) .

2- Tiny periapical foramen → no collateral circulation → so any Inflammation → pulp necrosis.

3- The tooth is embedded in the jaw bone results in spread of inflammation to bone.

Pulpitis

Inflammation of the pulp .

Histologically :-

Inflammation → oedema and swelling → rise in pressure (of inflammatory exudates) → local collapse of the venous microcirculation → local tissue hypoxia → local necrosis (no collateral circulation).

Chemical mediators (from necrotic tissue) → further inflammation → inflammation .

Reactionary dentin formation (before onset of pulpitis) → pulp protection from further injury, by increase thickness between pulp and carious lesion.

Untreated pulpitis → pulp death → inflammation spread to periapical Area .

Etiology

Pulpitis due to :-

1- Microbial injury

- It's commonest cause .
- Dental caries (recurrent caries and root caries) ⟶ bacteria and it's toxin can reach the pulp ⟶ pulpitis .
- Attretion, abrasion, traumatic restorative procedures associated with pulp exposure.
- Advanced periodontal disease (periodontal pocket involving the periapical tissue or lateral root canals) ⟶combined periodontal- endodontic lesion .

2- Thermal injury :-

- Cavity preparation, tooth polishing with no cooling ⟶heat ⟶pulpitis
- Large metallic restoration with inadequate lining⟶ heat to pulp ⟶ pulpitis .

3- Chemical injury :-

-Direct application of irritant material to the exposed pulp .
- Diffusion of acidic material through dentinal tubules (ex. composite filling).
- In many instances pulp may respond to such agents by forming reactionary dentin, sclerosing dentin, dead tract that D.T. sealed, rather than the irritation leading to symptomatic pulpitis.

4- Mechanical injury :-

Traumatic accident (fractured crown), attrition, abrasion, dental procedure (traumatic pulp exposure) .

Classification of pulpitis :-

1- Focal reversible pulpitis (hyperemia).

- earliest form of pulpitis.

Clinically :-

-sharp or intense pain to hot and cold and with immediate onset (sudden Pain change in temperature).

-pain remain less than 20 min., disappear with stimuli removal.

-affected tooth easily localized.
-tooth with deep carious lesion or incorrect filling.

- Not tender to percussion.
- Electrical pulp testing ⟶ low level current response.
- ***Histological:-***
- dilatation and congestion of blood vessel with slight oedema.
- ***Treatment:-***
- Caries removal, restoration with lining material (pulp protection).
- Early treatment ⟶ reversible.
- No treatment ⟶ pulpitis (irreversible).

Acute pulpitis:-

Follow hyperemia, or as exacerbation of chronic pulpitis(increase virulence of M.O., increase number of bacteria, decrease immunity of patient).

Clinically:-

- tooth with deep caries or filling with defective margin (secondary caries).
- pain to hot and cold, later heat is more significant.
- Spontaneous, sever, throbbing (pulsating) pain, at time lancinating in type.
- pain remain after stimuli removal.(characteristic feature is continuous pain).
- Pain increase at night (increase blood pressure)⟶ patient awake.
- Difficult to localized tooth.
- Pain radiating to adjacent jaw, face, ear, neck (same affected site) patient with low pain threshold.
- ***Histopathology:-***

1- Vascular dilatation (increase permeability of blood vessel).
2- Exudation and oedema.
3- Migration of polymorph (neutrophil).
4- Death of odontoblast (local) in area of inflammation.

3-Chronic pulpitis:-

- outcome of a cut pulpitis, or chronic from the beginning (mild stimulation, high resistance, for long period duration).

Clinically:-

- mild, dull, intermittent pain (not continuous).
- Long duration (one hour or more).
- Decrease thermal reaction (degenerated nerve fiber).
- ***Histopathology:-***
- Chronic inflammatory cell infiltrate(lymphocytes, plasma cells).
- Dense collagen fibers a round inflammation area (fibrous pulp).
- Treatment:-
- Root canal treatment or extraction.

Reversible	Irreversible
1- Elicited	1- spontaneous
2- Sharp	2- Dull
3- Less than 20 mints, duration.	3- more than 20 mints.
4- Unaffected by body position.	4- affected(lying down).
5- Easily localized.	5- difficult.

4-Pulp polyp:-

Chronic hyperplastic pulpitis (in children in erupted molar)

- Special type of polyp formation in the center of caries tooth.
- ***Clinically:-***

1- mostly in the deciduous molars and 1st permanent molar with large carious lesion(wide).(large apical foramina more blood supply, high tissue resistance).

2- Painless, dark, red or pink nodule protruding into cavity sometime bleed.

Histopathology:-

1- mass of granulation tissue (healing tissue has newly formed blood vessel. collagen, lymphocyte, macrophage, plasma cells).

- Few odontoblast survive.
- Polyp may be epithelialized grafting(implantation) of stratified squamous epithelial cells in saliva.

- **Gingival polyp:-**

Proliferation of gingival tissue through proximal cavity(tracing base attachment).

Treatment :-
Root canal treatment, extraction.
No correlation between clinical features and extend of inflammation (histologically).
No symptoms ⟶ not indicated normal pulp.
pulpitis ⟶ pulp death ⟶ no pain

Pulp vitality measured by pulp testing
Thermal test:- cold ⟶ cotton contain ethyl chloride
Hot ⟶ warm getta percha. If there's pain it's reversible.
Electrical pulp tester:-
Device with electrical current
Pain and pulpitis ⟶ decrease pointer.
2- Tooth color : pulpitis (dead tooth) lead to grey black discolored tooth.
3- Percussion : tender to percussion ⟶ periapical inflammation.
others :- x-ray, palpitation of surrounding area, history of

5-Pulp necrosis (death of pulp)

- pulpitis (untreated) lead to traumatic injury to apical blood vessel ⟶ cutting blood vessel supply to pulp.
- Decrease blood supply ⟶ ischemia ⟶ coagulation necrosis.
- Pulpitis ⟶ breakdown of inflammation cells ⟶ liquefaction necrosis ⟶ infected by putrefaction bacteria from caries(gangrenous necrosis).
- ***Clinically :-***
  1- foul odour (during root canal treatment).
  2- Discoloration of tooth(necrotic material pass into dentinal tubules and show through the translucent enamel) greenish-black, grey.

Pulpitis if not treated lead to pulp necrosis either it progress to :
a- coagulative necrosis(ischemia ⟶ injury to blood vessel).
b- liquifactive necrosis (gangrene).

Pulp stone (calcification of pulp):-

- Pulp stone (denticales) : gross calcified body in the pulp

- Very common, increase in size and number with age.
- Radiographically appear as small rounded radiopaque mass.
- Unknown cause, more after operative procedure.
- Painless, interfere with root canal treatment.
- Denticales ,some composed of dentin.

Classified according to:-

1- composition:

a- true stone : dentinal tubules, outer predentin layer and adjacent odontoblast.

b- False stone : concentric layers of calcified material, no dentin tissue.

2-*location:-*

a- free

b- adherent

c- interstitial that surrounded by reactionary or secondary dentin.

3-Dystrophic calcification;-

Granules of amorphous calcified material seen scattered along collagen fiber or aggregated into larger masses.

Common in root canals lead to obstruct root canal treatment.

Age changes in pulp

-Pulp size decrease due to continued secondary dentin production.

- decrease vascularity, decrease cellularity, increase collagen fibers which may impair tissue response to injury and it's healing potential.

- diffuse calcification increase with age.

Oral Pathology

Lec :5

Diseases of periapical tissue (Periapical periodontitis)

Periapical inflammation

The extension of inflammation of the pulp beyond the tooth into the periodontal Ligament space or area.

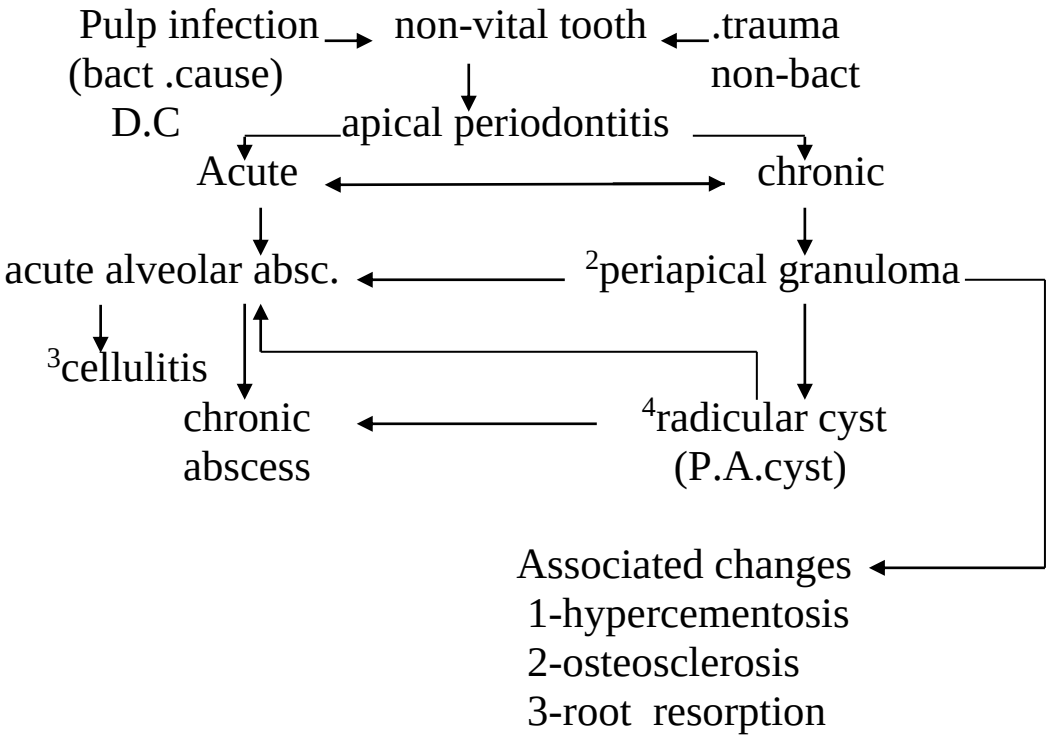
It's the same inflammation process, but because of confined spaces the process develop with it a particular feature of infl .occur that

- adjacent bone and root apex resorb.
-easily detected radiographically.

Difference between pulpitis and periapical periodontitis(p.A.periodontitis) :-

(pulpitis)	(p.A.periodontitis)
1-No healing in damaged pulp	1- Healing occur, if cause of inflam. removed because rich controlled Blood supply which enhanced healing(Basis endodontic treatment).
2-affected tooth not localized (loss of properioceptive NF.)	2- localized tooth(stimulation Of propreoceptive N.ending in P.D.L. Facilitate this accurate location).

Changes that occur around the apex of non-vital tooth:



Response of P.D.L irritations (acute or chronic) depend on factors:

1-No. and virulence of any m.o. involved.

2-type and severity of any mechanical or chemical irritant.

3-Effeciency of the host defenses (patient resistance).

Etiology:

1-infection:

bact. and it's toxin , inflam. product ⟶

p.A area w time P.A. periodontitis.

2-Trauma : a- direct blow on tooth.

b- occlusal trauma (high spot filling)

c- under pressure during or through treatment.

d- biting on hard body in food.

3-Endodontic treatment:

a- mechanical instrumentation ⟶ bact to P.A.area (infect & trauma)
b- chemical irritation from R.C. filling material.

Periapical periodontitis :e.g.:-

1- Periapical Granuloma (chronic peridontitis)
(apical granuloma)

Commenst sequalae of pulpitis and pulp necrosis (persistent irritation from bact. may lead to chronic inflammation)

Characterized by resorption of P.A. alveolar bone will replaced chronically by inflam. granulation tissue (P.A.G.).

Clinically:

- Asymptomatic ⟶ vitality test ⟶ pulp necrosis
- Some cases show mild pain ,slight tenderness to percussion.

Radiographically:

Oval or round radiolucency with a well demarcated outlines (cortical margin Separate P.A.G. from surrounding bone).

-This radiolucency located at apex.
-Radiolucency may be laterally (rare).

P.A.G.=slow mild reaction to inflammation ⟶ time for sclerosis bone Formation around it.

Histopathology:

-Circumscribed mass of granulation tissue.
-Fibrous t. capsule (condensed collagen F.) separate granulation t. from a Surrounding bone.
-Central portion composed of:
1-Chronic inflammatory cell (lymphocyte, plasma, macrophages)
2-Deposit of cholesterol and hemosiderin (from RBCs break down).

(cholesterol crystals appear as empty needle spindle like space ⟶ dissolving of cholesterol in slide preparation).

3-multinucleated giant cell (foreign body) grouped around cholesterol crystals.
4-Foci of foams cells (lipid laden macrophages).
5-Endothelium lined capillaries.
6-Prolifrated fibroblast (⟶ collagen fiber).
7-Epithelial cell rests of malassez incorporated with granulation t. (remainent of root sheaths).
8-prolifrated sq. epi. form anastomosing cords throughout granulation t.

*Sequalae of P.A.G. (fate or and result)

1-Remain localized within bone.(resistance of body equal to virulence of m.o.)
decreased resistance &/or increase virulence of m.o. lead to
2-suppuration and abscess formation.
3-Radicular cyst (P.A. cyst).(from ep. cell proliferation (malassez))
4-osteosclerosis.
5-Hypercementosis.

Treatment

1-R.C.T. 2-Extraction.

Radicular cyst (periapical cyst)

-Commonest cystic lesion in the jaw.
-Derived from untreated long standing P.A.G.
-True cyst (Radicular cyst pathological cavity lined by epithelium)

Pathogenesis :

P.A.C. arise from **proliferation of ep:. Rests of malassez** within P.A.G. (not all P.A.G progress to cyst).

Cyst formation follows two mechanism:
1- Continuous proliferation ⟶ mass of epi. cell⟶ mass increase in size⟶ central part lost nutrition ⟶ degeneration and necrosis (liquifactive)⟶ cavitation ⟶ cyst formation with continuous expansion due to osmotic pressure

(draining fluid from surrounding t. lead to uniform enlargement).
2-Degeneration and liquifactive necrosis of granulation t.(deep pulp and m.o. release toxic product ⟶ necrosis) ⟶ epithelial proliferation to surrounded this area will lead to cyst formation.
1st theory is most common.

Clinically :

1-Asymptomatic (unless exacerbation ⟶ progress to abscess formation ⟶ pain)
2-Mobility of adjacent teeth .

Radiographically:

Well circumscribed radiolucency at root apex surrounded by thin radio opaque margin.

Histopathology :

1-cavily lined by str . sq . ep. (nonkeratinized, ep. thickness correlated with degree of in flamm.)
2-wall composed of:
⟶c.t rich in collagon fiber.
⟶Infl. Cell infltrate (plasma , lymphocyte)
⟶Foam cell.
⟶Cholestrol crystal surrounded by foriegn body macrophage.
3-fibrous t. capsule surrounding the wall.
4-lumen contain thick protinaeous fluid and cellular debries.

Treatment:

1-exo. with socket curettage
2-apicectomy.
3-R.C.T

*Residual cyst:

radicular cyst remain in a jaw and failed to resolve after exo. of involved tooth.
20% of radicular cyst is residual.

*lateral radicular cyst:

-uncommon.
-extension of inft. from pulp to P.D.L along lateral root canal.

Perapical abscess:

Suppurative process at apex of tooth.

Clinically:

1-sever pain pus and edema at apex ⟶ pr. transmitted through fluid
exudation ⟶ Sensory N.in
PDL ⟶ pain

2-Extrusion of tooth from socket.
Infl exudate push against
root ⟶ extrusion.

3-tenderness to percussion.
4-fever , malaise , regional lymphadenitis.
5-swelling and redness of area near apex.
6-well localized tooth (stimulation properioceptive NF. in P.D.L)

Radiographically:

Acute abscess ⟶ no radiographic indication or slight P.D.L. widening at apex.

Chronic abscess ⟶ radiolucency, no distinct demarcated line (abscess rapid lytic Process)

Histopathology : (mostly for chronic)
1-outer fibrous t. capsule.
2-wide zone of granulation t. ⟶ neutrophil ,lymphocyte , plasma cell , macrophages and proliferated B.V.

Treatment:

1-drainge of abscess (emergency)
2-Analgesic and antibiotic prescription.
3-R.C.T.
4-Exo. (when acute symptoms subside).

Spread of inflammation of P.A.A:

-No removal of causative factors ⟶ continuous suppuration ⟶ abscess enlarged.
balance between host resistance and irritant ⟶ localized, chronic abscess.
-Progressive suppuration and increase hydrostatic pr. ⟶ pus will tract (drain)into:
a- through root canal (if its open to mouth) .

b- through P.D.L, ⟶ discharge in gingival sulcus.
c- through chancellors bone ⟶ cortical plate perforation ⟶ subperiosteal abscess
⟶ pr. and pain (common one).

-Most abscess pointed buccally.
-Upper lateral incisors and palatal roots of upper molars and premolar pointed palately → 1)pus directly discharged into oral cavity through a sinus appear

1- painless swelling.
2- Gumboil.
(=nodule of granulation tissue mark the sinus opening).
2) palatal abscess : e.g. upper left lateral incisor infection.
3) abscess of molar regions in either jaw, it's spreading appear as:
a- cellulitis (spread of inflammation to soft tissue of face and neck).
b- localized soft tissue abscess → may track to skin (sinus in the skin) extra oral sinus ⟶ scarring (if chronic).

Cellulites:

-rapidly spreading inflammation of soft tissue, associated with streptococcal infection.
- not well localized in contrast to circumscribed abscess.
- the rapid spread of cellulites due to streptococcal production of streptokinase, hyaluronidaze.

Clinically:

Diffuse, tense, painful soft swelling associated with fever and malaise.
- cellulites of upper half of face due to maxillary teeth infection.
- Cellulites involving eye is serious because the risk of cavernous sinus thrombosis.
- Cellulites of mandibular teeth involve lower half of face extended to submandibular and cervical tissue cause respiratory embarrassment.

Ludwig's Angina:

- Sever cellulites of submandibular, sublingual and submental spaces.
- Board-like swelling of floor of mouth, tongue elevated posteriorly → difficulty in eating, swallowing and breathing.
- edema of glottis lead to death by suffocation.

ORAL PATHOLOGY

DEVELOPMENTAL DEFECTS OF THE ORAL AND MAXILLOFACIAL REGION

DEVELOPMENTAL CYSTS OF THE ORAL AND MAXILLOFACIAL REGION.

(non odontogenic cyst)

Cysts are epithelium-lined pathological cavities, usually filled with fluid, semi-solid material, or cellular debris.
Also are called **fissural cysts or occlusion cysts**, because they arise from embryonic epithelium that becomes entrapped during embryogenesis.
Clinically, they present as a soft or fluctuant swelling.
Cysts of the oral and maxillofacial region are divided into odontogenic, nonodontogenic, pseudocysts, and neck cysts.
Pseudocysts differ from true cysts in that **they lack an epithelial lining.**

1-**Nasolabial Cyst (Nasoalveolar cyst)** is a rare developmental soft-tissue cyst that develops in the upper lip in the canine region.
Etiology: Unclear. Although there are two major theories:-
One theory considers this cyst to be a fissural cyst arising from epithelial remnants entrapped along the line of fusion of the maxillary, medial nasal and lateral nasal processes.
A second theory suggests that these cysts develop from misplaced epithelium of the nasolacrimal duct.

Clinical and radiographical features: - It appears as a soft-tissue swelling in the mucobuccal fold of the maxilla, lateral to the midline . Occasionally, the patient may complain of nasal obstruction, discomfort, or difficulties in wearing dentures. The cyst is more common in women, usually between 40 and 50 years of age. Because this cyst arises in soft tissues, in most cases there are **no radiographic changes**, but resorption of the underlying bone may occur.

Histopathological examination shows lining of the cyst by pseudo stratified columnar epithelium, often show goblet cells and cilia. The cyst

wall is composed of fibrous connective tissue with adjacent skeletal muscle.

Differential diagnosis:-

Soft-tissue abscess, tooth abscess, mucocele, radicular cyst, salivary gland neoplasms, and mesenchymal neoplasms.

Treatment: Surgical excision.

3- Nasopalatine duct cyst(Incisive canal cyst) :

It is the **most common** non-odontogenic cyst of the oral cavity.

Etiology: It arises from epithelial rests in the incisive foramen.

Clinical and radiographical features: It appears as a slow-growing soft swelling of the palatine papilla, covered with normal mucosa. The cyst, after mechanical irritation, may be inflamed and becomes painful due to local infection.

Radiographically: usually demonstrates a well circumscribed RL in or near the midline of the maxilla, between and apical to the central incisor teeth. **It may be difficult to distinguish a small nasopalatine duct cyst from a large incisive foramen**. It is generally accepted that a diameter of (6 mm) is the upper limit of normal size for incisive foramen. Therefore, a radiolucency that is (6 mm) or smaller in this area is usually considered a normal foramen unless other clinical signs and symptoms are present.

The clinical diagnosis should be confirmed by histopathological examination that showed epithelial lining composed of either:-

1- Stratified squamous epithelium.
2- Pseudostratified columnar epithelium.
3- Simple columnar epithelium.
4- Simple cuboidal epithelium.

Differential diagnosis: - Tooth and periodontal abscesses, mechanical trauma of the palatine papilla, fibroma, lipoma.

- **N.B.:** to distinguish between the nasopalatine cyst & P.A. cyst:
- **1-** N.P.cyst, the tooth is vital, but in case of P.A. cyst the associated tooth is nonvital.
- **2-** Because the N.P.cyst is not related (attached) to the apex of the root, so by changing the direction of the X-ray beam we see if the lesion remain attached to the apex of the root, so it mean it's radicular cyst, if not it means N.P. cyst.

Treatment: Surgical removal.

3-Globulomaxillary cyst

Globulomaxillary cyst were once considered fissural cyst, located between the globular and maxillary processes. The former theory of origin related to epithelial entrapment within a line of embryologic closure with subsequent cystic change Other evidence now shows that , are of odontogenic origin.

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Radiolucencies in this location, when reviewed microscopically, have been shown to represent radicular cysts, periapical granulomas, lateral periodontal cysts, OKCs, central giant cell granulomas, calcifying odontogenic cysts, and odontogenic myxomas. Thus today the termglobulomaxillary can be justified only in an anatomic sense, with definitive diagnosis of lesions located in this area made by combined clinical and microscopic examination.

Radiologically: a globulomaxillary lesion appears as a well-defined radiolucency, often producing divergence of the roots of the maxillary lateral incisor and canine teeth. Radicular cyst and periapical granuloma can be ruled out with **pulp vitality testing.**

Because of the array of potential diagnoses, the histology varies considerably from case to case.

Histologically: - lining epithelium is stratified squamous and some times pseudostratified ciliated columnar respiratory epithelium. Thin C.T. wall which is free from inflammation.

Treatment and prognosis are determined by the definitive microscopic diagnosis.

4-Lymphoepithelial Cyst

Definition: Lymphoepithelial cyst is an uncommon developmental lesion of the oral mucosa.

Etiology: Probably caused by cystic degeneration of glandular or surface epithelium entrapped in lymphoid tissue during embryogenesis.

Clinical features: It presents as an asymptomatic, mobile, well-defined nodule, usually firm on palpation and elevated, with a yellowish or whitish color. The size ranges from 0.5 cm to 2 cm in diameter. **The floor of the mouth** is the most frequent location, followed by the posterior lateral border and the ventral surface of the tongue.

Lymphoepithelial cysts are **histologically** similar to the branchial cleft cysts that develop in the lateral neck.

Histopathological examination which showed epithelial lining of stratified squamous that may or may not be keratinized. The wall of the cyst typically contains lymphoid tissue often demonstrating germinal center formation.

Differential diagnosis: lymphoid tissue aggregation, dermoid cyst, mucocele, lipoma, fibroma and other benign tumors.
Treatment: Surgical removal.

5-Thyroglossal Duct Cyst

Definition: Thyroglossal duct cyst is a rare developmental lesion that may form along the thyroglossal tract.
Etiology: Remnants of thyroglossal duct epithelium.
Clinical features: The cyst is usually located under the hyoid bone but can be located anywhere from the suprasternal notch to the foramen cecum of the dorsal tongue. **Intraorally,** it appears as a painless, fluctuant swelling usually 1–3 cm in diameter, located in the midline of the dorsum of the tongue close to the foramen caecum. Occasionally, a fistula may form following infection. The cyst is most often diagnosed in patients less than 20 years of age.
Histopathological examination, showed a lining epithelium of stratified squamous, or columnar or small intestinal epithelium, or mixture of them. The C.T. tissue wall may contain normal thyroid tissue.
Differential diagnosis: Median rhomboid glossitis, benign and malignant tumors.
Treatment: Surgical removal.

6-Median mandibular cysts:-

Like globulomaxillary cysts, were once considered fissural cysts, in which a fissural origin was based on the theory of epithelial entrapment in the midline of the mandible during the "fusion" of each half of the mandibular arch. And recently it is thought to be of odontogenic origin.
Clinical and radiographical features: Swelling In the midline of the mandible .**In x-ray** it appears as a well circumscribed RL between the two lower central incisors in the midline.

HISTOPATHOLOGY: Lining epithelium is mainly stratified squamous. C.T. wall is free from inflammation.

Treatment: surgical removal

7-**Median palatal cyst (palatine cyst):**

It is rare fissural cyst that develops from epithelium entrapped along the embryonic line of fusion of lateral palatal shelves. This cyst may be difficult to distinguish from nasopalatine duct cyst.

Clinical and radiographical features:

This cyst is present as firm or fluctuant swelling in the midline of the hard palate posterior to the palatine papilla. Most of these cysts are asymptomatic, but sometimes pain may be present.

X-ray: occlusal radiograph showed a well –circumscribed RL in the midline of the hard palate.

A midline RL without clinical evidence of expansion is probably a nasopalatine duct cyst.

Histopathology: - Cyst is usually lined by stratified squamous epithelium. Areas of ciliated pseudostratified columnar epithelium may be present in some cases. Chronic inflammation may be present in the cyst wall.

Treatment: surgical removal.

8-**Oral lympho-epithelial cyst**

It occurs intraorally and usually located in the **posterior part of the tongue** or in the **floor of the mouth** and sometime near the soft palate and the pharynx and in the tonsilar area (lymphoid tissue).

Cliically: asymptomatic swelling in the oropharynx area, lateral border of the tongue and floor of the mouth.

9-**Dermoid & Epidermoid cyst**

These represents a simple form of cystic teratoma derived from skin epithelium entrapped during embryonic development. Most of these cysts occur in the head & neck region, primarily in the skin around the eyes & the anterior upper neck, extending superiorly into the floor of the mouth.

Clinically: Mostly occur in young adults, present as painless swelling exhibiting a doughy consistency on palpation,& may cause elevation of the tongue & can interfere with eating & speaking.

Histopathology: The cyst lined by a layer of orthokeratinized squamous epithelium, surrounding by C.T. capsule. In dermoid cyst in addition to these, the lesion exhibiting variable numbers of dermal appendages including hair follicles, sebaceous glands.

Treatment: surgical excision.

Dermoid cyst:

These cysts probably form as a result of some abnormality of development of the branchial arches or pharyngeal pouches. It is generally classified as a benigin form of Teratoma.

Clinical features

Dermoid cysts develop between the hyoid and jaw or may form immediately beneath the tongue. They are sometimes filled with desquamated keratin giving them a semi- solid consistency

If the cyst develops above the geniohyoid muscle a sublingual swelling may displace the tongue upward and create difficulty in eating, speaking or even breathing. Cysts that occur below the geniohyoid muscle often produce a submental swelling with a double chin appearance.

Dermoid cyst is more deeply placed than a **ranula;** the latter is obviously superficial, having a thin wall and a bluish appearance. A dermoid cyst causes no symptoms until large enough to interfere with speech or eating.

Pathology:

The lining of epidermoid cysts is keratinising stratified squamous epithelium alone. Less often, cysts also have dermal appendages (sebaceous gland, hair follicle or sweat gland) in the wall and are then referred to as dermoid cysts.

These cysts should be **removed surgically.**

Oral Pathology

Lecture

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 colour 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 characrerized 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 epirhelium. 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.

SINONASAL PAPILLOMAS

Sinonasal papillomas are benign, localized proliferations

of the sinonasal mucosa and include three histomorphologically

distinct types:

1. Fungiform. 2. Inverted. 3. Cylindrical cell

About half of sinonasal papillomas arise from the lateral nasal wall; the remainder predominantly involves the maxillary and ethmoid sinuses and the nasal septum

The etiopathogenesis of sinonasal papillomas remainsunclear**.**

A variable association with HPV infection has been reported

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, yellowwhite, 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_

SEBORRHEIC KERATOSIS

- Seborrheic keratosis is an extremely common skin lesion of older people and represents an acquired, benign proliferation of epidermal basal cells. The cause is unknown, although there is a positive correlation with chronic sun exposure, sometimes with a hereditary (autosomal dominant) tendency.In addition, somatic mutations in the *fibroblast growth factor receptor 3 (FGFR3)* and *phosphatidylinositol3-kinase, catalytic subunit alpha (PIK3CA)* genes may contribute to the pathogenesis of these lesions. In some cases, HPV DNA has been detected, but this finding may be

coincidental. Seborrheic keratosis does not occur in the mouth.

SEBACEOUS HYPERPLASIA

- is characterized by a localized proliferation of sebaceous glands of the skin. It has no known cause and is common on the facial skin. In some cases an association with cyclosporine, systemic corticosteroids, hemodialysis

- Cutaneous sebaceous hyperplasia usually affects adults older than 40 years of age. It occurs most commonly on the skin of the face, especially the nose, cheeks, and forehead. Less commonly, lesions may involve the genital area, chest, and areola. The condition is characterized by one or more soft, nontender papules with white, yellow, or normal coloration

Histopathological feature:sebaceous hyperplasia is characterized by a collection of enlarged normal sebaceous gland lobules grouped around one or more centrally located sebaceous ducts

EPHELIS

An ephelis is a common small hyperpigmented 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 pregnanc

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 thenevus 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.

SMOKELESS TOBACCO

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 nonfermented 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 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 keratoses

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

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 sun-exposed 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

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.

Precancerous Lesions of the Oral,Pharyngeal, and Laryngeal Mucosa (Clinical Terms Only) Malignant Transformation Potential

Proliferative verrucous leukoplakia(PVL)*★★★★★★

Nicotine palatinus in reverse smokers† ★★★★★

Erythroplakia ★★★★★

Oral submucous fibrosis ★★★★★
Erythroleukoplakia ★★★★
Granular leukoplakia ★★★★
Laryngeal keratosis ★★★
Actinic cheilosis ★★★
Smooth, thick leukoplakia ★★
Smooth, red tongue of Plummer-Vinson syndrome ★★
Smokeless tobacco keratosis ★
Lichen planus (erosive forms)‡ ★?
Smooth, thin leukoplakia +/

1-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. Focal cemento-osseous dysplasia.
3. Periapical cemento-osseous dysplasia.
4. Ossifying fibroma.

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):

FD is a skeletal anomaly in which normal bone is replaced and distorted 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***.

- **<u>Clinical Features of FD:</u>**

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*** & ***2nd decade of life***.

Monostotic FD usually exhibits an equal sex distribution & the polyostotic form tends to occur more commonly in females.

- **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 shaped 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.

- **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.

Clinically & microscopically similar to cementifying fibroma, 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. 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:**

N.B. 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.

- **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** and (2) **Psammomatoid**. The latter neoplasm occur more than the trabecular type in a ratio of approximately 4:1

- **Histopathology:**

Both patterns are nonencapsulated 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 starnds are lined by plump osteoblast and in other areas by giant cells.

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

Cemento-osseous Dysplasia (COD):

The term COD refers to a disease process of the jaws for which the precise etiology is unknown.

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.

- The condition appears 1st as a *periapical lucency* that is continuous with the periodontal ligament space. *To be differentiated from* ***Periapical granuloma*** ⟶ ***vitality test***.
- As the condition progresses, the lucent lesion develops into a mixed or mottled pattern because of bone repair.
- The final stage appears as a solid, opaque mass that is surrounded by a thin, lucent ring (after months – years).

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.

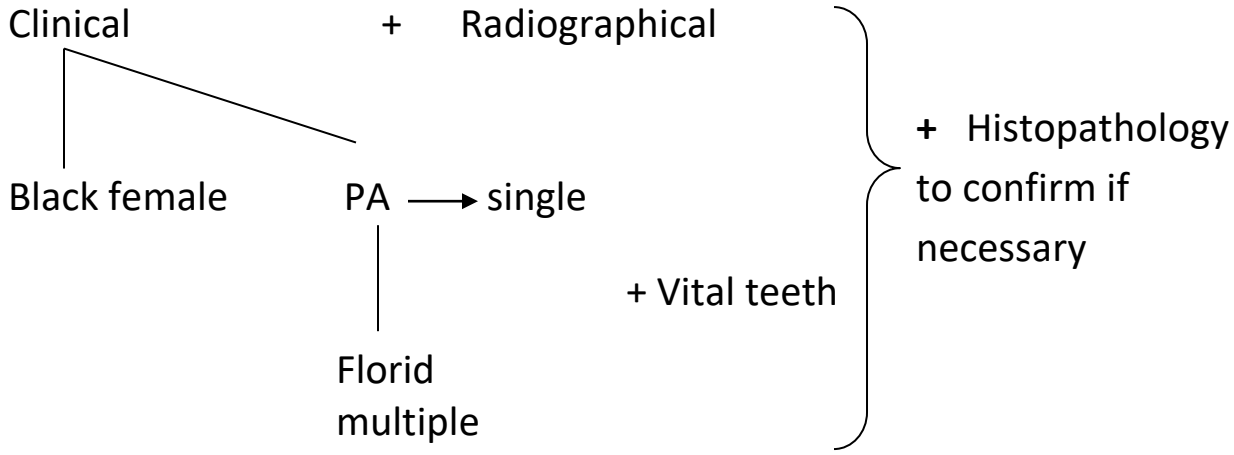
[1] Exuberant: excessive in size or extent.

- **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.

Lucent stage	⟶	***Mature radiopaque***
Less bone trabeculae		Solid sclerotic masses of bone or cementum

- **Diagnosis:**



Treatment: No treatment.

FCOD ⟶ sclerotic stage ⟶ ↓vascularity ⟶ prone to ***necrosis*** & ***osteomyelitis*** ⟶ instruction for good oral hygiene to prevent infection.

Oral pathology
Giant cell lesions

Giant cell lesions of the jaw include:-
1-Giant cell granuloma (central-peripheral)
2-Giant cell tumor (osteoclastoma)
3-Aneurysmal bone cyst
4-Cherubism
5-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 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 reddish-blue nodular mass. Most lesions are smaller than 2cm in diameter although larger ones are seen occasionally. The lesion can be sessile or pedunculated and may or may not be ulcerated.

The clinical appearance is similar to the more common pyogenic granuloma of the gingiva. 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.

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" showsproliferation 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.

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

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

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 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. 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, parasthesia, 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 granulomas 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.

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.

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.

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 alternativessurgery-(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.

Giant cell tumor:(osteoclastoma)

The question of whether true giant cell tumors, which most often occur in the epiphyses of long tubular bones, occur in the jaws has been argued for many years and still is unresolved. Although most central giant cell lesions can be distinguished histopathologically from the long bone tumors ,a number of jaw lesions are indistinguishable microscopically from the typical giant cell tumor of long bone.

In spite of the histopathologic similarity, these jaw lesions appear to have a biologically different behavior from long bone lesions, which have **higher recurrence rates** after curettage and show **malignant change in up to 10% of cases.**

Cherubism(hereditary bone disease)

Cherubism is a rare developmental jaw condition that is generally inherited as an autosomal dominant trait. The gene for cherubism was mapped to chromosome 4p16. 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.

Clinical and Radiographic Features

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 faces arises from bilateral involvement of the posterior mandible that produces angelic chubby checks. 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. Milder maxillary involvement occurs in the tuberosity areas; in severe cases, the entire maxilla can be affected.

In addition, there is an "**eyes upturned to heaven**" appearance that is due to a wide rim of exposed sclerae noted below the iris.

Radiographically:

The lesions are typically multilocular expansile radiolucencies. The appearance is virtually diagnostic as a result of their bilateral location. No unusual biochemical findings have been reported in patients with cherubism.

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.Foci of extravasated blood are commonly present. 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. 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 patients 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. Radiation therapy is contraindicated because of the risk of development of postirradiation 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. Others have suggested that aneurysmal bone cyst and giant cell granuloma are closely related. 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 intrabony lesion.

Clinical and Radiographic Features

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 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.

Radiographically:

It shows a unilocular or multilocularradiolucent 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 .

At the time of surgery, intact periosteum and a thin shell of bone are typically found covering the lesion. 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.

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, and removal of the bulk of the lesion is usually sufficient to control the bleeding. Rare cases require more extensive surgical resection grafting.

The reported recurrence rates are from8% - 60%. Mostly arise from inadequate or subtotal removal upon initial therapy. In spite of recurrences, the long-term prognosis appears favorable.

Hyperparathyroidism(metabolic bone disease)

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.

Hyperparathyroidism may be one of three types: **primary**, **secondary** and **hereditary** , *Primaryhyperparathyroidism*: is characterized by hyprersecretion of parathyroid hormone from hyperplastic parathyroid gland,parathyroid adenoma or an adenocarcinoma.

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.

Hereditaryhyperparathyroidism has been shown to be autosomal dominant condition

Clinical and Radiographic Features

The incidence increase with age ,and is greater in menopausal women. Early symptoms include, fatigue, weakness, arrythemias, polyuria, bone pain and headache.

Radiographically:

In the jaw bones,osteoporotic appearance of the mandible and maxilla showing well-demarcated unilocular or multilocular radiolucencies reflecting ageneralized resorption(ground glass appearance), overall cortical thinning loss of the lamina dura surrounding the roots of the teeth is also seen.longstanding lesions may produce significant cortical expansion.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 tissue specimen. which is usually a dark reddish-brown because of the abundant hemorrhage and hemosiderin deposition within the tumor.

Histopathologic Features:

Bone lesions of hyperparathyroidism although non -specific, are important in establishing diagnosis. Bone trabeculae show osteoclastic resorption .

The brown tumor of hyperparathyroidism is histopathologically identical to the central giant cell granuloma of the jaws. Both lesions are characterized by a proliferation of exceedingly vascular granulation tissue, which serves as a background for numerous multinucleated osteoclast- type giant cells. Accummulation of hemosiderin and extravasated RBCs,as a result the tissue may appear reddish brown accounting for the term**(brown tumor).**

Diagnosis:

Brown tumor of hyperparathyroidism is clinically **,**radiographically and histopathologically similar to central giant cell granuloma, therefore ,a bone chemistry profiling should reveal elevation of serum parathyroid hormone (PTH),serum calcium and alkaline phosphatase, with decrease of phosphorus.

Treatment and Prognosis

After diagnosis of hyperparathyroidism the patient should be referred to a surgeon for excision of the parathyroid glandor for kidney function evaluation.The jaw lesion should resolve after treatment.

ORAL PATHOLOGY
Healing of Oral wounds

Definition: The word healing refers to replacement of damaged tissue by living tissue to restore function.

Healing of wounds is one of the most interesting phenomenon which characterizes a living organism.

Healing of a wound is not an isolated, solitary phenomenon, healing of all tissues after injury has an essentially identical pattern, but may be modified considerably, depending upon numerous biological events.

It is a process consists of:

1- Wound contraction described at least in part to myofibroblasts, this contraction **causes reduction in the size of the wound in the first few weeks**

2- Replacement of lost tissue, brought about by division and migration of neighboring cells:

- **A- Replacement of the lost tissue by granulation tissue is known as 'repair' which results in scarring, and**
- **B- Replacement by similar type tissue is known as "regeneration".**

Causes of Oral Wound are common:

1. **Some sustained accidentally (e.g. jaw fractures).**
2. **Some inflicted by the dentist for a specific purpose (e.g. extraction wounds, biopsy wounds, etc.).**
3. **Others caused by disease process (e.g. various oral ulcers).**

Factors that contribute to modify the healing of the various wounds :-

1. **The unusual anatomic situation of the oral cavity—the teeth protruding from the bone.**
2. **The constant inflammation present in the gingival tissues.**
3. **The presence of countless microorganisms in a warm, moist medium of saliva.**

Factors Affecting Healing of Oral wounds:

A number of factors influence the healing process of wounds in the oral cavity, the dentist must recognize the possible causes:-

1-Location of Wound: Wounds in an area with a good vascular bed heal considerably more rapidly than wounds in an area which is relatively avascular.

2-Immobilization: If the wound is in an area subjected to constant movement so that formation of the new connective tissue is continuously disrupted (e.g. in the corner of the mouth), it will result in delayed

healing.

3-Physical Factors: Severe trauma to tissue will cause delay in wound healing. Under certain situations, however, mild traumatic injury may actually favor the healing process.

4-Local temperature in the area of a wound influences the rate of healing, probably by its effect on local circulation and cell multiplication.

5-X-ray radiation : data indicates that generally low doses of radiation tend to stimulate healing, while large focal doses of radiation or total body radiation tend to suppress healing.

6-Circulatory Factors Anemia has been reported to delay wound healing, similarly, dehydration has been found to affect the healing wound.

7-Nutritional Factors, delay in healing of wounds may occur in a person who is deficient in any of the essential foods.

Protein: is one of the most important substances, which may influence the speed of wound healing, so as its deficiency results in a delay in the appearance of new fibroblasts as well as a decreased rate of multiplication of fibroblasts in wounds.

Vitamins: One of these, which has been known for many years to influence the rate of wound healing, is vitamin C or ascorbic acid. It acts through regulation of collagen formation and formation of normal intercellular ground substance of the connective tissue.

8-Age of Patient: Wounds in younger persons heal considerably more rapidly than in elderly persons, and the rate of healing appears to be in inverse proportion to the age of the patient. The cause for this is unknown, but probably relates to the general reduction in the rate of tissue metabolism as the person ages.

9-Infection, severe bacterial infection slows the healing of wounds.

10- Hormonal Factors: Adrenocorticotropic hormone (ACTH) and cortisone are substances shown to interfere with the healing of wounds. Diabetes mellitus is one of the most widely recognized diseases in which there is significant, clinically evident retardation in repair of wounds after surgical procedures, including tooth extraction.

Healing of Biopsy Wound

The healing of a biopsy wound of the oral cavity is identical with the healing of a similar wound in any other part of the body and thus may be classified as either primary healing or secondary healing.

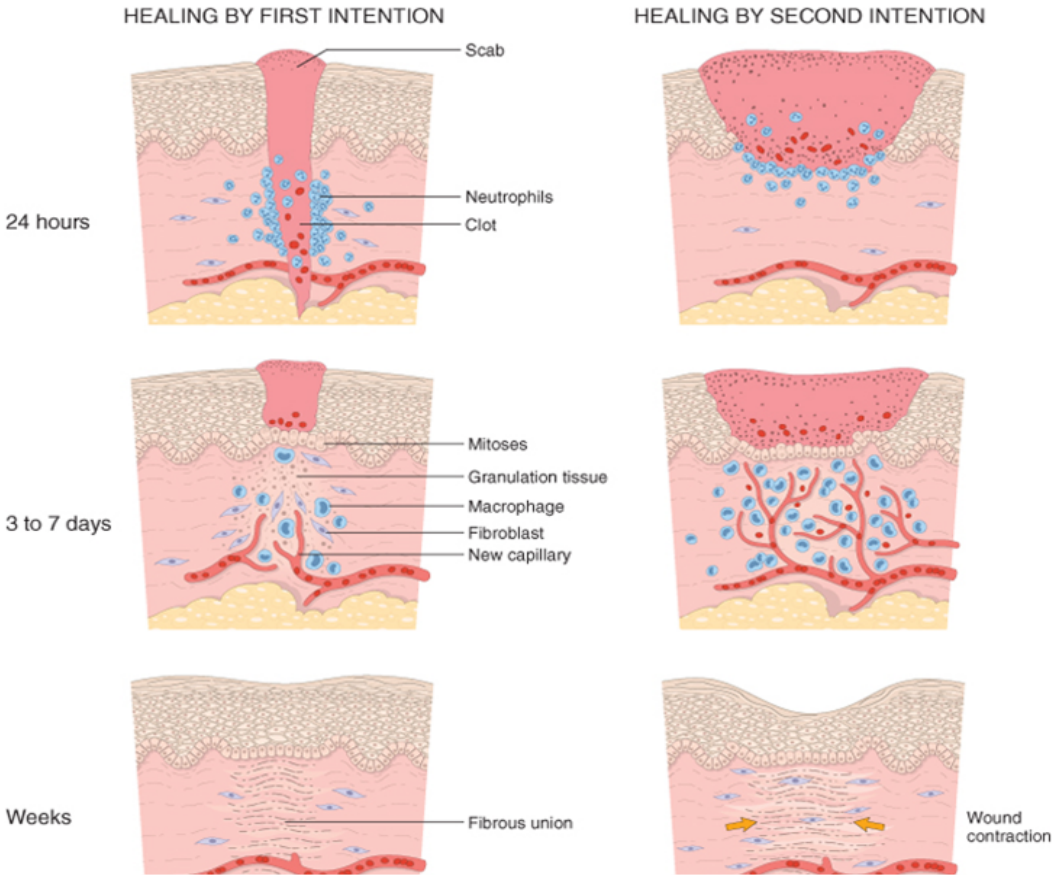
The nature of the healing process depends upon whether the edges of the wound can be brought into apposition, often by suturing, or whether the lesion must fill in gradually with granulation tissue.

Primary healing:

Healing by primary intention or healing by <u>first intention</u> is healing that occurs after the excision of a piece of tissue with the close apposition of the edges of the wound by sutures. Because there is no defect which must be filled with new tissue, this type of wound heals rapidly .

Secondary healing:

Healing by <u>second intention</u> or healing by <u>granulation</u> (the material which fills the defect during the healing process is called granulation tissue). This type of wound is a result of biopsy of a lesion or an open wound when there is loss of tissue in an area of the oral cavity in which the edges cannot be approximated, for example, removal of a lesion of the palate or a large lesion of the alveolar ridge.



Healing of extraction sockets

One of the most common oral wounds is an extraction socket after tooth removal. Wound healing in the socket follows similar principles as the soft tissue healing except that it also involves healing of the bone, namely:
(1) clotting (2) re-epithelialization (3) granulation tissue formation and (4) bone formation.
Within minutes after tooth extraction a blood clot forms into the extraction socket. Re-epithelialization starts as for any soft tissue wounds as described above. Granulation tissue also forms within a week it has replaced the blood clot. What happens next differs from soft tissue healing.

1-Osteogenic cells from the bottom and the walls of the socket are induced to migrate into the developing granulation tissue in which they differentiate and initiate bone deposition. It is likely that mesenchymal stem cells recruited locally together with bone marrow derived cells are induced for osteogenic differentiation by cytokines and growth factors released locally by platelets and inflammatory cells and bone cells.

2-In addition, wounding stimulates osteoclastic activity and remodeling at the socket walls, which process releases growth factors and cytokines that are stored in the bone matrix. Therefore, bony defect turns to bone rather than soft tissue.

3- Most of the socket is filled with bone within 8 weeks after extraction. Bone remodeling continues, however, often for 6 months or more, with great individual variation. During this remodeling phase of socket healing, dimensions of socket walls change. A significant amount of bone height and width is lost due to resorption of the socket walls.

Histological aspects:

The extraction of a tooth initiates a series of reparative processes involving both hard tissue (i.e. alveolar bone) and soft tissues (periodontal ligament, gingiva).
A gross classification of these tissues can be as following:

- **A- Blood clot (BC), consisting of erythrocytes and leukocytes embedded in a fibrin network.**
- **B- Granulation tissue (GT), rich in newly formed vascular structures, inflammatory cells and erythrocytes.**
- **C- Provisional matrix (PM), presenting densely packed mesenchymal cells, collagen fibers and vessels but no or only scattered inflammatory cells.**
- **D- Woven bone (WB), consisting of fingerlike projections of immature bone embedded in a primary spongiosa.**
- **E- Lamellar bone and bone marrow (LB/BM), i.e. lamellae of mature, mineralized bone harboring secondary osteons surrounded by marrow spaces rich in vessels, adipocytes, mesenchymal cells and inflammatory cells.**

Immediately after tooth extraction, the socket fills with blood and BC formation occurs. The BC fills the socket up to the soft tissue margins of the wound. Portions of the injured periodontal ligament, containing large numbers of mesenchymal cells, fibers and blood vessels, are in direct contact with the BC. In the center of the BC, firstly, and in the marginal portions of the BC, secondly, erythrocytes undergo lysis by coagulative necrosis.

Starting from the marginal portion of the socket, several areas of the BC are progressively replaced by GT. Later on, the residual principal fibers of the severed periodontal ligament, which are perpendicular to the surface of the hard tissue wall and inserted in the bundle bone, accompany the formation of a PM towards the center of the extraction socket. The PM replaces in part the fiber bundles of the periodontal ligament as well as residues of the BC and GT.

Healing after pulpal diseases

Inflammation of the pulp does not always result in pulpal necrosis. Resolution occurs in a considerable number of cases. Healing of pulp is the common outcome of pulpal inflammation in clinical conditions. But nevertheless, it depends on the degree of infection, inflammation, amount of the pulpal tissue involved, and the age of the patient. If the carious cavities are thoroughly cleaned and restored with suitable materials, the abscesses heal by reparative dentin formation.

When the pulp is exposed with the damage to the odontoblast layer**, healing process with dentin bridge is possible but requires recruitment of progenitor cells that can differentiate to odontoblasts. Although reparative dentinogenesis can happen spontaneously in the absence of bacteria, many materials have been used to stimulate the reparative dentin formation. Traditionally, calcium hydroxide has been used for pulp capping after exposure. More recently, mineral trioxide aggregate (MTA) has been recommended for this purpose. Nevertheless, infection of the dental pulp may result in inflammation and eventually tissue necrosis which is treated conventionally by pulpectomy and root canal treatment.**

Advances in regenerative medicine and tissue engineering along with the introduction of new sources of stem cells have led to the possibility of pulp tissue regeneration. Animal studies since 2010 carried to determine the ability of stem cell therapy to regenerate the dentine-pulp complex (DPC) and the success of clinical protocols. Stem or progenitor cells are induced to proliferate and migrate to the wound site where they differentiate into odontoblast-like cells that are able to synthesize proteins and vesicles involved in formation of reparative dentin. The origins of the stem/progenitor cells are still under investigation. Dental pulp stem cells constitute the most commonly used cell type. The majority of stem cells are incorporated into various types of scaffold and implanted into root canals. Some of the studies combine growth factors with stem cells in an attempt to improve the outcome. If the inflammation persists in the pulp, the development of reparative dentin is inhibited and pulpal necrosis may follow.

Healing after periapical diseases

Healing of periapical lesions may result in the formation of new bone or fibrosis in the involved area. In periapical lesions treated surgically, there is an outgrowth of fibroblasts and capillaries from the surrounding healthy connective tissue. Slowly this granulation tissue fills the entire defect. Osteoblasts appear in the granulation tissue towards the deeper portion adjacent to the healthy bone, and the granulation tissue is gradually replaced by bone in the course of time.

Wound Healing Around Dental Implants

The introduction of the 'modern dental implant' to dentistry has revolutionized the approach to patient care. In contrast with teeth that develop in occurrence with the surrounding periodontal tissues, dental implants are surgically placed directly into native or regenerated bone. This limits the number of cell types that migrate to, attach and differentiate on the implant surface during healing. In spite of that, soft and hard tissue healing following implant placement lead to marginal soft tissue attachment and Osseo-integration. The attachment between the peri-implant soft tissue and the implant surface plays an important role both in achieving and maintaining desired soft tissue contour around dental implants.

Osteointegration of dental implants is a very predictable procedure with success rates far above 90%, regardless of the implant loading protocol. Failure to osteointegrate or the development of peri-implant disease are often connected with patient associated factors such as smoking, diabetes and history of periodontal disease, which can all affect various phases of the initial wound healing response

Osteointigration and soft tissue healing around dental implants:

Dental implants have become part of routine treatment in oral rehabilitation. Placing an implant into the alveolar bone initiates a wound healing response that typically involves healing of both soft tissues and bone. Implant fixtures can be placed at the level of the alveolar bone crest or left above it. They can also be either covered completely with the mucosal tissue or left exposed to oral cavity with a healing abutment.

Wound healing response varies depending on the situation. In cases where an implant is placed at the level of bone with a cover screw and then completely covered with soft tissue with primary closure, the soft tissue will quickly heal following the principles described above with minimal granulation tissue formation.

1-Wound healing reaction in the osteotomy site is initiated by clot formation at the inner parts of the treads. This clot is then infiltrated by inflammatory cells, namely polymorphonuclear leukocytes and macrophages.

2-Fibroblastic progenitor cells then invade the provisional matrix and deposit granulation tissue that gets vascularized by migrating endothelial cells. These cells then differentiate to osteoblasts and start to deposit bone.

3- Bone deposition can be seen as early as 4 days after implant placement, but complete osteointegration with maximum bone–implant contact takes 1–3 months. Implant stability can be tested during healing with various devices.

4- Bone around the implant continues to remodel over the first year of implant placement and is dependent on the mechanical stress from occlusal forces.

When implants are immediately 'restored' with a healing abutment or a permanent abutment and restoration, the soft tissue healing response will differ from that associated with covered implants. In this case:

1-A blood clot forms now between the abutment or the collar of the implant and the gingival soft tissue.

2-During healing, epithelial cells from oral epithelium migrate towards the implant/abutment, flatten along the surface and create a peri-implant epithelium that mimics junctional epithelium. (The adhesion of this epithelium may not fully recapitulate that of junctional epithelium. During healing, fibroblasts apical to the peri-implant epithelium deposit collagen fibers that run parallel to the implant surface without insertion into the implant surface). This can be explained by the lack of cementum formation at the connective tissue–implant interphase.

Complications of Wound Healing:

1-Infection

Wounds may provide a portal of entry to microorganisms. Infections of the wound delay the healing process. It is a common phenomenon in maxillofacial trauma cases. The underlying systemic conditions such as diabetes mellitus, immunosuppressive state, etc. make the individual prone to infections.

2-Keloid and hypertrophic and hypertrophic scar formation

Keloids are overgrown scar tissues with no tendency for resolution, they occur in wounds, which heal without any complications. Hypertrophic scars occur in wounds where healing is delayed, these hypertrophic scars are more cellular and vascular. Keloids and hypertrophic scars are not seen in the wounds of the oral cavity. In the oral cavity, the wound remodeling rate is so high that even a normal scar is not seen most of the times.

3-Pigmentary changes:

These are common in healing of wounds on the skin. Though hypo pigmented scars are not common in the oral cavity, some lesions leave hyperpigmentation while healing (e.g. lichen planus, lichenoid reactions, etc.).

4-Cicatrization:

Refers to late reduction in the size of the scar .It is a complication due to burns of the skin.

5-Implantation cyst:

Epithelial cells may slide or get entrapped in the wound and later may proliferate to form implantation cysts.

ORAL pathology

Lec :3

Histopathology of Dental Caries

I- Enamel Caries

a-Smooth surface caries:-

The ***initial lesion (whit spot)*** form a cone (triangular) shape lesion , the apex toward DEJ and the base toward tooth surface.

The ***advanced lesion*** results from disintegration of enamel which lead to ***cavity formation***.

Ground section of an early lesion shows :-

Zone 1 =translucent zone:-

Demineralization occur, Fall in magnesium and carbonate, It's the earliest and deepest area of demineralization.

Zone 2 =Dark zone :-

Superficial to zone 1, remineralization due to repricipitation of minerals lost from zone1.

Zone 3= body of the lesion:-

Extend from surface zone to the dark zone, the area of maximal demineralization.

Zone 4 =The surface zone:-

surface zone remain unaffected because :-

1- this area is still exposed to fluoride and ca present in saliva and oral fluid.

2- ions from deeper area (diffusion outward) .

So it has higher content of fluoride , it's an area of active repricipition of minerals from plaque, and that dissolved from deeper area.

b-Pit and fissure caries:-

-It follow the enamel rod direction (perpendicular to DEJ and obliquely at cusp forming a cone shaped lesion, the apex at the outer surface and the base toward the DEJ.

-***Histologically,*** similar to smooth surface caries .

*More cavitation in pit and fissure caries than smooth surface.

1-Area of dentin involves is larger and wider.

2-Enamel is much thinner at the base of pit and fissure so lesion progress more faster lead to cavity.

II- Dentin caries :-

-It progress at much faster rate than enamel caries, (dentin more than enamel)

-Bacteria producing proteolytic enzyme are needed (acid producing bacteria in enamel caries)

-Dentin caries develops from enamel caries, enamel caries reach DEJ lead to lateral extension and greater dentinal tubule involvement , act as pathway for M.O spread to deeper area and then pulp.

-It form cone-shaped with apex toward pulp, base toward DEJ.

-Ground section shows 5 microscopic zone :-

-**zone 1=Early degeneration** :-

The earliest changes of caries infection.

-Bacterial enzyme will break down the cell membrane of the organic compound of dentin liberate lipid

-It's the deepest zone.

-**Zone 2 =translucent zone (=zone of sclerosis)**

-Band of hypermineralized dentin (=scleroting dentinal tubules)

-redeposition of Ca from the demineralization zone, and from odontoblasts (=defense mechanism).

-It's higher mineralized zone.

-Zone 3=zone of demineralization (=decalcification)

Dentin is softer than normal (= acid production of bacteria),sterile dentin (=no bacterial invasion).

-Zone 4=zone of bacterial invasion

Downward extension of bacteria, with it's multiplication with in dentinal tubules .

2types of bacteria to invade :-

Acidogenic (lactobacilli) produce acid lead to ***demineralization***.

Proteolytic produce proteolytic enzyme lead to ***organic destruction***.

Dentin soft enough to remove by hand instrument.

Coalescence of bacterial colonies in the adjacent dentinal tubules lead to irregular liquefactive foci parallel to dentinal tubules (ovoid or elliptical areas of dentin destruction filled with necrotic debris).

Zone 5 =destruction (=decomposition)of dentin.

No mineralization remain, the organic component dissolved liquifactive foci enlarge and increase in number.

Cracks or cleft appear at right angle to dentinal tubules forming transverse clefts (=coalescence of liquifactive foci on adjacent dentinal tubules).

Little remains of normal dentin architecture then cavitation occur.

Acute rapidly progressing caries that the necrotic dentin very soft, yellowish-white

Chronic caries, leathery consistency, brown-black.

Protective reaction against dental caries :-

-Mainly due to odontoblast activity.

-Not specific to dental caries, may occur due to attrition, abrasion restorative procedure.

1-Dental sclerosis :-

-Dentinal tubules sealed with calcified material to prevent bacterial penetration or invasion to pulp.

-It's minimal in acute caries and prominent in chronic caries.

By odontoblasts ca salt will deposited between pulp and DEJ irritation.

2-Reparative (tertiary, a tubular, reactionary)dentin :-

-Localized to irritated odontoblast (localized injury)

-irregular dentinal tubules, fewer in number.

-It increase depth of tissue between caries and pulp which delay pulp involvement.

-Reparative dentine main function is to seal off the injured area.

III- Root caries :-

-Root exposure to oral environment lead to root caries .
Actinomyces species present in large number, Streptococcus mutans , lactobacilli also present.

Microscopically :-

- Subsurface area with demineralization of root extending to dentin
-Hypermineralized surface layer(=zone of repricipitation of minerals removed from subsurface and of remineralization from minerals in plaque , saliva). Fluoride.
Deposit surface hypermineralization , progressive softening occur (within time) in active lesion.
Demineralization followed by bacterial invasion , fracture and loss of cementum layer.
Root caries **clinically** diagnosed as brown, saucer shaped cavity.
Occur in old age due to gum recession , bad oral hygiene.

IV- Arrested Caries :-

***Enamel:-**

-White spot arrested when adjacent tooth is removed.
-No stagnation area, lesion accessible to plaque control.
-Remineralization from saliva /topical calcifying solution application.

****Dentin :-***

Much enamel destruction (which removed by attrition and abrasion) lead to wide dentin area exposed to oral environment that result with hard polished surface, it appear as brown-black in color.
-Remineralization = from saliva /topical calcifying solution application.

****Cementum :-***

Have similar clinical appearance as above.

Immunological Aspect of dental caries :-

1-Natural active immunity (=serum and salivary Abs)is little effects by S. mutans is weakly antigenic.
2-Artificial active immunity (=vaccines):- induce Abs that cross react with heart tissue .(it produce dental caries reduction in experimental animal)
3-**Salivary IgA** act mainly by interfering with attachment of microorganism to tooth surface.

Oral Pathology

Immune-Mediated disorders

Recurrent aphthus stomatitis

Etiology: Although the cause of aphthous ulcerations is unknown, several possibilities have been postulated

There is considerable evidence that aphthous ulcers are related to a focal immune dysfunction in which T lymphocytes have a significant role.

Deficiencies of vitamin B12, folic acid, and iron as measured in serum have been found in only a small percentage of patients with aphthous ulcers. Correction of these deficiencies has produced improvement or cure in this small group. Patients with malabsorption conditions such as celiac disease (gluten-sensitive enteropathy or nontropical sprue) and Crohn's disease have been reported as having occasional aphthous-type ulcers, with the latter disease possibly related to an auto inflammatory process. In such cases, deficiencies of folic acid and factors related to underlying disease may be part of the cause.

Clinical Features. Three forms of aphthous ulcers have been recognized: minor, major, and herpetiform aphthous ulcers. All are believed to be part of the same disease spectrum, and all are believed to have a common etiology. Differences are essentially clinical and correspond to the degree of severity. All forms present as painful recurrent ulcers. Patients occasionally have prodromal symptoms of tingling or burning before the appearance of lesions. The ulcers are not preceded by vesicles and characteristically appear on the vestibular and buccal mucosa, tongue, soft

palate, fauces, and floor of mouth. Only rarely do these lesions occur on the attached gingiva and hard palate, thus providing an important clinical sign for the separation of aphthous ulcers from secondary herpetic ulcers. In patients with AIDS, however, aphthous-like ulcers may occur at any mucosal site.

Minor Aphthous Ulcers. Minor aphthous ulcers are the most commonly encountered form. This type usually appears as a single, painful, oval ulcer that is less than 0.5 cm in diameter, covered by a yellow fibrinous membrane and surrounded by an erythematous halo. Multiple oral aphthae may be seen. When the lateral or ventral surfaces of the tongue are affected, pain tends to be out of proportion to the size of the lesion. Minor aphthous ulcers generally last 7 to 10 days and heal without scar formation. Recurrences vary from one individual to another. Periods of freedom from disease may range from a matter of weeks to as long as years.

In some patients with reluctant aphthae, a diagnosis of Crohn's disease may be considered. This granulomatous disease may affect the gastrointestinal tract from mouth to anus. Oral manifestations include mucosal fissures and small, multiple, hyperplastic nodules on the buccal mucosa, producing a cobblestone appearance. Biopsy findings of these mucosal nodules show small, noncaseating granulomas characteristic of Crohn's disease. HIV-positive patients may develop minor aphthous ulcers, although proportionately more have major or herpetiform lesions.

Major Aphthous Ulcers. Major aphthous ulcers were previously thought to be a separate entity, and this form was referred to as periadenitis mucosa necrotica recurrens or Sutton's disease. It is now regarded as the most severe expression of aphthous stomatitis. Lesions are larger (>0.5 cm) and more painful and persist longer than minor aphthae. Because of the depth

of inflammation, major aphthous ulcers appear crateriform clinically and heal with scar formation. Lesions may take as long as 6 weeks to heal, and as soon as one ulcer disappears, another one starts. In patients who experience an unremitting course with significant pain and discomfort, systemic health may be compromised because of difficulty in eating and psychological stress. The predilection for movable oral mucosa is as typical for major aphthous ulcers as it is for minor aphthae. HIV-positive patients may have aphthous lesions at any intraoral site.

Herpetiform Aphthous Ulcers. Herpetiform aphthous ulcers present clinically as recurrent crops of small ulcers. Although movable mucosa is predominantly affected, palatal and gingival mucosa may also be involved. Pain may be considerable, and healing generally occurs in 1 to 2 weeks. Unlike herpes infection, herpetiform aphthous ulcers are not preceded by vesicles and exhibit no virus-infected cells. Other than the clinical feature of crops of oral ulcers, no finding can link this disease to a viral infection.

Histopathology

Because the diagnosis of these ulcers is usually evident clinically, biopsies usually are unnecessary and therefore are rarely performed. Aphthous ulcers have nonspecific microscopic findings, and no histologic features are diagnostic. At no time are virus-infected cells evident. Essentially, the same microscopic changes are found in all forms of aphthous ulcers. Studies have shown that mononuclear cells are found in submucosa and perivascular tissues in the preulcerative stage. These cells are predominantly CD4 lymphocytes, which soon are outnumbered by CD8 lymphocytes as the ulcerative stage develops. Macrophages and mast cells are common inhabitants of the ulcer.

Treatment: In patients with occasional or few minor aphthous ulcers,

usually no treatment is needed apart from a bland mouth rinse such as sodium bicarbonate in warm water to keep the mouth clean. However, when patients are more severely affected, some forms of treatment can provide significant control (but not necessarily a cure) of this disease.

Rational treatment would include drugs that can manipulate or regulate immune responses. In this category, corticosteroids currently offer the best chance for disease containment. In severely affected patients, systemic steroids may be used for immediate control.

Although nearly all topical compounds have been developed for use on the skin, it has been standard practice to prescribe these agents for use on mucous membranes. Intralesional injection of triamcinolone may be used for individual or focal problematic lesions.

Behçet's Syndrome

Behçet's syndrome is a rare multisystem inflammatory disease (gastrointestinal, cardiovascular, ocular, CNS, articular, pulmonary, dermal) in which recurrent oral aphthae are a consistent feature. Although the oral manifestations are usually relatively minor, involvement of other sites, especially the eyes and CNS, can be serious.

Clinical Features. Lesions of Behçet's syndrome typically affect the oral cavity (100% incidence), the genitalia (62% of cases), and the eyes. Other regions or systems are less commonly involved. Recurrent arthritis of the wrists, ankles, and knees may be associated. Cardiovascular manifestations are believed to result from vasculitis and thrombosis. CNS manifestations are frequently seen in the form of headaches, although infarcts have been reported.

Oral manifestations of this syndrome appear identical to the ulcers of

aphthous stomatitis. The ulcers are usually the minor aphthous form and are found in the typical aphthous distribution.

Ocular changes are noted in most patients with Behçet's syndrome. Uveitis, conjunctivitis, and retinitis are among the more common inflammatory processes.

Genital lesions are ulcerative in nature and may cause significant pain and discomfort. Painful ulcerative lesions may occur around the anus. Inflammatory bowel disease and neurologic problems have been described in some patients.

Histopathology.

T lymphocytes are prominent in the ulcerative lesions of Behçet's syndrome. However, neutrophilic infiltrates in which the cells appear within vessel walls (vasculitis) have been described. Immunopathologic support of a vascular target in this condition comes from the demonstration of immunoglobulins and complement within the vessel walls.

Diagnosis. The diagnosis of Behçet's syndrome is based on clinical signs and symptoms associated with the various regions affected. No specific findings are noted in biopsy tissue, and no supportive laboratory tests are available.

Treatment. No standard therapy is known for Behçet's syndrome. Systemic steroids are often prescribed

Immunosuppressive drugs, such as chlorambucil and azathioprine, may be used instead of or in addition to steroids. Dapsone, cyclosporine, thalidomide, interferon, and biological anti–tumor necrosis factor (TNF) agents may play a role in the treatment of these patients, depending on the degree of disease severity.

Mucosal and Skin Condition:

LICHEN PLANUS

Lichen planus is a relatively common, chronic dermatologic disease that often affects the oral mucosa. The strange name of the condition was provided by the British physician Erasmus Wilson, who first described it in 1869. Lichens are primitive plants composed of symbiotic algae and fungi. The term planus is Lat in for " flat. " Wilson probably thought that the skin lesions looked similar enough to the lichens growing on rocks to merit this designation.

A variety of medications may induce lesions that appear clinically identical to the idiopathic form of the condition: however, the term lichenoid mucositis (or lichenoid dermatitis, depending on the site involved) is probably a better name for the drug- related alterations. Similarly, foreign material that becomes inadvertently embedded in the gingiva may elicit a host response that is termed lichenoid foreign-body gingivitis.

Clinical Features

Most patient s with lichen planus are middle-aged adults. It is rare for children to be affected .Women predominate in most series of cases, usually by a 3:2 ratio over men. 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 of lichen plan us have been classically described as purple, pruritic, polygonal papules. These usually affect the flex or surfaces of the extremities. Excoriations may not be visible. despite the fact that the lesions itch , because it hurts the patient

when he or she scratches them. Careful examination of the surface of the skin papules reveals a fine, lacelike network of white lines (Wickham's striae). Other sites of extraoral involvement include the glans penis the vulvar mucosa, and the nails Essentially there are two forms of oral lesions: (1) reticular and (2) erosive. Reticular lichen planus. Reticular lichen planus is much more common than the erosive form, but the erosive form predominates in several studies. This is probably because of referral bias (because the erosive form is symptomatic).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's striae); however, the white lesions may appear as papules in some instances, 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.

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. In such cases, biopsy specimens should be obtained for light microscopic and immunofluorescent studies of perilesional tissue, because cicatricial pemphigoid and pemphigus vulgaris may appear in a similar fashion. If the erosive component is severe,

epithelial separation may occur. This results in the relatively rare presentation of bullous lichen planus.

Histopathologic Features

The histopathologic features of lichen planus are characteristic but may not be specific because other conditions such as lichenoid drug reaction, lichenoid amalgam reaction, lupus erythematosus, chronic ulcerative stomatitis, and oral mucosal cinnamon reaction may also show a similar histopathologic pattern. Varying degrees of orthokeratosis and parakeratosis may be present on the surface of the epithelium, depending on whether the biopsy specimen is taken from an erosive or reticular lesion.

The thickness of the spinous layer can also vary. The reteridges 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, band like 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.

No significant degree of epithelial atypia is expected in oral lichen planus although lesions having a superimposed candidal infection may appear worrisome. These should be reevaluated histopathologically after the candidal infection is treated.

The immunopathologic features of lichen planus are non specific. Most lesions show the deposition of a shaggy band of fibrinogen at the basement membrane zone.

Treatment and Prognosis

Reticular lichen planus typically produces no symptoms and no treatment is needed. Occasionally; Affected patients may have superimposed candidiasis. in which case they may complain of a burning sensation of the oral mucosa. Antifungal therapy is necessary in such a case. Some investigators recommend annual reevaluation of the reticular lesions of oral lichen planus.

Erosive lichen planus is often bothersome because of the open sores in the mouth because it is an immunologically mediated condition. corticosteroids are recommended. The lesions respond to systemic corticosteroids, but such drastic therapy is usually not necessary. One of the stronger topical corticosteroids (e.g.• Iluoclnonlde, betamethasone. clobetasol gel) applied several times per day to the most symptomatic areas is usually sufficient to induce healing within I or 2 weeks.

Erythema Multiforme

(EM) is an acute self-limiting hypersensitivity reaction characterized by target skin lesions and/or ulcerative oral lesions. It has been divided into two subtypes: a minor form, usually associated with an HSV trigger, and a major severe form, triggered by certain systemic drugs.

Etiology and Pathogenesis.

The basic cause of EM is unknown, although a hypersensitivity reaction is suspected. Some evidence suggests that the disease mechanism may be related to antigen-antibody complexes that are targeted for small vessels in the skin or mucosa. In about half of cases, precipitating or triggering factors can be identified. These generally fall into the two large categories

of infections and drugs. Other factors, such as malignancy, vaccination, autoimmune disease, and radiotherapy, are occasionally cited as possible triggers. Infections frequently reported include HSV infection (due to HSV types 1 and 2), TB, and histoplasmosis.

Clinical Features

EM is usually an acute, self-limited process that affects the skin or mucous membranes or both. Between 25% and 50% of patients with cutaneous EM have oral manifestations of this disease. It may on occasion be chronic, or it may be a recurring acute problem. In recurrent disease, prodromal symptoms may be experienced before any eruption. Young adults are most commonly affected. Individuals often develop EM in the spring or fall. The term erythema multiforme was coined to indicate the multiple and varied clinical appearances that are associated with cutaneous manifestations of this disease.

The classic skin lesion of EM is the target or iris lesion. It consists of concentric erythematous rings separated by rings of near-normal color. Typically, the extremities are involved, usually in a symmetric distribution. Other types of skin manifestations of EM include macules, papules, vesicles, bullae, and urticarial plaques.

Orally, EM characteristically presents as an ulcerative disease, varying from a few aphthous-type lesions to multiple superficial, widespread ulcers in EM major. Short-lived vesicles or bullae are infrequently seen at initial presentation. Any area of the mouth may be involved, with the lips, buccal mucosa, palate, and tongue being most frequently affected.

Symptoms range from mild discomfort to severe pain. Considerable Systemic signs and symptoms of headache, slightly elevated temperature, and lymphadenopathy may accompany more intense disease.

At the severe end of the EM spectrum (EM major), intense involvement of the mouth, eyes, skin, genitalia, and occasionally the esophagus and respiratory tract may be seen concurrently. This form of EM major, sometimes called Stevens-Johnson syndrome, has a strong relationship to medications, in particular analgesics, where oxicams or propionic acid derivatives have been used

Characteristically, the lips show crusting ulceration at the vermilion border that may cause pain. Superficial ulceration, often preceded by bullae, is common to all sites affected. Ocular inflammation (conjunctivitis and uveitis) may lead to scarring and blindness.

Histopathology.

The microscopic pattern of EM consists of epithelial hyperplasia and spongiosis. Basal and parabasal apoptotic keratinocytes are usually seen. Vesicles occur at the epithelium–connective tissue interface, although intraepithelial vesiculation may be seen. Epithelial necrosis is a frequent finding. Connective tissue changes usually appear as infiltrates of lymphocytes and macrophages in perivascular spaces and in connective tissue papillae.

Treatment

In EM minor, symptomatic treatment, including keeping the mouth clean with bland mouth rinses, may be all that is necessary. In EM major, topical

corticosteroids with antifungals may help control disease. The use of systemic corticosteroids remains controversial and is believed by some to be contraindicated,particularly as maintenance therapy. Acyclovir at 400 to 600 mg daily may be effective in preventing recurrences in patients who have an HSV-triggered disease, although the efficacy is not clear. Supportive measures, such as oral irrigation, adequate fluid intake, and use of antipyretics, may provide patients with substantial benefit.

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". 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 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 .

Clinical Features

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. 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. The lesions usually affect the palate, buccal mucosa, and gingivae. Sometimes they appear as lichenoid areas, but they may also look non specific or even some what 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, candidiasis, periodontal disease, and dysgeusia have been described, but the direct association of these problems with SLE remains to be proven.

Histopathologic Features

The histopathologic features of the skin and oral lesions of the various forms of lupus erythematosus show some features in common but are different enough to warrant separate discussions. The skin lesions of SLE are characterized by hyperkeratosis, often displaying keratin packed into the openings of hair follicles ("follicular plugging"). In all forms of lupus erythematosus, 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 .

Treatment and Prognosis

Patients with SLE should avoid excessive exposure to sunlight because ultraviolet light may precipitate disease activity. Mild active disease may be effectively managed using non-steroidal anti inflammatory agents combined with antimalarial drugs, such as hydroxychloroquine. For more severe, acute episodes that involve arthritis, pericarditis. thrombocytopenia. or nephritis, systemic corticosteroids are generally indicated.

Discoid Lupus Erythematosus. DLE is characteristically seen in middle age, especially in women. Lesions commonly appear solely on the skin, most commonly on the face and scalp. Oral and vermilion lesions are commonly seen, but usually in the company of cutaneous lesions. On the skin, lesions appear as disc-shaped erythematous plaques with hyperpigmented margins. As the lesion expands peripherally, the center heals, and formation of scar and loss of pigment are noted. Involvement of hair follicles results in permanent hair loss (alopecia).

Mucous membrane lesions appear in about 3% to 25% of patients with cutaneous DLE. The buccal mucosa, gingiva, and vermilion are most commonly affected. Lesions may be erythematous or ulcerative with delicate white, keratotic striae radiating from the periphery. The diagnosis of oral lesions may not be evident on the basis of clinical appearance. Progression of DLE to SLE is very unlikely, although the potential does exist.

Pemphigus Vulgaris

Pemphigus is a group of autoimmune mucocutaneous diseases

characterized by intraepithelial blister formation. It results from a breakdown or loss of intercellular adhesion, thus producing epithelial cell separation known as acantholysis. Widespread superficial ulceration following rupture of the blisters leads to painful debilitation, fluid loss, and electrolyte imbalance. Before the use of corticosteroids, death was not an uncommon outcome for patients with pemphigus vulgaris.

Clinical Features.

Lesions of pemphigus present as painful ulcers preceded by bullae. The first signs of the disease appear in the oral mucosa in approximately 60% of cases. Such lesions may precede the onset of cutaneous lesions by periods of up to 1 year. Bullae rapidly rupture, leaving a red, painful, ulcerated base. Ulcers range in appearance from small aphthous-like lesions to large maplike lesions. Gentle traction on clinically unaffected mucosa may produce stripping of epithelium, a positive Nikolsky's sign. A great deal of discomfort often occurs with confluence and ulceration of smaller vesicles of the soft palate, buccal mucosa, and floor of the mouth.

Histopathology and Immunopathology.

Pemphigus vulgaris appears as intraepithelial clefting with keratinocyte acantholysis Loss of desmosomal attachments and retraction of tonofilaments result in free-floating, or acantholytic, Tzanck cells. Bullae are suprabasal, and the basal layer remains attached to the basement membrane.

Treatment and Prognosis.

The high morbidity and mortality rates previously associated with pemphigus vulgaris have been reduced radically since the introduction of systemic corticosteroids.

Topical Steroids: Topical corticosteroids may be used intraorally as an adjunct to systemic therapy, with a possible concomitant lower dose of systemic corticosteroid.

Mucous Membrane Pemphigoid

Mucous membrane pemphigoid (MMP) is a chronic blistering or vesiculobullous disease that affects predominantly oral and ocular mucous membranes .It is also known as cicatricial pemphigoid, benign mucous membrane pemphigoid, ocular pemphigus, childhood pemphigoid, and mucosal pemphigoid; when it affects gingiva exclusively, it is referred to clinically as gingivosis or desquamative gingivitis,

Clinical Features

This is a disease of adults and the elderly and tends to affect women more than men. MMP has rarely been reported in children. Other mucosal sites that may be involved include the conjunctiva, nasopharynx, larynx, esophagus, and anogenital region. Oral mucosal lesions typically present as superficial ulcers, sometimes limited to attached gingiva . Bullae are not commonly seen because the blisters are fragile and short lived. Lesions are chronic and persistent and may heal with a scar (cicatrix)—particularly lesions of the eye. Risks include scarring of the canthus (symblepharon), inversion of the eyelashes (entropion), and resultant trauma to the cornea (trichiasis). To prevent corneal damage, many patients with ocular pemphigoid have their eyelashes permanently removed by electrolysis. With laryngeal involvement, voice alterations may result from supraglottic stenosis. Cutaneous lesions are uncommon and usually appear in the head

and neck and extremities.

Gingival lesions often present as bright red patches or confluent ulcers extending to unattached gingival mucosa with mild to moderate discomfort. Concomitant ulcers and erosions may be seen on marginal and attached gingiva. Additionally, lesions may be seen on the buccal mucosa, palate, labial mucosa, and lips. With chronicity, the pain associated with oral MMP typically diminishes in intensity. Intact epithelium, especially adjacent to ulcers, can often be stripped away with ease, leaving denuded submucosa. This is one of several mucocutaneous diseases in which a positive Nikolsky's sign may be elicited. Because of patient discomfort, routine oral hygiene is often compromised. This results in dental plaque accumulation, which in turn superimposes an additional, but nonspecific, inflammatory response.

Histopathology and Immunopathology.

MMP is a subepithelial clefting disorder with no acantholysis. In early stages, few lymphocytes are seen, but over time, the infiltrate becomes more dense and mixed.

Treatment and Prognosis.

Corticosteroids are typically used to control MMP ,Prednisone is used for moderate to severe disease, and topical steroids for mild disease and maintenance. Very high systemic doses occasionally are required to achieve significant results in some cases of recalcitrant gingival MMP. Because side effects of therapy may outweigh benefits, high-potency topical steroids are often used instead (e.g., clobetasol, betamethasone dipropionate, fluocinonide, desoximetasone

Epidermolysis Bullosa

Etiology and Pathogenesis.

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 feature common to all subtypes of epidermolysis bullosa is bulla formation from minor trauma, usually over areas of stress such as the elbows and the knees. Onset of disease is seen during infancy or early childhood for the hereditary forms, and greater with the inherited recessive forms. Blisters may be widespread and severe and may result in scarring and atrophy. Nails may be dystrophic in some forms of this disease.

Oral lesions are particularly common and severe in the recessive forms of this group of diseases and uncommon in the acquired form. Oral manifestations include bullae that heal with scar formation, a constricted oral orifice resulting from scar contracture, and hypoplastic teeth. These changes are most pronounced in the type known as recessive dystrophic epidermolysis bullosa.

Treatment and Prognosis.

The prognosis is dependent on the subtype of epidermolysis bullosa. Behavior ranges from life threatening in one of the recessive forms, known as junctional epidermolysis bullosa, to debilitating in most other forms. Therapy includes avoidance of trauma, supportive measures, and chemotherapeutic agents (none of which is consistently effective). Corticosteroids, vitamin E, phenytoin, retinoids, dapsone, and immunosuppressive agents all have been suggested as providing some

benefit to patients. More recently, IVIg and the monoclonal biologic agent, infliximab, have been associated with some therapeutic success.

Oral pathology

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.

Osteomyelitis

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.

The vast majorities of osteomyelitis cases are caused by bacterial infections and result in an expanding lytic destruction of the involved bone, with suppuration and sequestra formation. This condition (osteomyelitis) may appropriately be termed suppurative osteomyelitis, bacterial osteomyelitis or secondary osteomyelitis. Osteomyelitis may also result from bacteremia.

Another ill defined group of an idiopathic inflammatory disorder of bone that do not responds consistently to antibacterial medications and typically demonstrate sclerosis of bone without suppuration or sequestra formation. This second pattern of inflammatory bone disease is most appropriately termed primary chronic osteomyelitis but may be included under the term of diffuse sclerosing osteomyelitis. Other pattern unique patterns of inflammatory bone diseases include focal sclerosing osteomyelitis, proliferative periostits, and alveolar osteitis.

Suppurative osteomyelitis of the jaw is uncommon in developed countries, but it is a significant difficulty in developing nations. The most common cause is odontogenic infections and jaw fractures. In Africa an important cause is the presence of acute necrotizing gingivitis or NOMA.

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.

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.

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. The radiographs may be unremarkable or may demonstrate an ill-defined radiolucency. 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. 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. Because of an anatomic peculiarity, large portions of each jawbone receive their blood supply through multiple arterial loops originating from a single vessel. Involvement of this single feeder vessel can lead to necrosis of a large portion of the affected bone. 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 tissue 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 nonvital 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).

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.

DIFFUSE SCIEROSING 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

Etiology

Diffuse sclerosing osteomyelitis represents **an inflammatory** reaction in the mandible or maxilla, believed to be in response to a microorganism of low virulence. Bacteria are generally suspected as causative agents, although they are seldom specifically identified. **Chronic periodontal disease,** which appears to provide a portal of entry for bacteria, is important in the etiology and progression of diffuse sclerosing osteomyelitis. Carious non vital teeth are less often implicated.

Clinical Features

This condition may be seen in any age, in either sex, and in any race,. The disease is typified by a protracted chronic course with acute exacerbations of pain, swelling, and occasionally drainage.

Radiographically:

This process is diffuse, typically affecting a large part of the jaw. The lesion is ill defined. Early lucent zones may appear in association with sclerotic masses. In advanced stages, sclerosis dominates the radiographic picture. Periosteal thickening may also be seen. Scintigraphy may be particularly useful in evaluating the extent of this condition.

Histopathology

The microscopic changes of this condition are inflammatory, Fibrous replacement of marrow is noted; a chronic inflammatory cell infiltrate and occasionally a neutrophilic infiltrate are also seen. Bony trabeculae exhibit irregular size and shape and may be lined by numerous osteoblasts, Focal osteoclastic activity is also present. The characteristic sclerotic masses are composed of dense bone, often exhibiting numerous reversal lines.

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/infectious 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.

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, It is most common in children.

- The eponym Garré's osteomyelitis has been applied to this condition after the author, Dr. K. Garrés, who in1893 described the clinical features of 72 patients with osteomyelitis. The disease he described was most common in the femur, with only three cases occurring in the jaws. In the absence of histological and radiographic findings, which were unavailable at the time of the report, it is likely that Garrés was describing a form of recalcitrant, acute osteomyelitis that occurred in both adults and children. It was not chronic osteomyelitis with proliferative periostitis. Therefore, the term Garré's osteomyelitis, although widely used in reference to this condition, is inaccurate.

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. 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.

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.

Bisphosphonate-Associated Osteonecrosis

A similar type of jaw necrosis may be seen as a complication of bisphosphonate therapy (e.g., pamidronate, zoledronic acid). 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.

Bisphosphonates, taken for an extended period (greater than 1 year), but the patient at risk for non infectious jaw necrosis.

The typical presenting clinical symptom of bisphosphonate-associated osteonecrosis is pain, and the characteristic sign is bone exposure. The lesion usually follows tooth extraction or other form of jaw surgery, although many cases seem to be spontaneous. As with osteoradionecrosis, the mandible is more commonly affected than the maxilla.

Alveolar osteitis

(drysocket; fibrinolytic alveolitis)

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. This knowledge correlates well with the increased frequency of alveolar osteitis in association with inexperienced surgeons, traumatic extractions, oral contraceptive use and presurgical infections. In addition, inadequate irrigation at surgery and the use of tobacco products have been related to the development of the problem.

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 ext reaction of the tooth. The signs and symptoms may last from 10 to 40 days.

Treatment and Prognosis

On evaluation of the patient complaining of postextraction 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).

Oral pathology

Genetic and Metabolic diseases of bone

Genetic Bone Diseases:

1-Osteogenesis imperfecta

Osteogenesis imperfecta comprises a heterogeneous group of heritable disorders characterized by ***impairment of collagen maturation***. Collagen forms a major portion of bone, dentin, sclerae, ligaments, and skin; osteogenesis imperfecta demonstrates a variety of changes that involve these sites.

Abnormal collagenous maturation results in bone with a thin cortex, fine trabeculation, and diffuse osteoporosis.

Clinical and Radiographic Features

Osteogenesis imperfectais a rare disorder. Both autosomal dominant and recessive hereditary patterns occur, and many cases are sporadic.

In addition to bone fragility, some affected individuals also have blue sclera, altered teeth, hearing loss, long bone and spine deformities, and joint hyperextensibility.

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.

Four major types of osteogenesisimperfecta arc recognized

1-Type I osteogenesisimperfecta.

It is the most common and mildest form. It is inherited as an autosomal dominant trait. Characterized by osteoporosis, bone fragility, blue sclera and hearing loss in adolescents and adults, dentinogenesis imperfecta.

2-Type II osteogenesis imperfecta:

It 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.

3-Type IIIosteogenesis imperfecta:

Both autosomal dominant and recessive hereditary patterns are noted. It demonstrates moderately severe to severe bone fragility. Characterized by skeletal deformity. Discoloration is present, it fades as the child grows older. Hearing loss are common. Fractures may be present at birth, but there is a low mortality In Infancy. Blue sclera at birth but the color normalize with age adolescents and adults are with normal sclera. Dentinogenesis imperfecta may be found in some patients.

4-Type IV osteogenesis imperfect:

This variant is inherited as an autosomal dominant trait.It is associated with mild to moderately severe bone fragility. Bone fragility without other classic features of OI, normal color sclera. Some of the patients have opalescent dentin: others have normal teeth.

Histopathologic Features

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 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.

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.

2-Osteopetrosis (marble bone disease)

Is uncommon hereditary bone condition characterized by generalized symmetric increase in skeletal density and defective bone resorption. The characteristic feature is an **absence of physiologic bone resorption caused by reduced osteoclastic activity.** The number of osteoclasts present is often increased; however, because of their failure to function normally, bone is not resorbed.

The lack of bone remodeling results in accumulation of bone mass and manifest itself in skeletal disturbances, including sclerosis of bone marrow, decrease hemopoietic activity and growth retardation.

It can be divided into:

1-**Infantile-malignant**: it is inherited **as autosomal recessive** in nature and is fatal within 2-3 years of life if not treated.

2-**Intermediate autosomal recessive type:** nonfatal but clinically aggressive with onset usually within the first decade.

3-**Autosomal dominant form:**is the least severe form, with full life expectancy but with considerable morbidity resulting from orthopedic alteration.

Clinical features: Bone pain is the most common symptom. Cranial nerve compression due to narrowing of cranial foramina may result in blindness, deafness and facial paralysis. The normal bone is replaced by dense poorly structured fragile bone and has propensity for pathologic fractures. Excessive endosteal bone formation result in aneamia and pancytopenia. The patient may die as a result of anemia or secondary infection.

Dental findings: Include, delayed eruption, congenitally missing teeth, unerupted and malformed teeth. Decreased alveolar bone production with thickened periodontal ligament and marked mandibular prognathisim, elevated caries index due to enamel hypoplasia, increase development of osteomylitis resulting from inadequate host response because of the diminished vascular supply of osteopetrotic bone.

Radiographic findings:

An increase in bone density of the whole skeleton with no distinction between cortical and medullary bone. Jaw bone involvement is variable the bone appears so dense that dental root morphology in invisible on radiographs.

The laboratory values of blood indicate the type of anemia. **Calcium, phosphorus and alkaline phosphatase are normal.**

Histopathology: The involved bone showing thickened cortices and reduced marrow cavities.Tortuous lamellar trabeculae replacing the cancellous portion of the bone. Numerous osteoclasts may be seen, but there is no evidence that they function because Howship's lacunae are not visible.

Treatment: Because of the mild severity of the disease, adult osteopetrosis is usually associated with long- term survival. Bone marrow transplantation is the only hope for permanent cure. Recent medical advances designed to increase osteoclastic activity.

Dental extraction should be done in conjunction with antibiotic therapy to prevent osteomyelitis.

3-Cleidocranial dysplasia:(cleidocranial dysostosis).

Best known for its **dental** and **clavicular abnormalities**,cleidocranial dysplasia is a disorder of bone. 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.
It is aplasia or hypoplasia of the clavicles, it has autosomal-dominant mode of inheritance, characterized by craniofacial malformations, the presence of numerous supernumerary and unerupted teeth.

Clinical features:
1- Hypoplasia, Malformation, absence of clavicle
2- Short stature, Large head, Frontal bossing
3-Depressed nasal bridge
4- Open skull suture and fontanels

Oral findings of cleidocranial dysplasia
1-Cleft palate or narrow palate
2-Unerupted permanent and supernumery teeth
3- Narrow ascending mandibular ramus
4- Thin zygomatic arch
6-Maxillary hypoplasia gives mandible a relatively prognathic appearance

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.

4-Cherubism (discussed with the giant cell lesions)

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. .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

Once the diagnosis is established,by incisional biopsy, 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. 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 distinguishthe idiopathic lesions from those of inflammatory origin, confusion in terminology has resulted.

Clinical and Radiographic Features

the prevalence appears to be approximately slightly increased frequency in blacks and Asians. No significant sex predilection is seen. A 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.

Idiopathic osteosclerosis in variably asymptomatic, 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.

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. A radiolucent rim does not surround the radiodense area

Histopathologic Features

In the few microscopic studies that have been reported, the lesion consists of dense lamellar bone with scant fibrofatty marrow. Inflammatory cells are absent.

Diagnosis

Usually a diagnosis of idiopathic osteosclerosis may be 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.

Metabolic Bone Diseases

1-Hyperparathyroidism(discussed with the giant cell lesions)

2-Paget's disease of bone (osteitis deformans)

It is a chronic slowly progressive bone condition .It is a disease characterized by uncoordinated resorption and deposition of bone, producing larger but weaker bones. The cause of Paget's disease is unknown, but inflammatory, genetic mutation, viral (as paramyxovirus), or endocrine factors may be contributing agents .

A relationship to altered osteoclast development and function has been suggested. Paget's disease generally progresses through several stages including an initial resorptive phase, followed by a vascular phase, and by a sclerosing phase.

Clinical and Radiographic Features

1-The disease principally affects older people and is rarely encountered in patients younger than 40 years of age.

2- Men are affected more often than women

3-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.

4-Paget's disease affecting the skull generally leads to a progressive increase in the circumference of the head

5-Bones most affected are sacrum, spine, skull, femur and pelvis.

6-It is wide spread and symmetrical.

7-The most serious concern is the **involvement of base of the skull**, in this location lead to narrowing of various foramina and this can result in compression of the spinal cord and cranial nerves and lead to **facial paralysis, blindness and deafness.**

DENTAL FINDINGS: Jaw involvement is present in approximately 17% of patients diagnosed with Paget's disease.

1-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).

2-Nasal obstruction, enlarged turbinates, obliterated sinuses, and deviated septum may develop secondary to maxillary involvement.

3-The alveolar ridges tend to remain symmetric but become grossly enlarged.

4- If the patient is dentulous, the enlargement causes spacing of the teeth.
5-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. 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.

Asymptomatic disease often is discovered in radiographs taken for unrelated reasons or from an unexpected elevation in serum alkaline phosphatase.

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 **"jigsaw puzzle**." or **"mosaic."** appearance of the bone. In the less active phases, large masses of dense bone showing prominent reversal lines are present.

Diagnosis

Patients with Paget's disease show: elevations in serum alkaline phosphatase levels but usually have normal blood calcium and phosphorus levels. 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.

Oral Pathology

ODONTOGENIC CYSTS

Odontogenic cysts and tumors constitute an important aspect of oral and maxillofacial pathology.

With rare exceptions, epithelium- lined cysts in bone are seen only in the jaws. Other than a few cysts that may result from the inclusion of epithelium along embryonic lines of fusion, most jaw cysts are lined by epithelium that is derived from odontogenic epithelium. These are referred to as odontogenic cysts. Odontogenic cysts are sub classified as developmental or inflammatory in origin. Developmental cysts are of unknown origin. but they do not appear to be the result of an inflammatory reaction. Inflammatory cysts are the result of inflammation.

DEVELOPMENTAL

1. **Dentigerous cyst**
2. **Eruption cyst**
3. **Odontogenic keratocyst**
4. **Orthokeratinized odontogenic cyst**
5. **Gingival (alveolar) cyst of the newborn**
6. **Gingival cyst of the adult**
7. **Lateral periodontal cyst**
8. **Calcifying odontogenic cyst "**
9. **Glandular odontogenic cyst**

INFLAMMATORY

1. Periapical (radicular) cyst

2. Residual periapical (radicular) cyst

3. Buccal bifurcation cyst

A *cyst* is defined as an epithelial-lined pathologic cavity. Cysts of the maxilla, mandible, and perioral regions vary markedly in histogenesis, incidence, behavior, and treatment. Cysts are divided into odontogenic cysts, non odontogenic cysts, pseudocysts, and neck cysts. In contrast to true cysts, pseudocysts lack an epithelial lining.

Dentigerous Cyst

Dentigerous or follicular cysts are the **second most common type of odontogenic cyst**, and the **most common developmental cyst of the jaws**. In children from 2 to 14 years of age, dentigerous cysts account for 49% of intraosseous cystic lesions, with eruption cysts, odontogenic keratocysts, and radicular cysts accounting for more than 10% each. **By definition, a dentigerous cyst is attached to the tooth cervix at the enamel-cementum junction, and it encloses the crown of the unerupted tooth**.

Etiology and Pathogenesis. A dentigerous cyst develops from proliferation of the enamel organ remnant or reduced enamel epithelium.

As with other cysts, expansion of the dentigerous cyst is related to an increase in cyst fluid osmolality and the release of bone-resorbing factors.

Clinical Features. Dentigerous cysts are most commonly seen in association with **third molars** and **maxillary canines**, which are the most commonly impacted teeth. The highest incidence of dentigerous cysts occurs during the **second and third decades**. A greater incidence in males has been noted, with a ratio of 1.6: 1 reported. Symptoms generally are absent, and delayed eruption is the most common indication

of dentigerous cyst formation. This cyst is capable of achieving significant size, occasionally with associated cortical bone expansion, but rarely does it reach a size that predisposes the patient to a pathologic fracture.

Radiographically

a dentigerous cyst presents as a **well-defined, unilocular radiolucency** with corticated margins in association with the **crown of an unerupted tooth**. The unerupted tooth is often displaced. These cysts range in size from several millimeters to several centimeters, where they may compromise jawbone integrity and produce facial asymmetry. In the mandible, associated radiolucency may extend superiorly from the third molar site into the ramus or anteriorly and inferiorly along the body of the mandible. In maxillary dentigerous cysts involving the canine region, extension into the maxillary sinus or to the orbital floor may be noted. Resorption of roots of adjacent erupted teeth may occasionally be seen.

The cyst-to-crown relationship shows several radiographic variations. **In the central** variety, which is the most common, the cyst surrounds the crown of the tooth and the crown projects into the cyst. **The lateral *variety*** is usually associated with mesioangular impacted mandibular third molars that are partially erupted. The cyst grows laterally along the root surface and partially surrounds the crown. In the **circumferential *variant***, the cyst surrounds the crown and extends for some distance along the root so that a significant portion of the root appears to lie within the cyst. Rarely, a third molar may be displaced to the lower border of the mandible or higher up into the ascending ramus. Maxillary anterior teeth may be displaced into the floor of the nose, and other maxillary teeth may be moved through the maxillary sinus to the floor of the orbit. Dentigerous cysts may displace the involved tooth for a considerable distance. Root resorption of adjacent erupted teeth can occur.

A variant of the dentigerous cyst arising at the bifurcation of molar teeth is the ***paradental cyst* or *buccal bifurcation cyst***. Originally, this cyst was described along

the buccal root surface of partially erupted mandibular third molar teeth, but later, .Radiographically, paradental cysts are characterized as well-circumscribed radiolucencies in the buccal bifurcation region. Often buccal tipping of the crown can be demonstrated by occlusal radiography.

Histopathology:

Microscopically, the dentigerous cyst is formed by a fibrous connective tissue wall and is lined by stratified squamous epithelium. In an uninflamed dentigerous cyst, the epithelial lining is nonkeratinized and tends to be approximately four to six cell layers thick. On occasion, numerous mucous cells, ciliated cells, and, rarely, sebaceous cells may be found in the lining of the epithelium. The epithelium–connective tissue junction is generally flat, although in cases of secondary inflammation, epithelial hyperplasia may be noted.

Treatment:

Removal of the associated tooth and enucleation of the pericoronal soft tissue component constitute definitive therapy in most instances. In cases in which cysts affect significant portions of the mandible, an acceptable early treatment approach involves exteriorization or marsupialization of the cyst to allow for decompression and subsequent shrinkage of the lesion, thereby reducing the extent of surgery to be done at a later date.

Potential complications of untreated dentigerous cysts include transformation of the epithelial lining into an ameloblastoma and, rarely, carcinomatous transformation of the epithelial lining. It has been suggested that the presence of mucous cells may indicate the potential for development of the rare intraosseous mucoepidermoid carcinoma.

Odontogenic Keratocyst/Keratocystic Odontogenic Tumor

Odontogenic keratocysts (OKCs) or keratocystic odontogenic tumors (KCOTs) may exhibit aggressive clinical behavior, a significant recurrence rate, and an association with *nevoid basal cell carcinoma syndrome (NBCCS).* They are found anywhere in the jaws and can radiographically mimic other types of cysts. Microscopically, however, they have a consistent and unique appearance.

Etiology and Pathogenesis. It is generally agreed that OKCs/KCOTs develop from dental lamina remnants in the mandible and maxilla. However, origin of this cyst from extension of basal cells of the overlying oral epithelium has also been suggested

This cyst shows a different growth mechanism and biologic behavior from the more common dentigerous cyst and radicular cyst. Most auth ors believe that dentigerous and radicular cysts continue to enlarge as a result of increased osmotic pressure within the lumen of the cyst. This mechanism does not appear to hold true for odontogenic keratocysts. and their growth may be related to unknown factors inherent in the epithelium itself or enzymatic activity in the fibrous wall. Several investigators suggest that odontogenic keratocysts be regarded as benign cystic neoplasms rather than cysts. Although there are wide variations in the reported frequency of odontogenic keratocysts compared with that of other types of odontogenic cysts. *several* studies that include large series of cysts indicate that odontogenic keratocysts make up 3% to II% of all odontogenic cysts.

Clinical Features:

OKCs/KCOTs are relatively common jaw cysts. They occur at any age and have a peak incidence within the second and third decades. Lesions found in children are often reflective of multiple cysts as a component of NBCCS. OKCs/KCOTs represent

5% to 15% of all odontogenic cysts. Approximately 5% of patients with OKCs/KCOTs have multiple cysts, and another 5% have NBCCS.

OKCs /KCOTs are found in the mandible in approximately a 2 : 1 ratio. In the mandible, the posterior portion of the body and the ramus region are most commonly affected, and in the maxilla, the third molar area is most commonly affected.
Radiographically, an OKC/KCOT characteristically presents as a well-circumscribed radiolucency with smooth radiopaque margins. Multilocularity is often present and tends to be seen more commonly in larger lesions. Most lesions, however, are unilocular, with as many as 40% noted adjacent to the crown of an unerupted tooth (dentigerous cyst presentation). Approximately 30% of maxillary and 50% of mandibular lesions produce buccal expansion. Mandibular lingual enlargement is occasionally seen.

Histopathology:

The epithelial lining is uniform, generally ranging from 6 to 10 cell layers thick. The basal layer exhibits a characteristic palisaded pattern with polarized and intensely stained nuclei of uniform diameter. The luminal epithelial cells are parakeratinized and produce an uneven or corrugated profile. Focal zones of orthokeratin are occasionally seen. Additional histologic features that may occasionally be encountered include budding of the basal cells into the connective tissue wall and microcyst formation. The fibrous connective tissue component of the cyst wall is often free of an inflammatory cell infiltrate and is relatively thin. The epithelium–connective tissue interface is characteristically flat with no epithelial ridge formation. All so-called primordial cysts (cyst in place of a tooth), when examined microscopically, are OKCs/KCOTs.

An *orthokeratinized odontogenic cyst* has been described and is about one twentieth as common as the OKC/KCOT. Histologic distinction between parakeratinized and orthokeratinized cysts is made because the latter type of cyst is less clinically

aggressive, has a lower rate of recurrence, and generally is not syndrome associated. In the orthokeratotic odontogenic cyst, a prominent granular layer is found immediately below a flat, noncorrugated surface. The basal cell layer is less prominent and has a more flattened or squamoid appearance in comparison with the parakeratotic type.

Treatment and Prognosis:

Surgical excision with peripheral osseous curettage or ostectomy is the preferred method of management. This more aggressive approach for a cystic lesion is justified by the high recurrence rate associated with OKCs/KCOTs. Some have advocated marsupialization to permit cyst shrinkage, followed by enucleation as an alternative.

The recurrence rate of 10% to 30% appears to be associated with several physical factors. The friable, thin connective tissue wall of the cyst may lead to incomplete removal. Small dental lamina remnants or satellite cysts in the bone adjacent to the primary lesion may contribute to recurrence

Follow-up examinations are important for patients with this lesion. Patients should be evaluated for completeness of excision, new keratocysts, and NBCCS. Most recurrences become clinically evident within 5 years of treatment. Aside from the recurrence potential, ameloblastic transformation is a rare complication. Patients with multiple keratocysts have a significantly higher rate of recurrence than those with single keratocysts (30% and 10%, respectively).

Nevoid basal cell carcinoma syndrome (gorlin syndrome)

Nevoid basal cell carcinoma syndrome (Gorlin syndrome) is an autosomal dominant inherited condition that exhibits high penetrance and variable expressivity. It is caused

by mutations In patched (PTCH) , a tumor suppressor gene that has been mapped to chromosome 9q22,3-q31, The chief components are multiple basal cell carcinomas of the skin , odontogenic keratocysts, intracranial calcification, and rib and vertebral anomalies. Many other anomalies have been reported in these patients and probably also represent manifestations of the syndrome, The prevalence of Gorlin syndrome is estimated to be about 1 in 60,000.

Clinical and Radiographic Features

The patient often has a characteristic facies, with frontal and temporoparietal bossing, which results in an increased cranial circumference, The eyes may appear widely separa ted, and many patients have true mild ocular hypertelorism. Mild mandibular prognathism is also commonly present. Basal cell carcinomas of the skin are a major component of the syndrome. They usually begin to appear at puberty or in the second and third decades of life, although they can develop in young children. The tumors may vary *from* flesh- colored papules to ulcerating plaques. They are often appear on non-sun exposed skin but are most commonly located in the mid face area. The number of skin tumors may vary from only a few to many hundreds. Blacks with the syndrome tend to have fewer basal cell carcinomas than whites, probably because of protective skin pigmentation. Palmar and plantar pits are present in about 65% of patients. These punctate lesions represent a localized retardation of the maturation of basal epithelial cells. Basal cell carcinomas may develop at the base of the pits.

Lateral Periodontal Cyst

A lateral periodontal cyst is a nonkeratinized developmental cyst occurring adjacent or lateral to the root of a tooth. *Gingival cysts of the adult* are histogenetically and pathologically similar and are also discussed here.

Etiology and Pathogenesis:

The origin of this cyst is believed to be related to proliferation of rests of dental lamina. The lateral periodontal cyst has been pathogenetically linked to the gingival cyst of the adult; the former is believed to arise from dental lamina remnants within bone, and the latter from dental lamina remnants in soft tissue between the oral epithelium and the periosteum (rests of Serres). .

Clinical Features:

Most lateral periodontal cysts and gingival cysts of the adult occur in the mandibular premolar and cuspid regions and occasionally in the incisor area. In the maxilla, lesions are noted primarily in the lateral incisor region. A distinct male predilection has been noted for lateral periodontal cysts, with a greater than 2: 1 distribution. Gingival cysts show a nearly equal gender predilection. The median age for both types of cysts is between the fifth and sixth decades of life, with a range of 20 to 85 years for lateral periodontal cysts, and 40 to 75 years for gingival cysts of the adult.
Clinically, a gingival cyst appears as a small soft tissue swelling within or slightly inferior to the interdental papilla. It may assume a slightly bluish discoloration when it is relatively large. Most cysts are less than 1 cm in diameter. Radiography reveals no findings.

A lateral periodontal cyst presents as an asymptomatic, well-delineated, round or teardrop-shaped unilocular (and occasionally multilocular) radiolucency with an opaque margin along the lateral surface of a vital tooth root. Root divergence is rarely seen. The term *botryoid odontogenic cyst* is sometimes used when the lesion is multilocular.

Histopathology:

Both the lateral periodontal cyst and the gingival cyst of the adult are lined by a thin, non keratinized epithelium. Clusters of glycogen-rich, clear epithelial cells may be noted in nodular thickenings of the cyst lining.

Treatment and Prognosis. Local excision of both gingival and lateral periodontal cysts is generally curative. The multilocular variant, botryoid odontogenic cyst, seems to have increased recurrence potential. Follow-up, therefore, is suggested for treated multilocular odontogenic cysts.

Gingival Cyst of the Newborn

Gingival cysts of the newborn are also known as *dental lamina cysts of the newborn*, or *Bohn's nodules*. These cysts typically appear as multiple nodules along the alveolar ridge in neonates. It is believed that fragments of the dental lamina that remain within the alveolar ridge mucosa after tooth formation proliferate to form these small, keratinized cysts. In the vast majority of cases, these cysts are self-limiting and degenerate, and they involute or rupture into the oral cavity within a few weeks to a few months.

Histologically:

This cyst is lined by a bland stratified squamous epithelium. Treatment is not necessary because nearly all involute spontaneously or rupture before the patient is 3 months of age. Similar epithelial inclusion cysts may occur along the midline of the palate *(palatine cysts of the newborn*, or *Epstein's pearls).* These cysts are of developmental origin and are derived from epithelium that is included in the fusion line between the palatal shelves and the nasal processes. No treatment is necessary because they fuse with the overlying oral epithelium, discharge their contents, and resolve spontaneously.

Eruption Cyst

An eruption cyst results from fluid accumulation within the follicular space of an erupting tooth. The epithelium lining this space is simply reduced enamel epithelium. With trauma, blood may appear within the tissue space, forming an *eruption hematoma*. No treatment is needed because the tooth erupts through the lesion. Subsequent to eruption, the cyst disappears spontaneously without complication.

Glandular Odontogenic Cyst

The rare glandular odontogenic cyst, or *sialo-odontogenic cyst,* was first described in 1987 and has some histologic features that suggest a mucus-producing salivary gland tumor (low-grade mucoepidermoid carcinoma).

Clinical Features:

A strong predilection is seen for the mandible (80%), especially the anterior mandible. Maxillary lesions tend to be localized to the anterior segment. A slow growth rate is characteristic and symptoms are absent. Jaw expansion is not uncommon, particularly in association with mandibular lesions. The gender ratio is approximately 1:1. The mean age is 50 years, with a wide age range from the second through ninth decades.

Radiographic Features:

Most cases are radiographically multiloculated. In cases in which a unilocular radiolucency has been noted initially, recurrent lesions have tended to be multiloculated. Lesions that have been reported have exhibited a wide variation in size, from smaller than 1 cm to involving most of the mandible bilaterally. Radiographic margins are well defined and sclerotic and scalloped. Teeth may be displaced, and root resorption is noted in some cases. More aggressive lesions have shown an ill-defined peripheral border.

Histopathology:

this multilocular cyst is lined by nonkeratinized epithelium with focal thickenings in which the epithelial cells assume a swirled appearance. The epithelial lining consists of cuboidal cells, often with cilia at the luminal surface. Mucous cells are clustered in the cyst lining along with mucin pools. The overall histomorphology is reminiscent of a cystic low-grade mucoepidermoid carcinoma.

Treatment and Prognosis. This lesion can be considered locally aggressive; therefore, surgical management should be dictated by the clinical and radiographic extent of the disease. Where adequate healthy bone remains beyond the extent of the cystic lesion, peripheral curettage or marginal excision is appropriate. Long-term follow-up is essential given the local aggressiveness and recurrence rate (approximately 25%) of this lesion.

Calcifying Odontogenic Cyst

The calcifying odontogenic cyst is an uncommon lesion that demonstrates considerable histopathologic diversity and variable clinical behavior .

Lesions with a cystic component represent 85% of the cases, whereas a solid pattern reminiscent of a neoplastic process is seen in 15%. A summary of the basic features follows:

• Cystic, nonproliferative. In this predominantly cystic lesion, the epithelial lining may only be a few cells thick. Sparse dentinoid may be present, but no other hard tissues are seen. Such lesions constitute approximately 45% of all cystic calcifying odontogenic cysts.

• Cystic, proliferative/ameloblastomatous. A prominent central cystic component is usually associated with various satellite cysts in the wall. Odontogenic epithelial proliferations that superficially resemble ameloblastoma extend into the lumen as well as the connective tissue wall of the lesion.

• Odontoma-associated. Odontoma-like tissues are seen in the wall of the lesion.

• Epithelial odontogenic ghost cell tumor. This form has a growth pattern that is most consistent with a neoplasm, characterized by ameloblastoma-like strands and islands of odontogenic epithelium that infiltrate the connective tissue. Varying amounts of an eosinophilic calcified material (dentinoid) are typically present; thus, this lesion has been termed dentinogenic ghost cell tumor, although epithelial odontogenic ghost cell tumor and odontogenic ghost cell tumor are other names that have also been used.

Etiology and Pathogenesis:

COCs are believed to be derived from odontogenic epithelial remnants within the gingiva or within the mandible or maxilla. *Ghost cell keratinization,* the characteristic microscopic feature of this cyst, is also a defining feature of the cutaneous lesion known as *calcifying epithelioma of Malherbe,* or *pilomatrixoma.* In the jaws, ghost cells may be seen in other odontogenic tumors, including odontomas, ameloblastomas, adenomatoid odontogenic tumors, ameloblastic fibro-odontomas, and ameloblastic fibromas. Mutations of genes in the WNT signaling pathway, including the beta-catenin gene, have been reported in COCs.

Clinical Features:

A wide age range has been reported for this cyst, with a peak incidence in the second decade. It usually appears in individuals younger than 40 years of age and has a decided predilection for females. More than 70% of COCs are seen in the maxilla. Rarely, COCs may present as localized extraosseous masses involving the gingiva. Those presenting in an extraosseous or peripheral location are usually noted in individuals older than 50 years of age and are found anterior to the first molar region.
Radiographically, COCs may present as unilocular or multilocular radiolucencies with discrete, well-demarcated margins. Within the radiolucency may be scattered, irregularly sized calcifications. Such opacities may produce a salt-and-pepper type of pattern, with an equal and diffuse distribution. In some cases,

mineralization may develop to such an extent that the radiographic margins of the lesion are difficult to determine.

Histopathology:

Most COCs present as well-delineated cystic proliferations with a fibrous connective tissue wall lined by odontogenic epithelium. Intraluminal epithelial proliferation occasionally obscures the cyst lumen, thereby producing the impression of a solid tumor. The epithelial lining is of variable thickness. The basal epithelium may be prominent focally, with hyperchromatic nuclei and a cuboidal to columnar pattern. Above the basal layer are more loosely arranged epithelial cells, sometimes resembling the stellate reticulum of the enamel organ. The most prominent and unique microscopic feature is the presence of so-called ghost cell keratinization. Ghost cells are anucleate and retain the outline of the cell membrane. These cells undergo dystrophic mineralization characterized by fine basophilic granularity, which may eventually result in large sheets of calcified material. On occasion, ghost cells may become displaced in the connective tissue wall, eliciting a foreign body giant cell response.

Treatment and Prognosis. Because of the unpredictable biological behavior of this lesion, treatment is usually more aggressive than simple curettage. Patients should be monitored following treatment because recurrences are not uncommon. Management of the extraosseous or peripheral variant is conservative because recurrence is not characteristic.

Oral Pathology

Lec-12

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

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.

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 one 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.

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. Malignant lesions should be managed as carcinomas.

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 molar-ramus 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 so-called 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.

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.

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 forms 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.

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.

MESENCHYMAL TUMORS

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 osteoblastorna, 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 lymphnodes 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

CLINICAL FEATURES

Age over 60 years; women affected more often than men

Either jaw

Occasionally painful

HISTOPATHOLOGY

Nests/cords of clear cells, some palisades

Some glycogen; mucin negative

MICROSCOPIC DIFFERENTIAL DIAGNOSIS

Calcifying epithelial odontogenic tumor

Mucoepidermoid carcinoma

Renal cell carcinoma

BEHAVIOR

Recurrence and metastasis (neck nodes/lung)

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 nonkeratinized mucosa, whereas recurrent herpes simplex infections occur almost exclusively on the keratinized mucosa.

In general, oral mucosal lesions could be divided into:

- Oral infections
  - Fungal
  - Bacterial
  - Viral
- Vesiculobullous diseases
- Ulcerative conditions
- White lesions

To better describe the appearances of lesions and communicate these features to others, 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.

Microscopical changes of oral mucosa:

- Divided into epithelial and connective tissue changes

<u>Epithelial changes:</u>

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. An increase in the prickle cell layer is termed (acanthosis).

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:

Viral infections:

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. Physical contact with an infected individual or with body fluids is the typical route of HSV inoculation and transmission.

During the primary infection, only a small percentage of individuals show clinical signs and symptoms of infectious systemic disease, whereas a vast majority experience only subclinical disease. After resolution of primary herpetic gingivostomatitis, the virus is believed to migrate, through some unknown mechanism, to the trigeminal ganglion.

Reactivation of virus may follow exposure to sunlight (“fever blisters”), exposure to cold (“cold sores”), trauma, stress, or immunosuppression causing a secondary or recurrent infection.

Clinical Features

Primary Herpetic Gingivostomatitis. Primary disease is usually seen in children, although adults who have not been previously exposed to HSV may be affected. The vesicular eruption may appear on the skin, vermilion, and oral mucous membranes. Intraorally, lesions may appear on any mucosal surface. This is in contradistinction to the recurrent form of the disease, in which lesions are confined to the lips, hard palate, and gingiva. The primary lesions are accompanied by fever, arthralgia, malaise, anorexia, headache, and cervical lymphadenopathy.

After the systemic primary infection runs its course of about 7 to 10 days, lesions heal without scar formation. By this time, the virus may have migrated to the trigeminal ganglion to reside in a latent form.

Secondary, or Recurrent, Herpes Simplex Infection. Secondary herpes represents the reactivation of latent virus. Antibodies to HSV are present in a large majority of the population (up to 90%), and up to 40% of this group may develop secondary herpes.

Patients usually have prodromal symptoms of tingling, burning, or pain in the site at which lesions will appear. Within a matter of hours, multiple fragile and short-lived vesicles appear. These become unroofed and unite to form maplike superficial ulcers. The lesions heal without scarring in 1 to 2 weeks and rarely become secondarily infected. Regionally, most secondary lesions appear on the vermilion and surrounding skin. This type of disease is usually referred to as herpes labialis. Intraoral recurrences are almost always restricted to the hard palate or gingiva.

Herpetic Whitlow. Herpetic whitlow is a primary or a secondary HSV infection involving the finger(s). Before the universal use of examination gloves, this type of

infection typically occurred in dental practitioners who had been in physical contact with infected individuals. Contact could result in a vesiculoulcerative eruption on the digit (rather than in the oral region), along with signs and symptoms of primary systemic disease. Pain, redness, and swelling are prominent with herpetic whitlow and can be very pronounced. Vesicles or pustules eventually break and become ulcers. The duration of herpetic whitlow is protracted and may be as long as 4 to 6 weeks.

Histopathology. Microscopically, intraepithelial vesicles containing exudate, inflammatory cells, and characteristic virus-infected epithelial cells are seen. Virus-infected keratinocytes contain one or more nuclear inclusions.

Treatment: Symptomatic. In severe cases, systemic aciclovir or valaciclovir.

Varicella-zoster virus infection

Primary varicella-zoster virus (VZV) infection is known as varicella or chickenpox; secondary or reactivated disease is known as herpes zoster or shingles

Varicella is believed to be transmitted predominantly through the inhalation of contaminated droplets. The condition is very contagious and is known to spread readily from person to person.

Clinical features

Varicella

Fever, chills, malaise, and headache may accompany a rash that involves primarily the trunk and head and neck. The rash quickly develops into a vesicular eruption that becomes pustular and eventually ulcerates.

The infection is self-limiting and lasts several weeks. Oral mucous membranes may be involved in primary disease and usually demonstrate multiple shallow ulcers that are preceded by vesicles.

Herpes zoster Herpes Zoster. Zoster is essentially a condition of the older adult population and of individuals who have compromised immune responses. The sensory nerves of the trunk and head and neck are commonly affected. Involvement of various branches of the trigeminal nerve may result in unilateral oral, facial, or ocular lesions. Involvement of facial and auditory nerves produces the *Ramsay Hunt syndrome*, in which facial paralysis is accompanied by vesicles of the ipsilateral external ear, tinnitus, deafness, and vertigo.

After several days of prodromal symptoms of pain and/or paresthesia in the area of the involved dermatome, a well-delineated unilateral maculopapular rash appears. This may occasionally be accompanied by systemic symptoms. The rash quickly becomes vesicular, pustular, and then ulcerative. Remission usually occurs in several weeks.

Histopathology:

Essentially the same as those with HSV

Treatment:

For varicella in normal individuals, supportive therapy is generally indicated. However, for immunocompromised patients, more substantial measures are warranted. These include systemically administered acyclovir, vidarabine, and human leukocyte interferon. Corticosteroids generally are contraindicated

Herpangina

Herpangina is an acute viral infection caused by Coxsackie type A virus. It is transmitted by contaminated saliva and occasionally through contaminated feces.

Clinical Features. Herpangina is usually endemic, with outbreaks occurring typically in summer or early autumn. It is more common in children than in adults. Those infected generally complain of malaise, fever, dysphagia, and sore throat after a short incubation period. Intraorally, a vesicular eruption appears on the soft palate,

faucial pillars, and tonsils and persists for 4 to 6 days. A diffuse erythematous pharyngitis is also present. No associated skin lesions are typically seen.

Signs and symptoms are usually mild to moderate and generally last less than a week.

Treatment. Because herpangina is self-limiting, is mild and of short duration, and causes few complications, treatment usually is not required.

Hand-Foot-and-Mouth Disease

HFM disease is a highly contagious viral infection that usually is caused by Coxsackie type A16 or enterovirus 71. The virus is transferred from one individual to another through airborne spread or fecal-oral contamination.

Clinical Features. This viral infection typically occurs in epidemic or endemic proportions and predominantly (about 90%) affects children younger than 5 years of age. After a short incubation period, the condition resolves spontaneously in 1 to 2 weeks.

Signs and symptoms are usually mild to moderate in intensity and include low-grade fever, malaise, lymphadenopathy, and sore mouth. Pain from oral lesions is often the patient's chief complaint. Oral lesions begin as vesicles that quickly rupture to become ulcers. Lesions can occur anywhere in the mouth, although the palate, tongue, and buccal mucosa are favored sites, while the lips and gingiva are usually spared. Multiple maculopapular lesions, typically on the feet, toes, hands, and fingers, appear concomitantly with or shortly after the onset of oral lesions. These cutaneous lesions progress to a vesicular state; they eventually become ulcerated.

Histopathology. The vesicles of this condition are found within the epithelium because of obligate viral replication in keratinocytes. Eosinophilic inclusions may be seen within some of the infected epithelial cells

Treatment. Because of the relatively short duration, generally self-limiting nature, and general lack of virus-specific therapy, treatment for HFM disease is usually symptomatic

Measles (Rubeola) and German measles (Rubella)

Measles is a highly contagious viral infection caused by a member of the paramyxovirus family of viruses. Typically, oral eruptions consist of early pinpoint elevations over the soft palate that combines with ultimate involvement of the pharynx with bright erythema.

German measles, or rubella, is a contagious disease that is caused by an unrelated virus of the togavirus family. It shares some clinical features with measles, such as fever, respiratory symptoms, and rash. However, these features are very mild and short lived in German measles.

Clinical Features. After an incubation period of 7 to 10 days, prodromal symptoms of fever, malaise, coryza, conjunctivitis, photophobia, and cough develop. In 1 to 2 days, pathognomonic small erythematous macules with white necrotic centers appear in the buccal mucosa, these lesion spots, known as Koplik's spots. Koplik's spots generally precede the skin rash by 1 to 2 days. The rash initially affects the head and neck, followed by the trunk, and then the extremities.

Histopathology. Infected epithelial cells, which eventually become necrotic, overlie an inflamed connective tissue that contains dilated vascular channels and a focal inflammatory response. Lymphocytes are found in a perivascular distribution. In lymphoid tissues, large characteristic multinucleated macrophages, are seen.

Treatment. No specific treatment for measles is known. Supportive therapy of bed rest, fluids, adequate diet, and analgesics generally suffices

Bacterial infections

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 pseudomembrane. 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 in a host whose systemic health is significantly compromised.

Clinical Features. It typically affects children. 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.

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.

Tertiary syphilis begins after a period of 4–7 years. Oral lesions are gumma, atrophic glossitis, and interstitial glossitis. 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. Gummas may show necrosis and greater numbers of macrophages, resulting in a granulomatous lesion that is similar to other conditions, such as tuberculosis (TB).

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.

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.

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 five clinical varieties: pseudomembranous (thrush) , erythematous, papillary hyperplasia of the palate, and Candida-associated lesions (angular cheilitis, median rhomboid glossitis, denture stomatitis).

***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 nonhealing, 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 antimicrobials 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 strenght 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 periodontotis
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

<u>Oral Manifestaton of Aquired immunodyficiency system (AIDS)</u>

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. This unusual pattern of gingivitis appears with a distinctive linear band of erythema that involves the free gingival margin and extends 2 to 3 mm apically

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 in tense

***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 approxtmately 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

Precancerous or premalignant conditions and Squamous cell carcinoma (SCC), basal cell carcinoma .

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 it self 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

<u>Histological features of epithelial dysplasia:-</u>

1-increased and abnormal mitoses. Mitoses may be increased in number, occur in higher number in the epithelium that is usual away 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 rete pegs

3-drop-shaped rete pegs. 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-abnormal keratinization. Keratinization occurring below the normal keratine 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 upgrading 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 as being due to any other conditions, erythroplakic 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 others it 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 a field 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 per cent 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 over 2:1.

Aetiological factors in oral cancer

Tobacco smoking: Much indirect 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, bidis.

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, a site usually spared by this

disease.

Smokeless tobacco

Snuff dipping, tobacco sachets and tobacco chewing Betel chewing, betel quid, arecanut:

The betel or paan quid is a compound of natural substances (i.e., areca palm nuts, betel leaf. slaked lime. 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 the aetiology of oral cancer

Ultraviolet light and Radiation

The effects of ultra violet radiation on the lips x-irradiation, decrease s immune reactivity and produces abnormalities in chromosomal material. It should not seem surprising that radiotherapy 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 aetiological agents in oral carcinoma

human papilloma viruses

HPV types 16 and 18 are important factors in the aetiology 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-Barr virus

It has an aetiological 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 have been reported that risk of carcinoma of the lip in patients following renal and other organ transplantation due to immunosuppressive 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- inhibiting 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 inactivated The result in both cases leads to deregulation of cell proliferation and tumor formation.

Oncogenes

Oncogenes(for example, the c-myc and ras families) encode For a range of growth-promoting proteins such as growth factor receptors, signal- transmitting proteins, and stimulatory cell-cycle regulating proteins. In contrast, tumor-suppressor genes encod 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 G1 phase (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, checkpoint 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 area 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 anatomic sites

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 intra oral sites, carcinoma arising on the hard palate and dorsum of the tongue are relatively rare

Early lesions are usually asymptomatic. Common modes of presentation are a 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 induration 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.

Carcinoma developing on the vermilion border of the lip is clearly visible and so may be noticed at an early 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 crater like 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 around, 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 show 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 a reaction by the host immune system to tumor antigens as well as a response to tumor necrosis and ulceration. The lymphatic spread to the regional lymph nodes is a variable feature, but the frequency of cervical metastasis tend 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; polypoid squamous cell carcinoma)

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 5 years. 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 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 consist of cytologically malignant basaloid cells, arranged in a variety of patterns, invading adjacent tissue.

BOX 2-16 TNM CLINICAL STAGING SYSTEM FOR ORAL SQUAMOUS CELL CARCINOMA

T—Tumor

- T1: tumor <2 cm
- T2: tumor 2-4 cm
- T3: tumor >4 cm
- T4: tumor invades deep subjacent structures

N—Nodes

- N0: no palpable nodes
- N1: single ipsilateral node <3 cm
- N2A: single ipsilateral node 3-6 cm
- N2B: multiple ipsilateral nodes ≤6 cm
- N2C: contralateral or bilateral nodes ≤6 cm
- N3: node >6 cm

M—Metastasis

- M0: no distant metastasis
- M1: distant metastasis

TABLE 2-6 TNM CLINICAL STAGING OF ORAL SQUAMOUS CELL CARCINOMA

Stage	TNM Designation
I	T1, N0, M0
II	T2, N0, M0
III	T3, N0, M0 T1-3, N1, M0
IV	T4, N0, M0 T4, N1, M0 T any, N2-3, M0 T any, N any, M1

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.

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.

MUCOCELE

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. Unlike the salivary duct cyst (see page 457), the mucocele is not a true cyst because it lacks an epithelial lining.

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 adult. The lower lip is by far the most common sit, The lesions often burst, leaving shallow, painful ulcers that heal within a few days.

Histopathologic Features

the mucocele shows an area of spilled mucin surrounded by a granulation tissue response.the inflamation usually includes numerous foamy histiocytes (macrophages). In some cases a ruptured salivary duct may be identified feeding into the area. The adjacent minor salivary glands often contain a chronic inflammatory cell infiltrate and dilated ducts.

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 .

Ranula

Ranula is a term used for mucoceles that occur in the floor of the mouth.

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.

Histopathologic Features

The microscopic appearance of a ranula is similar to that of a mucocele in other locations.

Treatment And Prognosis

Treatment of the ranula consists of removal of the feeding sublingual gland and/or marsupialization. Marsupialization (exteriorization) entails removal of the roof of the intraoral lesion, which often can be successful for small, superficial ranulas associated with the ducts of Rivini. However, marsupialization is often unsuccessful for larger ranulas .

Salivary Duct Cyst (Mucus Retention Cyst; Mucus Duct Cyst; Sialocyst) The salivary duct cyst is an epithelium-lined cavity that arises from salivary gland tissue. Unlike the more common mucocele (see page 454), it is a true developmental cyst that is lined by epithelium that is separate from the adjacent normal salivary duct .

Clinical Features Salivary duct cysts usually occur in adults and can arise within either the major or minor glands. Cysts of the major glands are most common within the parotid gland, presenting as slowly growing, asymptomatic swellings. Intraoral cysts can occur at any minor gland site, but most frequently they develop in the floor of the mouth, buccal mucosa, and lip.

Histopathologic Features The lining of the salivary duct cyst is variable and may consist of cuboidal, columnar, or atrophic squamous epithelium surrounding thin or mucoid secretions in the lumen.

Treatment And Prognosis Isolated salivary duct cysts are treated by conservative surgical excision. For cysts in the major glands, partial or total removal of the gland may be necessary. The lesion should not recur.

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 ma 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 though 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 & candidal 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 increase 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 easinophilic coagulum.
2. The tumor epithelial cells may be arranged in sheets or strands about these tubular structures. Some time 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

ADENOMA)

The **oncocytoma** 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

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

Mucoepidermoid carcinoma

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 histopathologic 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; palataltumors 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 anastamosing 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. Some time 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