PATHOLOGY OF THE JAW (MANDIBLE)

DR. BOTOND TIMÁR

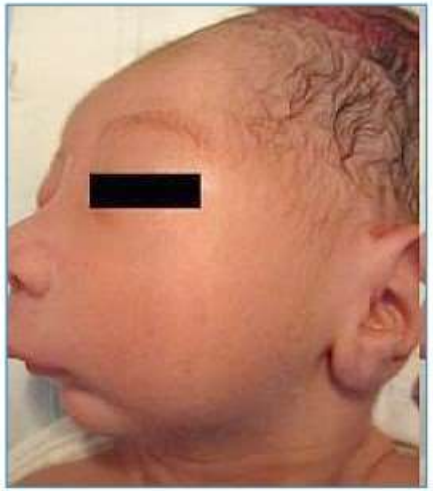
24.02.2020

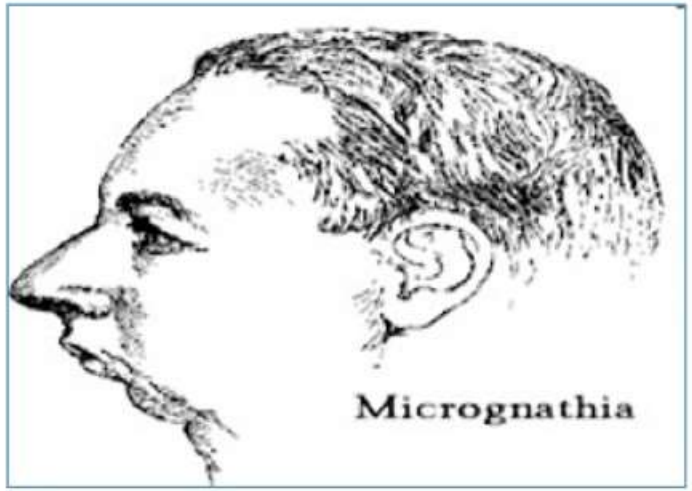
LECTURE OUTLINE

Hereditary bone lesions
Bone lesions of metabolic origin
Bone lesions of unknown etiology
Inflammatory (Infectious) bone diseases
Neoplastic lesions of the jaw
Cystic lesions of the jaw and oral cavity region

HEREDITARY BONE LESIONS

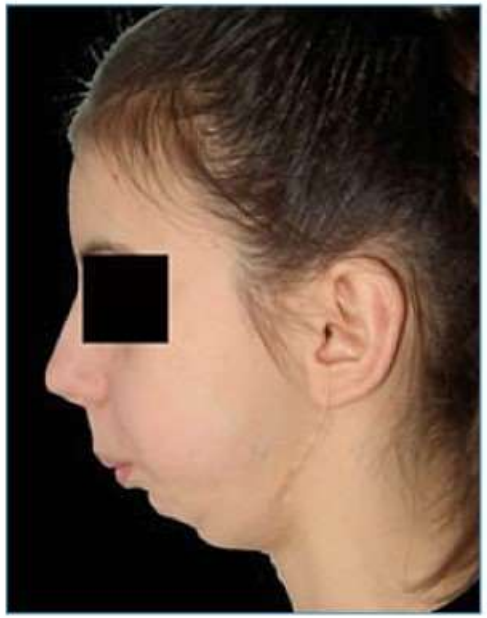
MICROGNATHIA / RETROGNATHISM





Retrognathism:
A type of malocclusion which refers to an abnormal posterior positioning of the maxilla or mandible, particularly the mandible, relative to the facial skeleton and soft tissues.

- *Micrognathia (undersized jaw)*
- Rarely maxillary anteroposition or hyperplasia



Micrognathia

- Potentially life-threatening condition in neonates (airway obstruction!)
- Frequent spontaneous correction in puberty

MICROGNATHIA

Can be part of different syndromes

Cri-du-chat syndrome (deletion in Chr 5)

Marfan-syndrome

Pierre-Robin syndrome

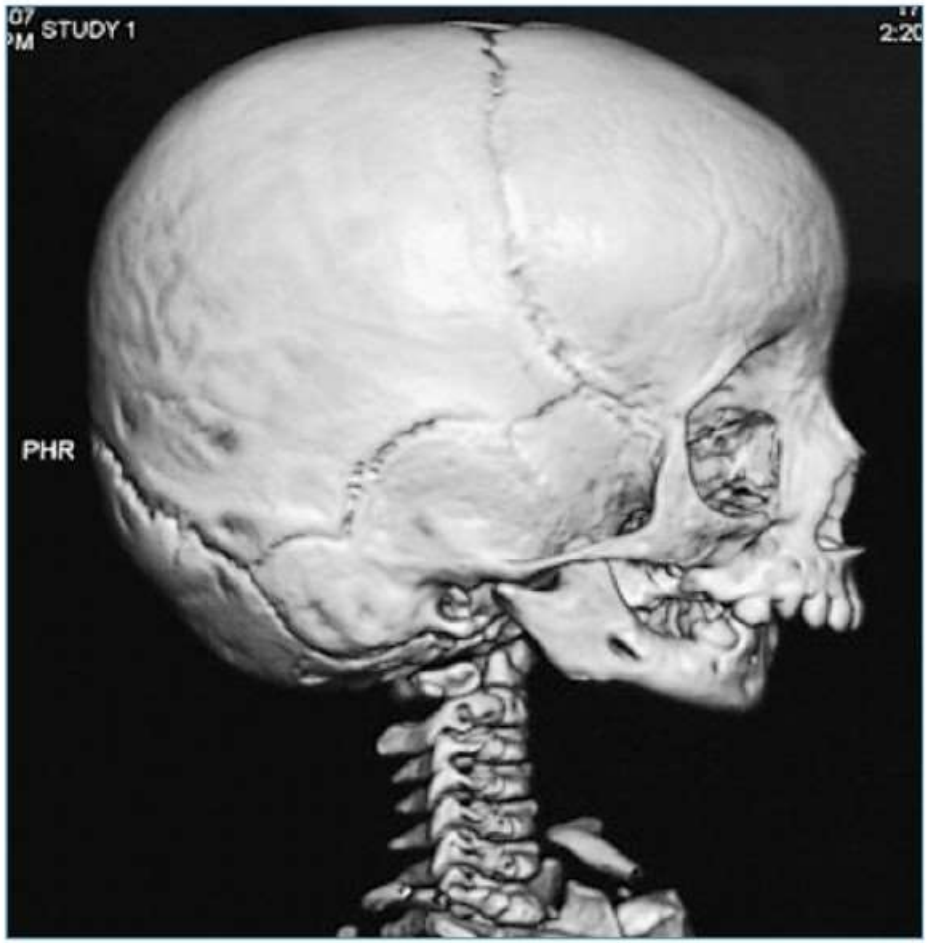
- (micrognathia, cleft palate, glossoptosis)
- can be part of other syndromes
- eating difficulty, difficulty of speach
- crowded teeth

Progeria

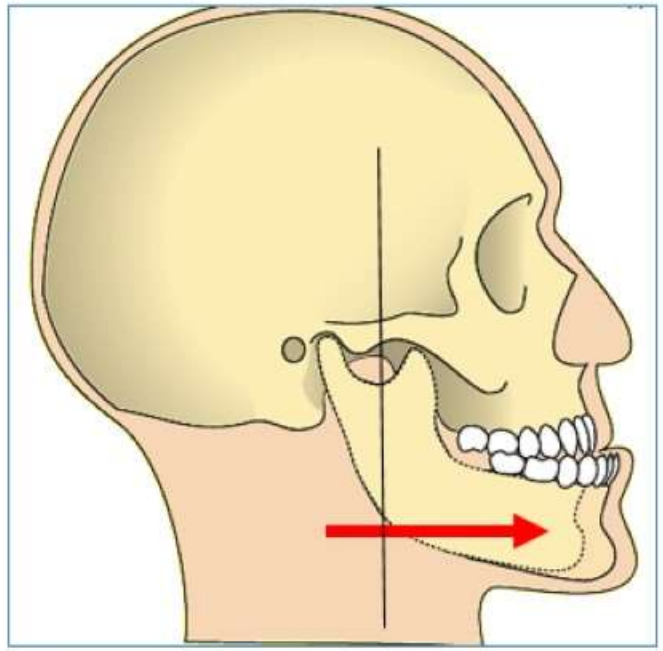
Edwards-syndrome (trisomy 18)

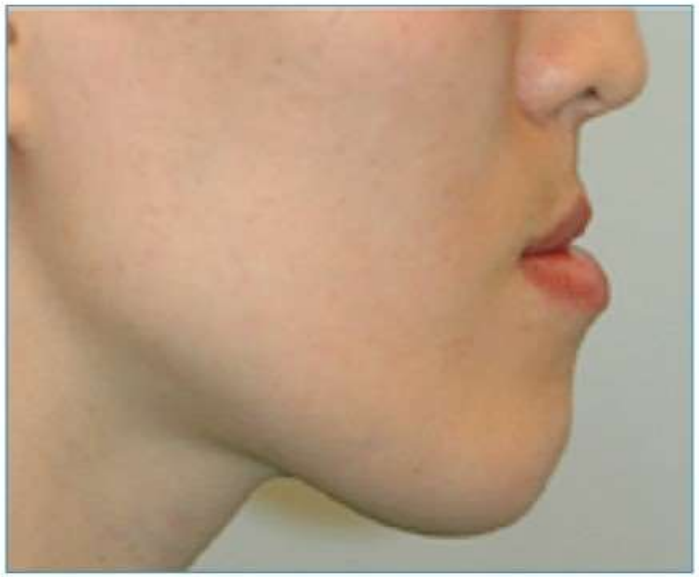
Patau-syndrome (trisomy 13)

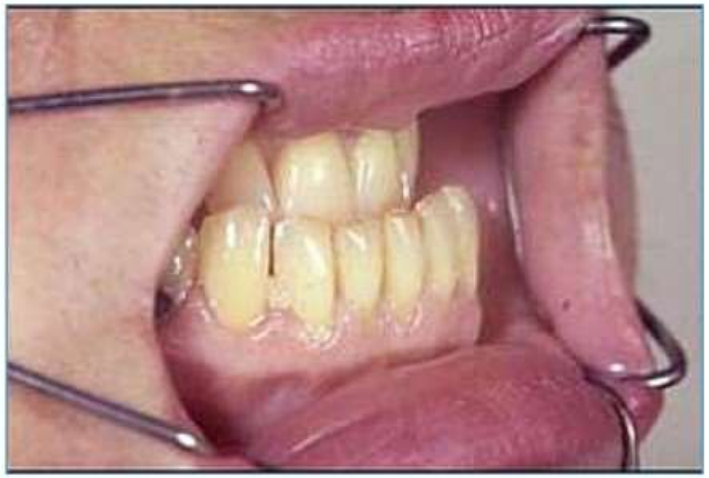
Turner-syndrome



PROGNATHISM







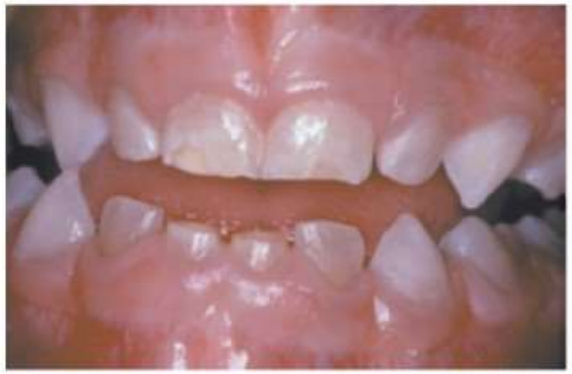
Hereditary (AD)

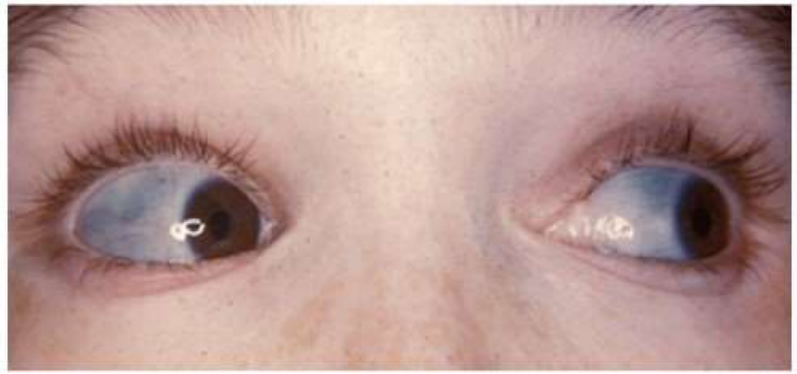
- Spanish Habsburgs

May also be normal variant

HEREDITARY BONE LESIONS

OSTEOGENESIS IMPERFECTA ("BRITTLE BONE DISEASE")

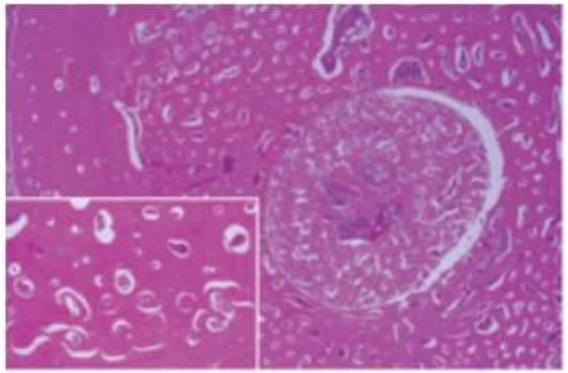


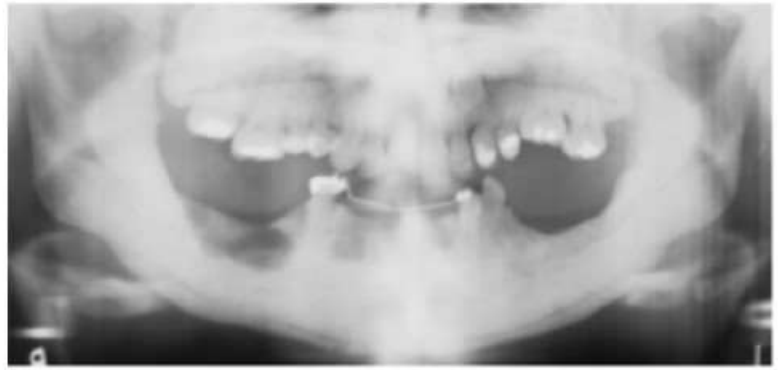


- Rare;AD inheritance;mutation in COL1A1 or COL1A2 genes
- Defective collagen synthesis
- Impaired bone matrix formation (osteogenesis)

- Growth retardation, Skeletal deformities
- Brittle bones, and recurrent fractures from minimal trauma
- Blue sclerae
- Progressive hearing loss; Brittle, opalescent teeth

OSTEOPETROSIS (ALBERS-SCHÖNBERG DISEASE; MARBLE BONE DISEASE)

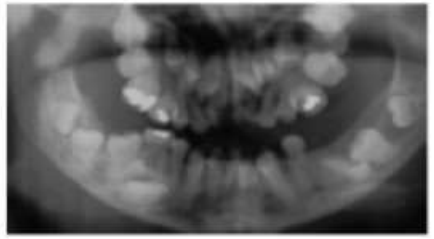


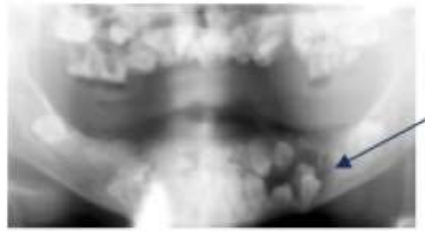


- Rare; AD, AR inheritance; mutation in different genes
- markedly increased bone density

- bone is dense but prone to pathologic fracture
- On dental radiographs, tooth roots often are difficult to visualize because of the density of the surrounding bone
- bone marrow failure, frequent fractures, cranial nerve
- compression, and growth impairment

CLEIDOCRANIAL DYSPLASIA (CLEIDOCRANIAL DYSOSTOSIS)





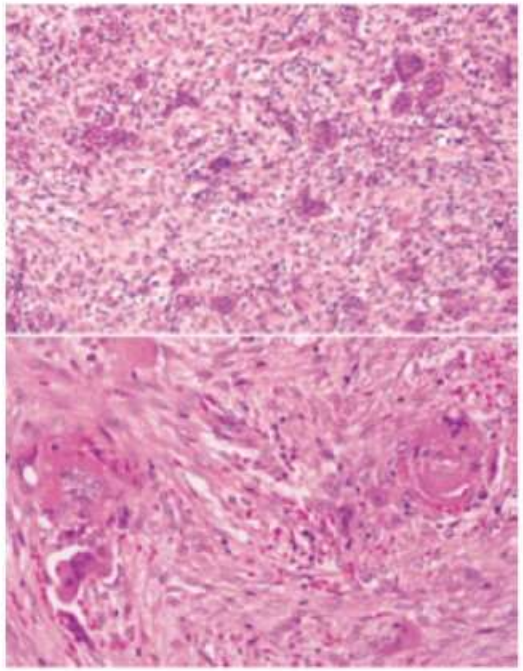
Multiple unerupted teeth

- mutation in RUNX2 gene (AD)
- dental and clavicular abnormalities
- clavicles typically are hypoplastic or discontinuous
- short stature, enlarged skull, brachycephaly, ocular hypertelorism

CHERUBISM

- Rare developmental jaw condition
- Can be inherited as an AD trait with variable expressivity
- Many cases appear to represent *de novo* mutations
- Most are caused by gain-of-function mutations in *SH3BP2* gene

- clinical alterations typically progress until puberty, then stabilize and slowly regress
- plump cheeks result from painless, bilaterally symmetric expansion of the posterior mandible



Scattered giant cells within a background of cellular, hemorrhagic mesenchymal tissue.

RAFFAELLO SANZIO

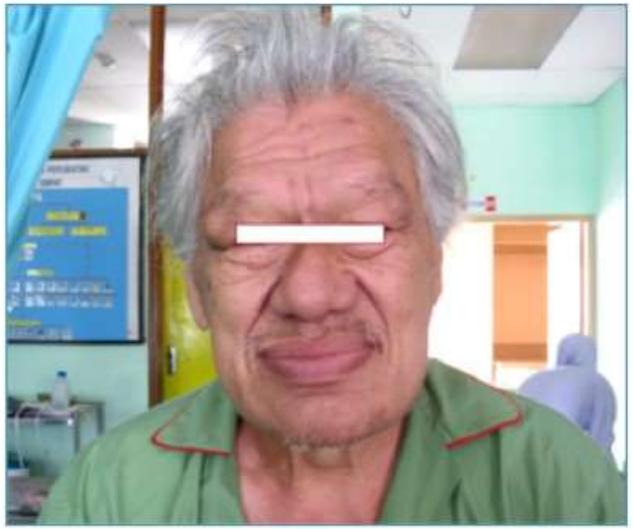
Angeli (particolare)

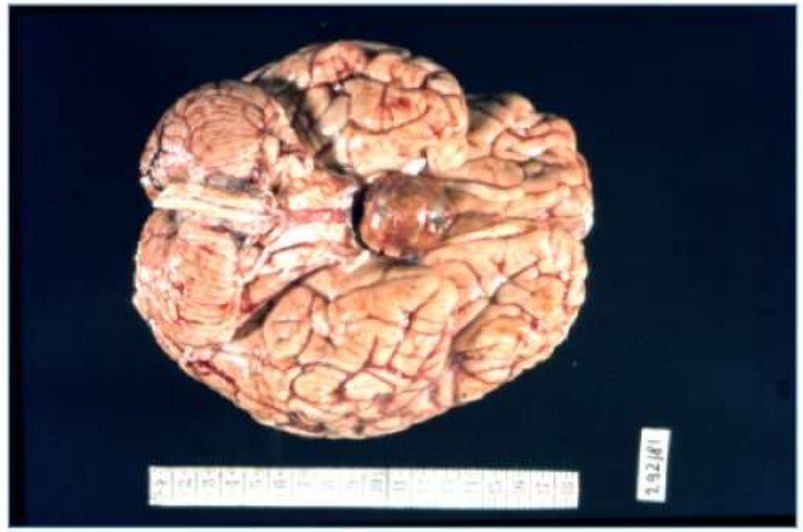
The name *cherubism* was applied to this condition because the facial appearance is similar to that of the plumpcheeked little angels (cherubs) depicted in Renaissance paintings.

no relationship to fibrous dysplasia of bone!

BONE LESIONS OF METABOLIC ORIGIN

ACROMEGALY





Etiology

- Benign GH-secreting pituitary adenoma (> 95% of cases)
- Very rare: neuroendocrine or hypothalamic tumors, paraneoplastic syndromes

- Teeth malpositioning
- Malocclusion

Skeletal effects

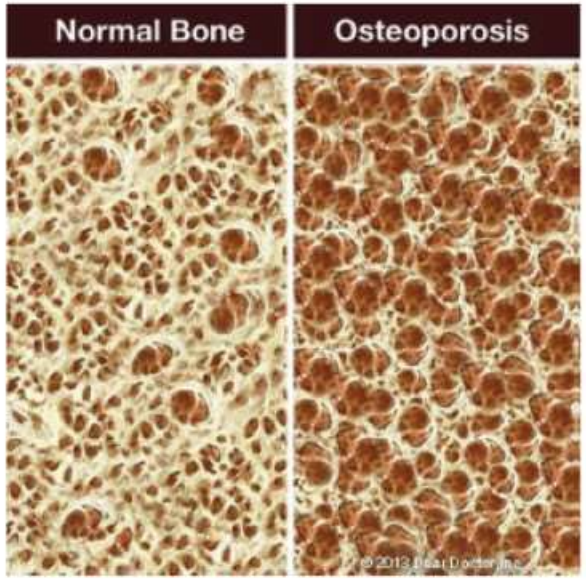
- Large skull, coarsened features:
- Enlarged nose, forehead, and jaw (macrognathia)
- Widened hands, fingers, and feet
- Painful arthropathy (ankles, knees, hips, spine)

OSTEOPOROSIS

- insufficient bone strength with increased susceptibility to fractures

Primary osteoporosis (most common)
- Postmenopausal osteoporosis: Estrogen stimulates osteoblasts and inhibits osteoclasts. Increased bone resorption.
- Senile osteoporosis: gradual loss of bone mass as patients age (especially > 70 years)

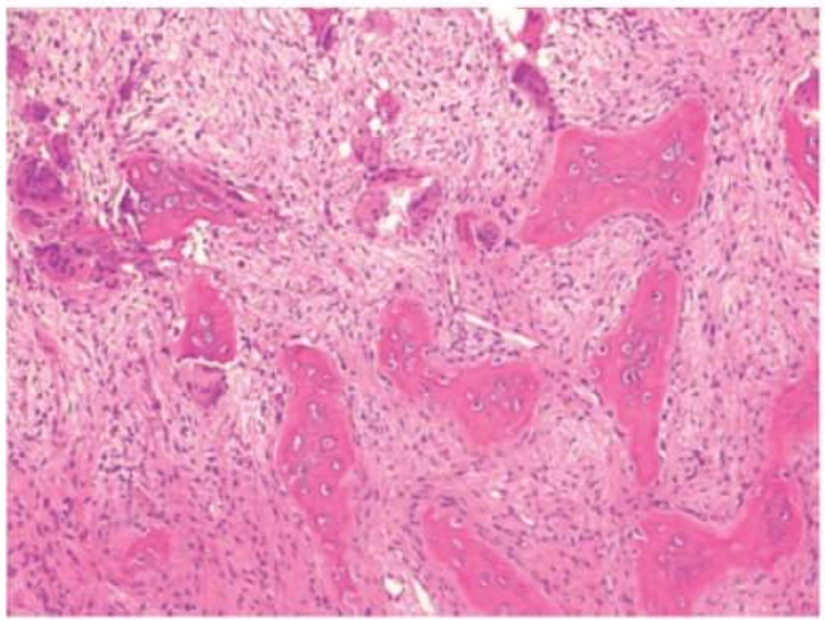
Secondary osteoporosis:
- Drug-induced/iatrogenic



HYPERPARATHYREODISM

- Leads to **osteitis fibrosa cystica**

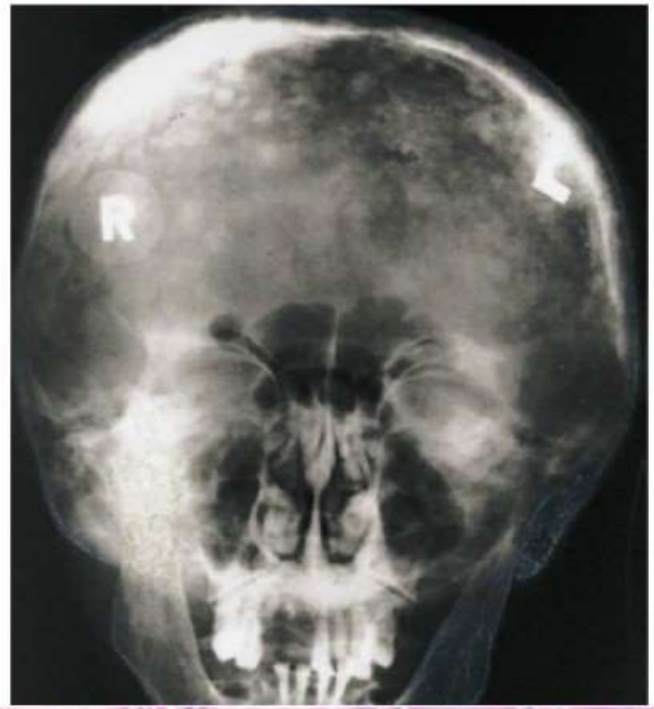
See more: Endocrinology



BONE LESIONS OF UNKNOWN ETIOLOGY

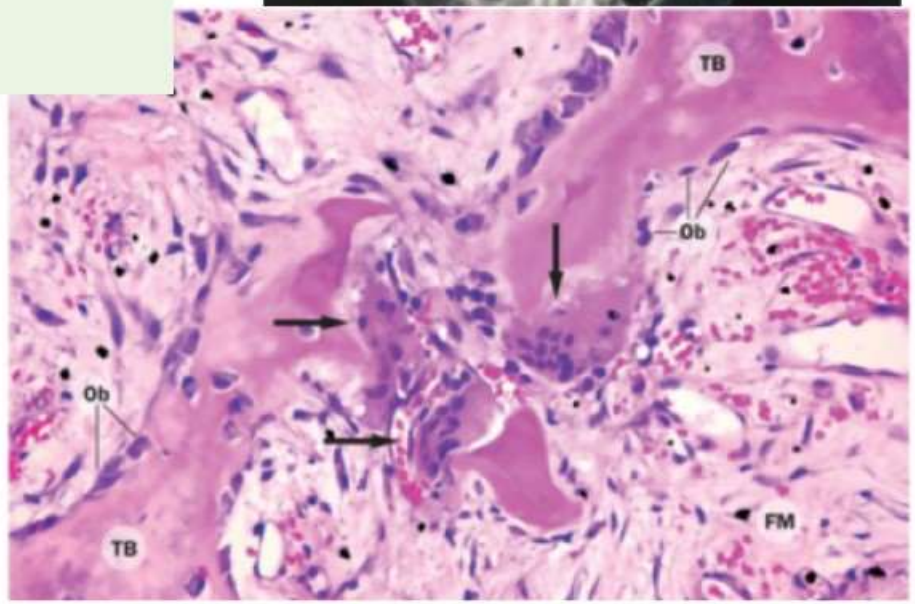
PAGET DISEASE OF BONE (OSTEITIS DEFORMANS)

- Still unknown etiology
- abnormal, anarchic resorption and deposition of bone, resulting in skeletal distortion and weakening
- Second most prevalent skeletal disease after osteoporosis
- Sex: ♂ > ♀ (1.2:1)
- Age of onset: > 55 years
- Approximately 70–90% of cases are asymptomatic.
- Bone pain, which may be associated with erythema and elevated skin temperature over the affected bones
- Bony deformities; e.g., bowing of legs (saber shin)
- Skull involvement (in ~ 40% of cases), Skull enlargement (increasing hat size)
- Cranial nerve deficits, Impaired hearing, Headache
- Pathological fractures



Microscopic examination shows uncontrolled resorption and formation of bone

1. Resorptive phase,numerous hyperactive osteoclasts surround the bone trabeculae
2. Mixed lytic and blastic phase: increased osteoclastic activity is accompanied by an increased number of osteoblasts
3. Sclerotic phase, there are large masses of dense bone with prominent reversal lines.



FIBRO-OSSEOUS LESIONS OF THE JAWS

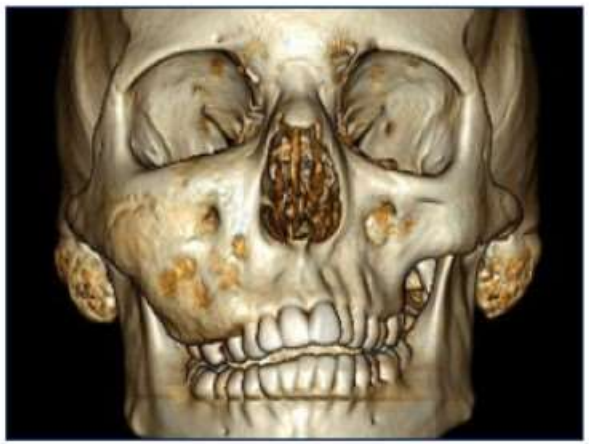
- **FIBROUS DYSPLASIA**
- **CEMENTO-OSSEOUS DYSPLASIA**
- **OSSIFYING FIBROMA**

developmental tumorlike condition, characterized by

FIBROUS DYSPLASIA

Non-hereditary, hamartomatous tissue proliferation
Activating mutation in GNAS gene (20q13.3)

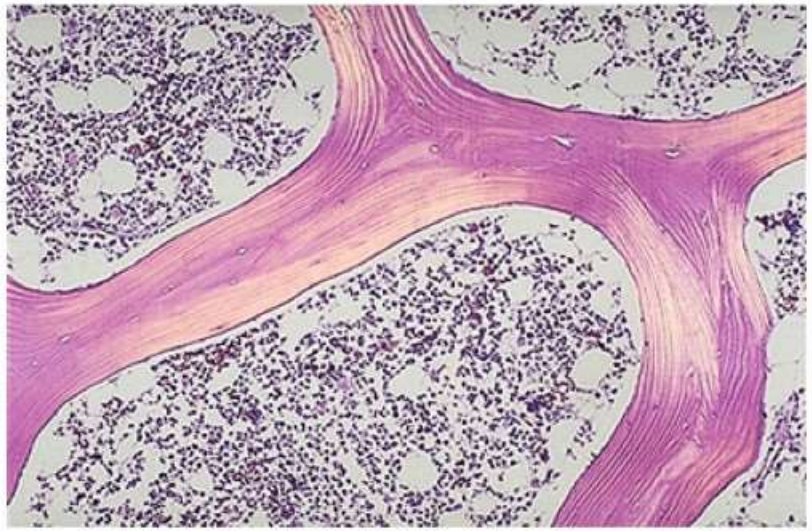
- Osteoprogenitor cells: expansion → decreased marrow→ fibrosis
- Osteoblasts: abnormal bone matrix production, irregular trabecules
- replacement of normal bone by a proliferation of cellular fibrous connective tissue with irregular bony trabeculae
- Monostotic – polyostotic
- Mainly in childhood or in puberty
- Slowly growing, painless, spindle-shaped
- Arrested eruption, movement of teeth
- Facial asymmetry
- Maxilla > mandible
- Mandible: mainly molar/praemolar
- Maxilla: may spread into the sinuses

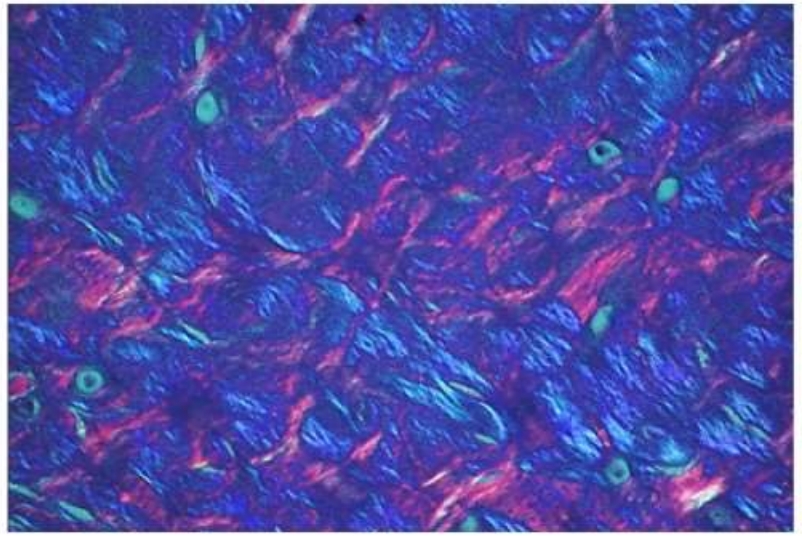


FIBROUS DYSPLASIA

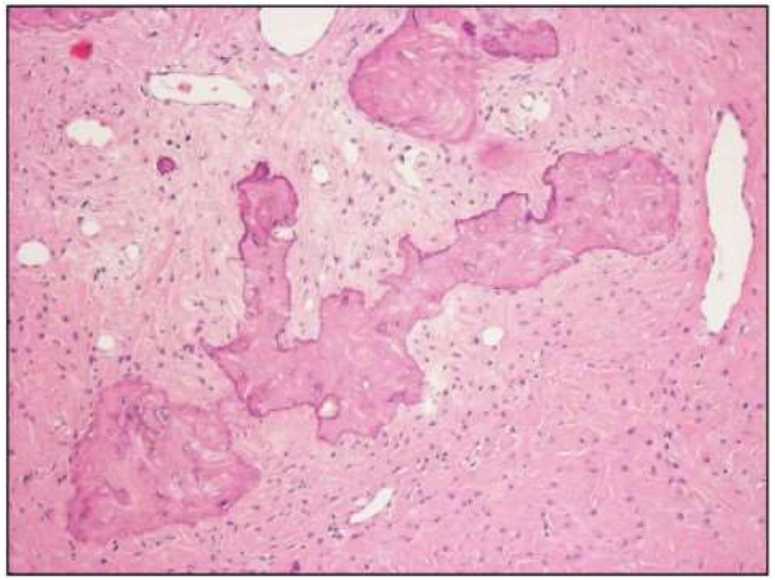
Normal bone structure

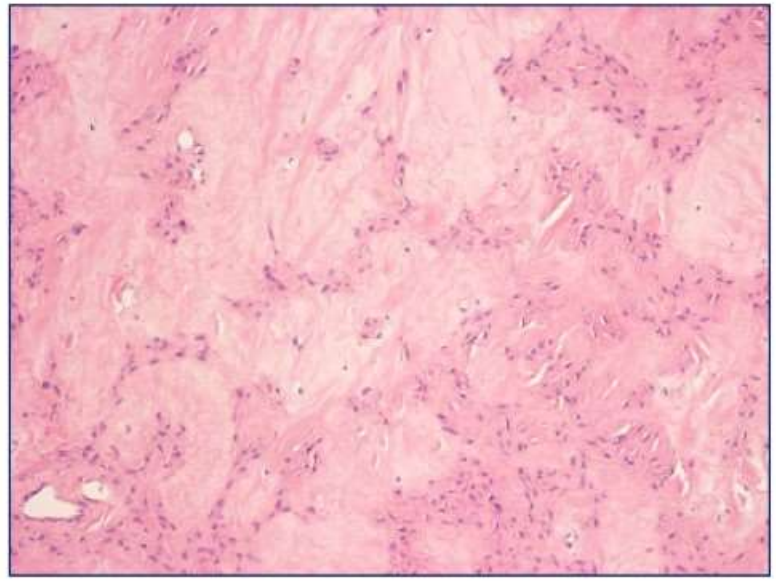
Lamellar bone

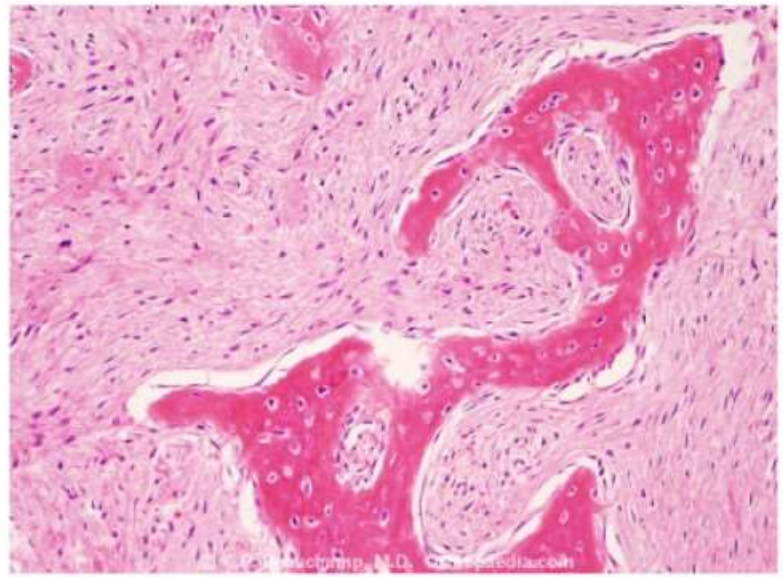




Fibrous dysplasia:
Woven bone

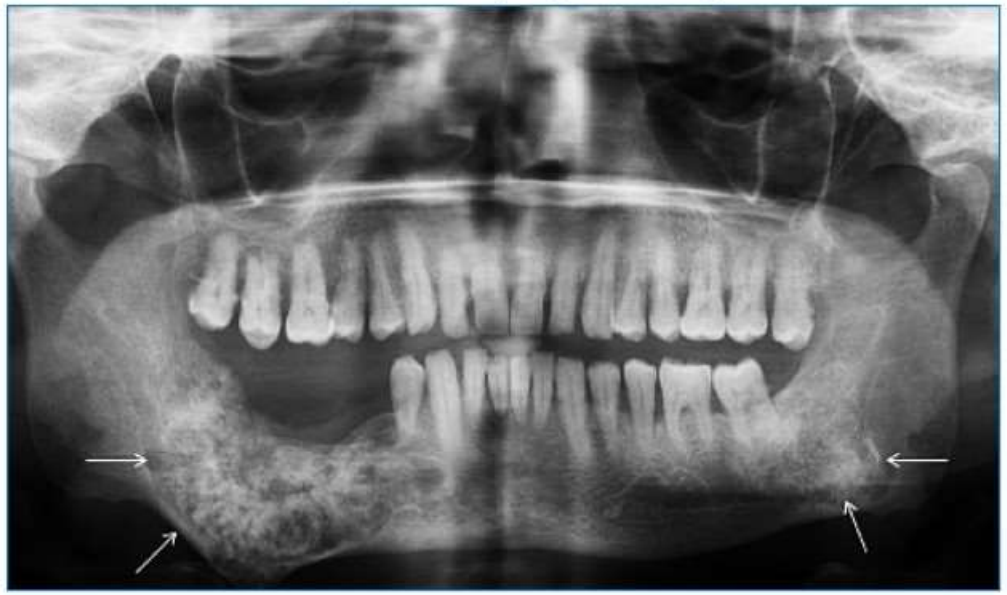


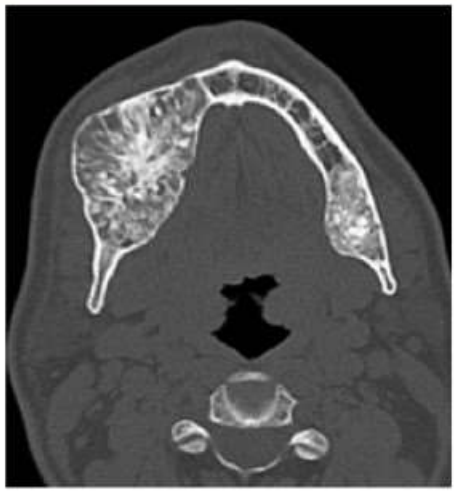


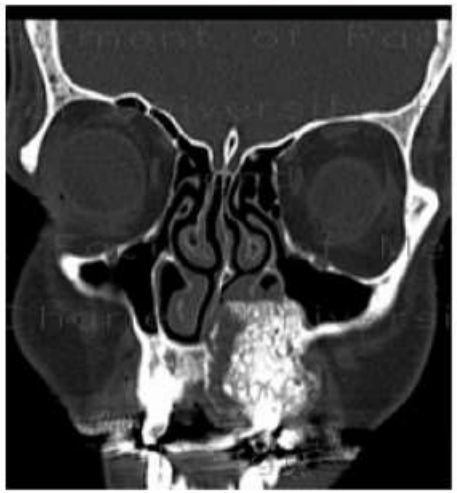


FIBROUS DYSPLASIA

X-Ray: variable appearance
Ill-defined border (⇆ ossifying fibroma)



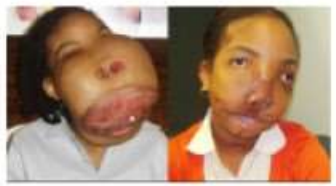


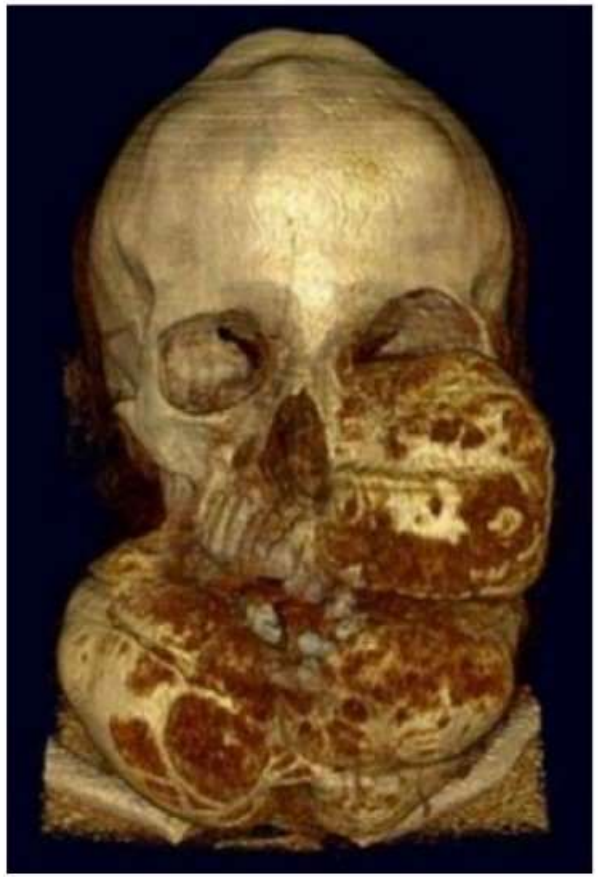


Facultative praeblastomatosis (1 – 4 %)

Radioresistent!

(irradiation may cause malignant transformation [fibrosarcoma])

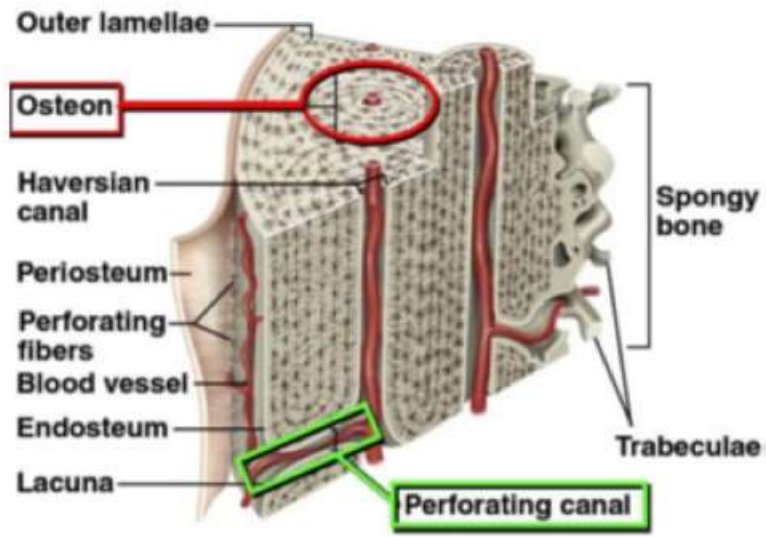




NONODONTOGENIC INTRAOSSEOUS LESIONS

I. EXOSTOSES (TORI)
II. OSTEOMYELITIS (INFLAMMATIONS/INFECTIONS)
III. OSTEONECROSIS

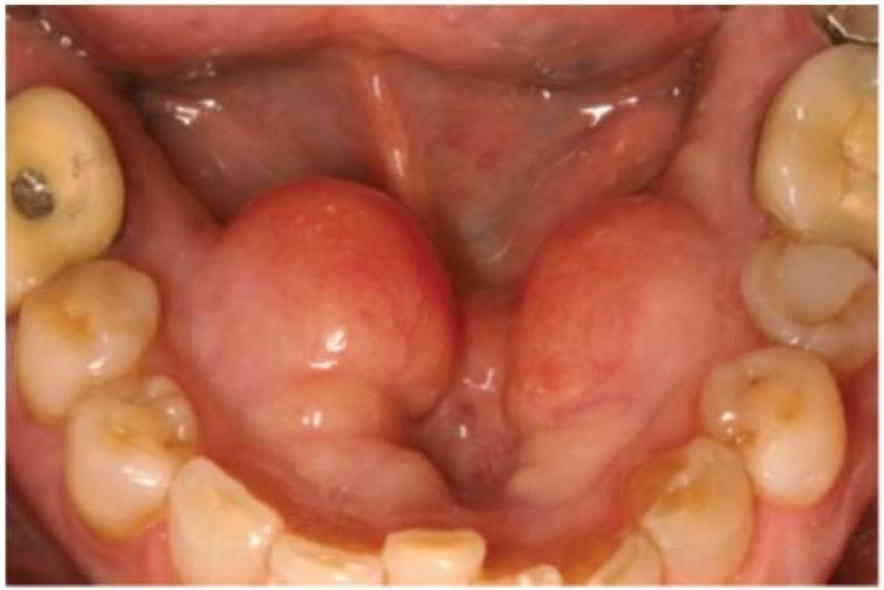
PERIOSTITIS
Inflammation of the periosteum
OSTEITIS
Inflammation in the vicinity of the perforating canals (around vessels) in the bone substance
OSTEOMYELITIS
Inflammation of the bone and the bone marrow



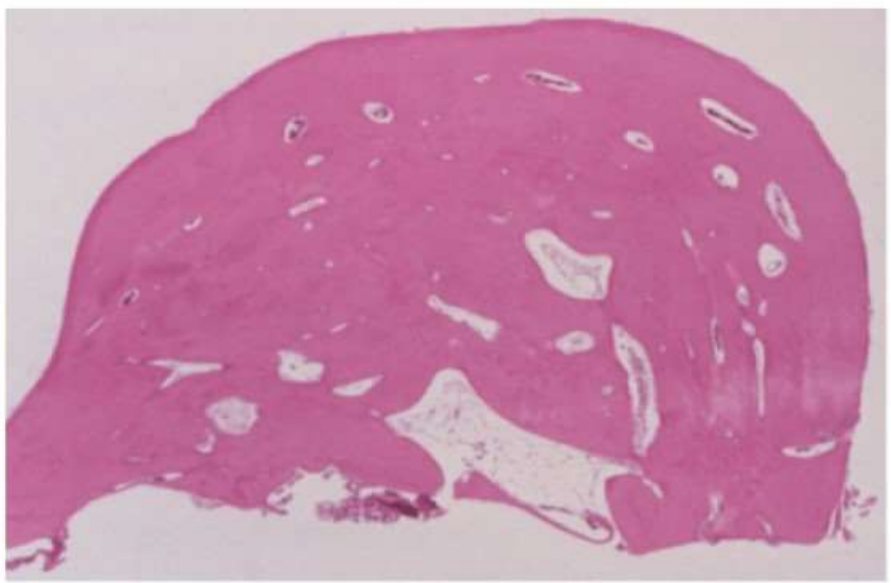
TORUS MANDIBULARIS

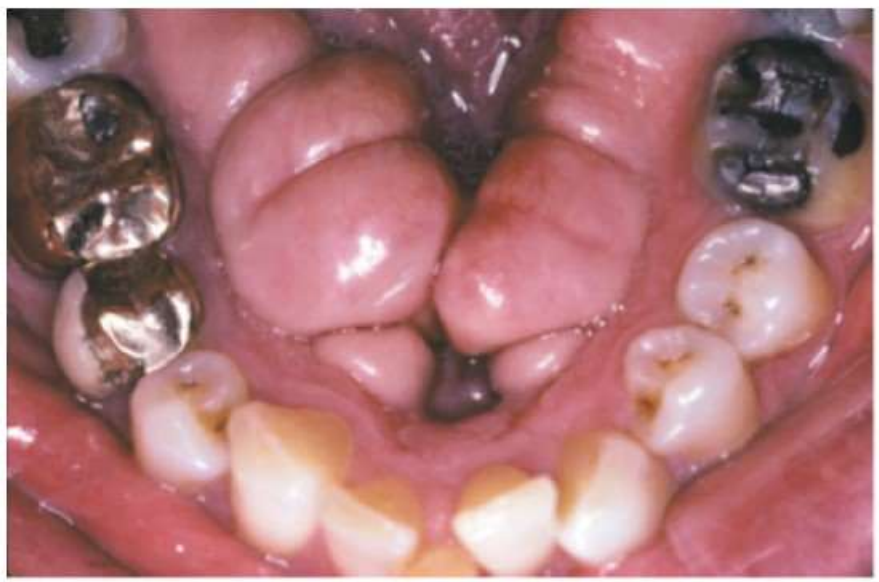
The **torus mandibularis** is a common exostosis that develops along the lingual aspect of the mandible.

- Palate or mandible
- Following chronic, local traumas or surgical interventions
- Mandible: lingual surface, praemolar region
  frequently bilateral
  may be multiple
  slowly growing bony mass



The *histopathologic* appearance of the torus mandibularis is similar to that of other exostoses, consisting primarily of a nodular mass of dense, cortical lamellar bone





OSTEOMYELITIS

Osteitis: general term for inflammation of the bone
Osteomyelitis: infection of the bone marrow

Acute form: develops within days or weeks
Chronic form: develops slowly (over months or years) and is associated with avascular bone necrosis and sequestrum formation within the bone

- Osteomyelitis of the jaws was a common complication of dental sepsis before the advent of antibiotics, it is now a rare disease
- Various clinical subtypes may be recognised

Factors predisposing to osteomyelitis:

Local:
Trauma
Radiation injury
Paget's disease
Osteoporosis

Systemic factors (impaired host defense)
Immundeficiency
Immunosupression
Diabetes mellitus
Malnutrition

Etiology

- Odontogenic infections
- Dental extraction while there is ongoing inflammation
- Soft tissue abscess
- Infected cysts
- Purulent sinusitis maxillaris
- Bacterial:
  - Polymicrobial infection
  - Anaerobs
  - Staphylococcus, Actinomyces

OSTEOMYELITIS

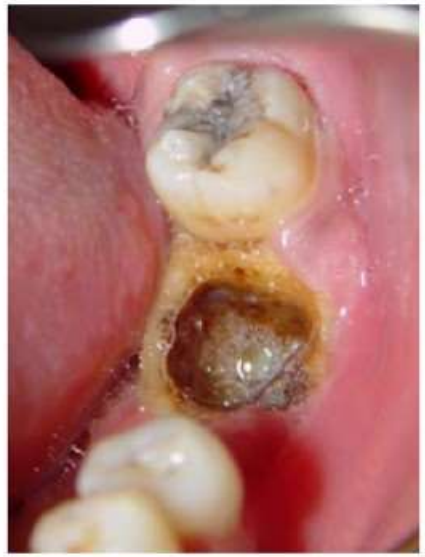
Acute (purulent) osteomyelitis

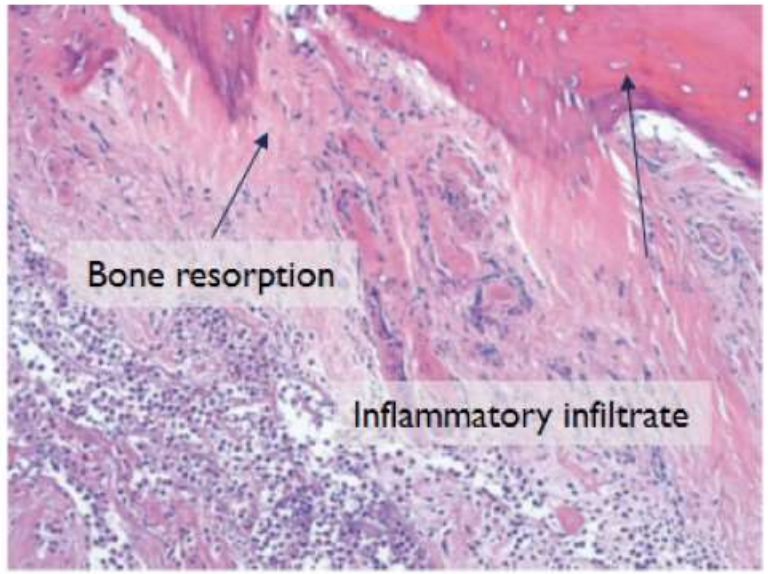
Onset
- usually gradual, over several days

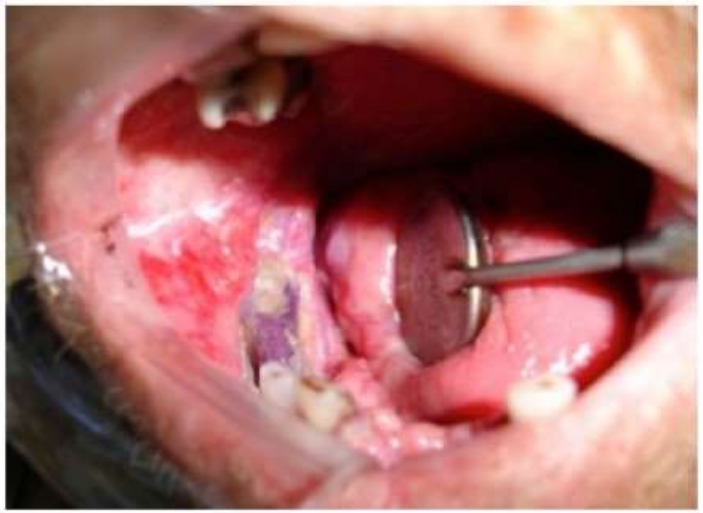
Chief complaint:
- pain at the site of infection, possibly related to movement

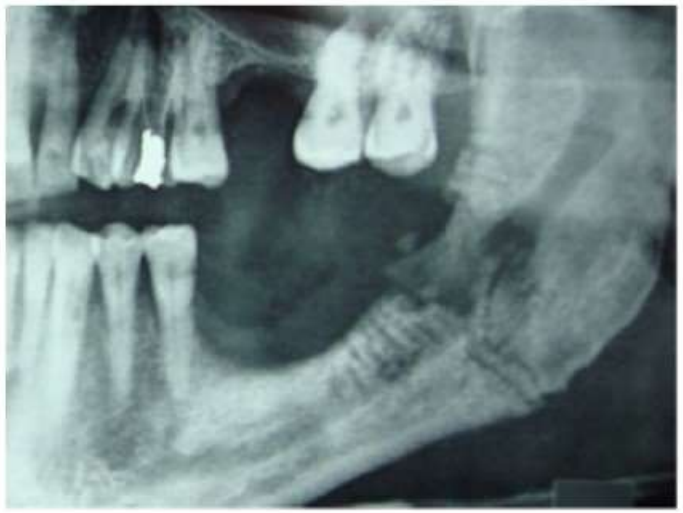
Localized findings:
- point tenderness, swelling, redness, warmth

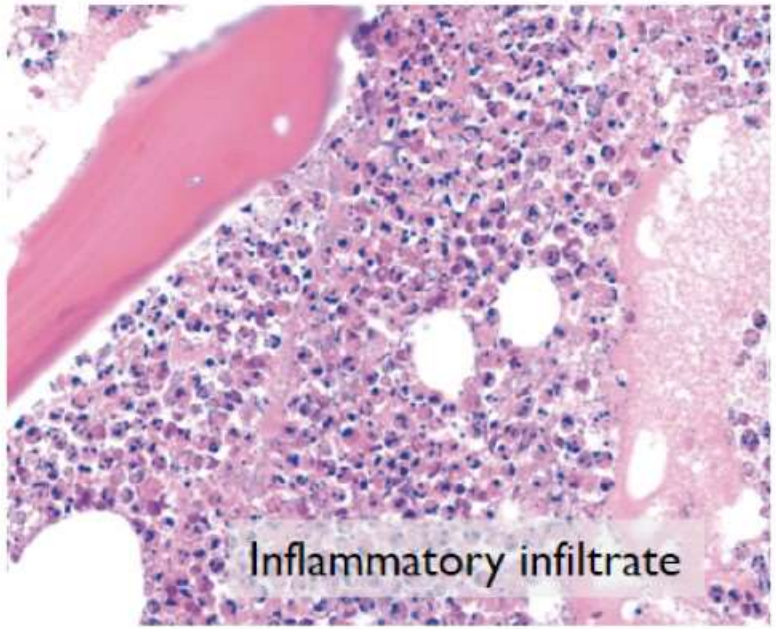
Systemic findings:
- malaise, fever, chills











OSTEOMYELITIS

Acut → Chronic (slow process)

Acute inflammation of marrow tissues

Spread of purulent exudate along the marrow spaces and bone canals

Thrombosis of the vessels due to compression (oedema)

Ischaemia, Microcirculation disorder

Bone necrosis

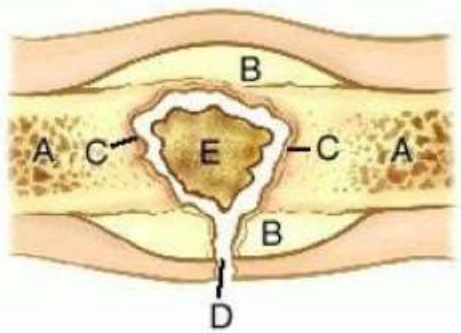
Lifting periosteum causing further necrosis

Osteoclast activity increases

Sequestrum

Sequestrum

- Dead piece of bone
- Gradually separated from living bone by granulation tissue
- May pass through sinus tract
- Avascular and dense on Xray
- Involucrum: sleeve of living tissue created by periosteum which is deposited around sequestrum

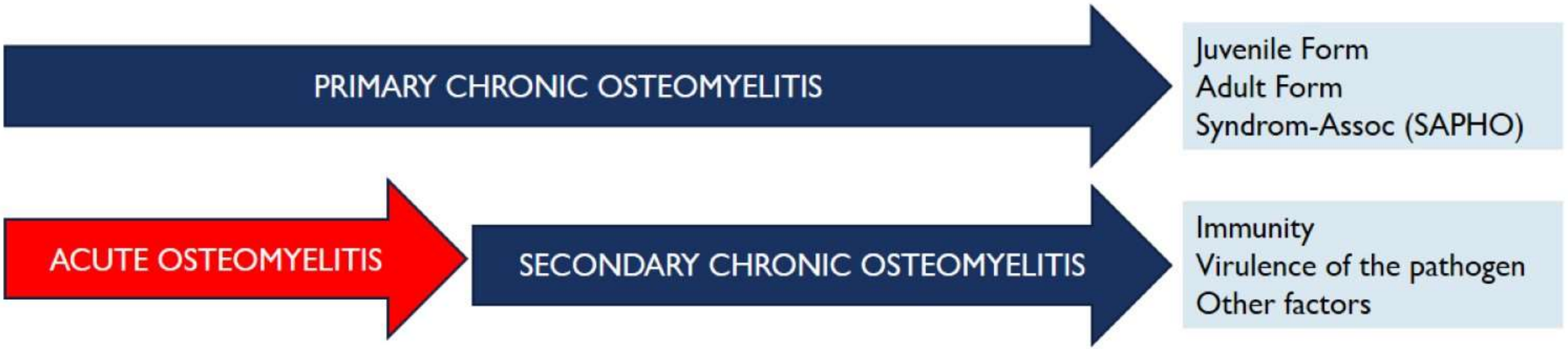


A: healthy bone
B: periosteum
C: involucrum
D: sinus tract
E: sequestrum

CHRONIC OSTEOMYELITIS

Several classification schemes!

1. Acute osteomyelitis (< 1 month)
2. Chronic osteomyelitis
   - chronic suppurative (secondary chronic osteomyelitis)
     (spread from dental focus)
   - chronic non-suppurative osteomyelitis
     (no pus, no fistule)
3. Diffuse sclerosing osteomyelitis
   (unknown etiology)
4. Chronic recurrent multifocal osteomyelitis
5. Garré-osteomyelitis
   (ossifying periostitis; immature bone tissue outside the cortical)



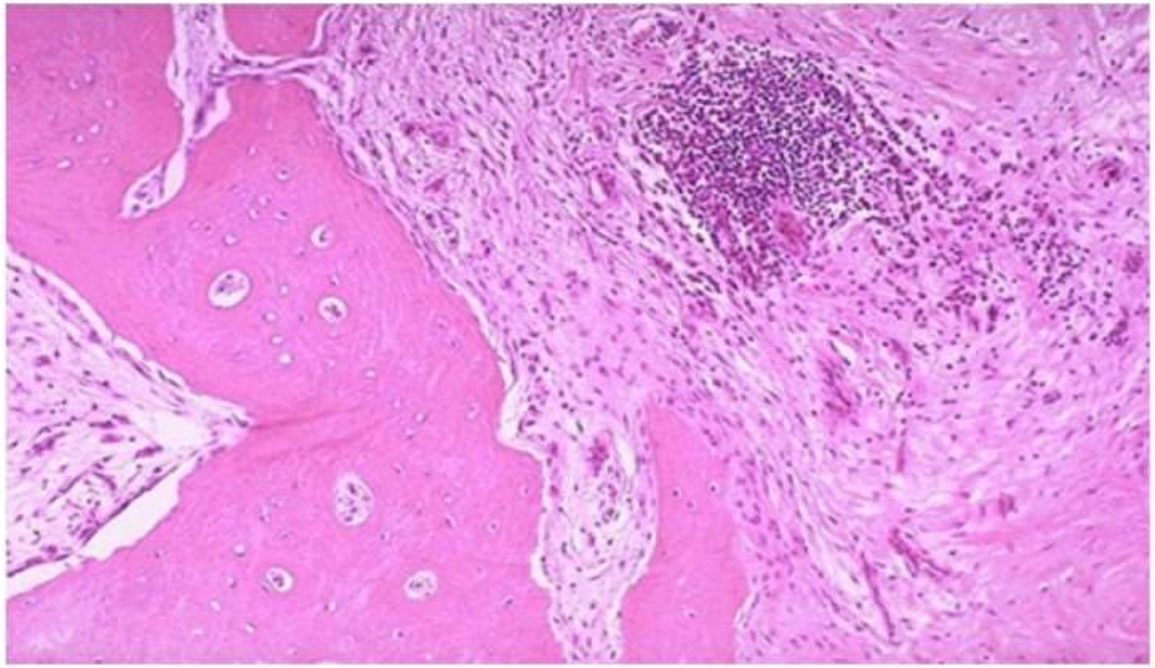
OSTEOMYELITIS

Chronic suppurative osteomyelitis

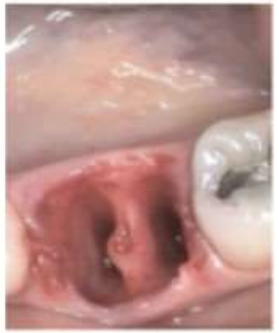
- develops in 15-30%
  - due to delayed treatment,
  - inadequate antibiotics,
  - incomplete surgical debridement of necrotic bone,
  - weakened host defenses

Onset
- usually following a prior episode of osteomyelitis; may last for months

Complaint
- recurrent pain
- Swelling, redness
- Local sinus tract formation, with draining pus



ALVEOLAR OSTEITIS (DRY SOCKET)
- higher freq in the mandible and the posterior areas



If acute osteomyelitis is not resolved expeditiously, the entrenchment of chronic osteomyelitis occurs, or the process may arise primarily without a previous acute episode.

DIFFUSE SCLEROSING OSTEOMYELITIS (DSO)

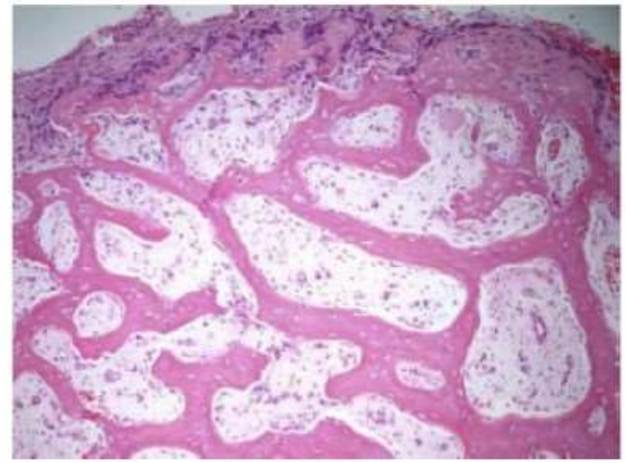
Diffuse sclerosing osteomyelitis is an ill-defined, highly controversial area of dental medicine.

1. Diffuse sclerosing osteomyelitis
2. Primary chronic osteomyelitis
3. Chronic tendoperiostitis

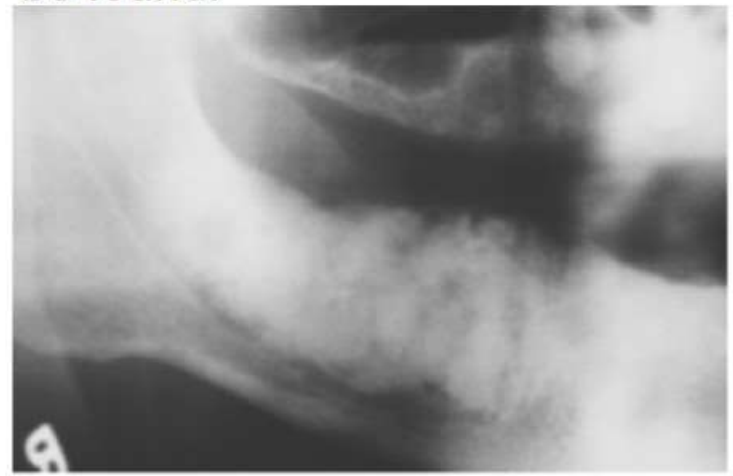
Group of presentations that are characterized by:

- Pain
- Inflammation
- Varying degrees of gnathic periosteal hyperplasia
- Sclerosis

DSO histology demonstrates sclerosis and remodeling of bone. The haversian canals are scattered widely and little marrow tissue can be found.



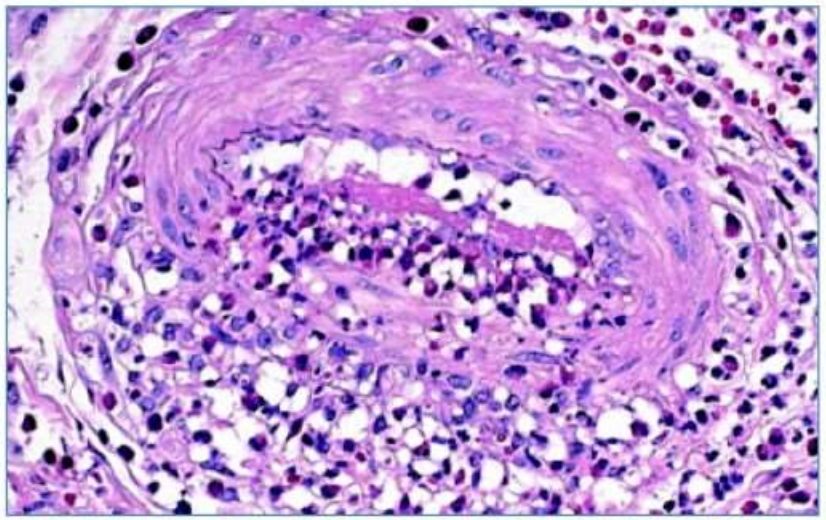
Diffuse area of increased radiodensity



NECROSIS OF THE JAW

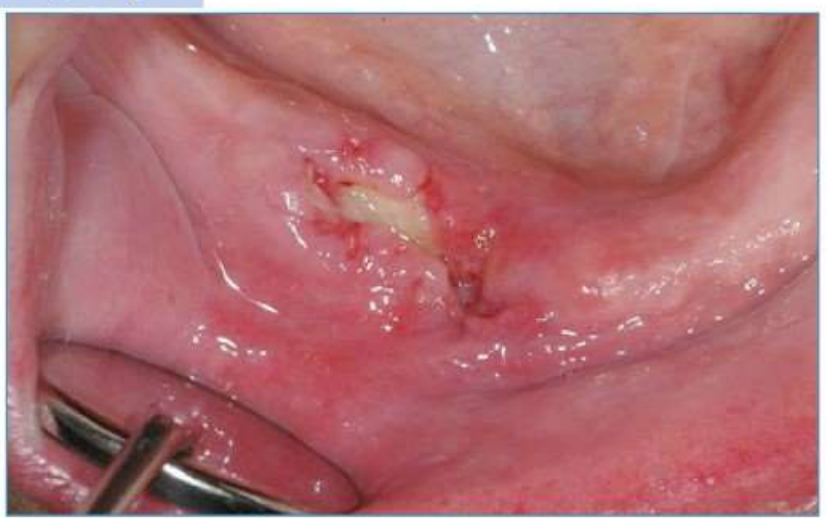
Osteoradionecrosis

- 20% following local irradiation
- endarteritis obliterans
- end arteries → coagulative necrosis
- sterile, symptomless
- prone to fracture, infection
- infected: rapid spread → osteomyelitis

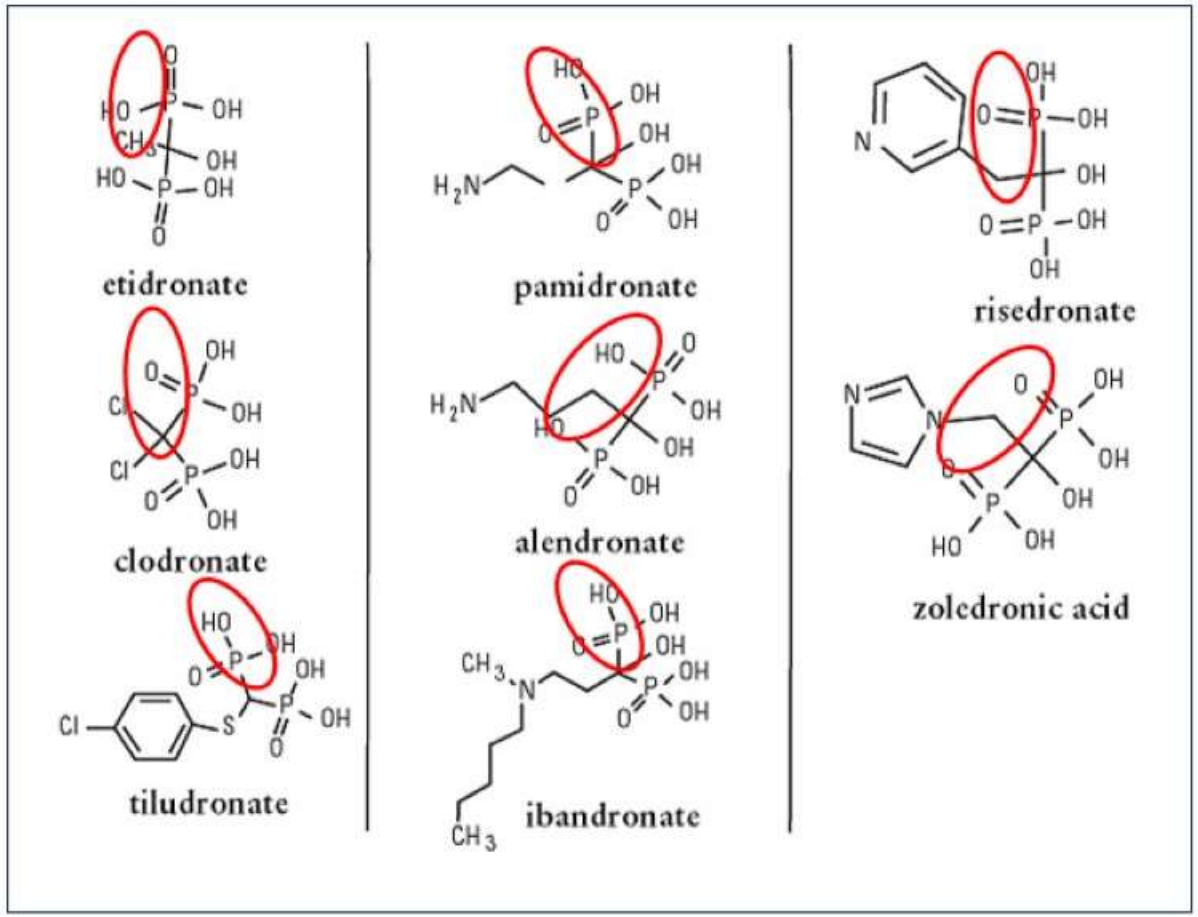


Bisphosphonate-necrosis (BRONJ – Bisphosphonate related ON of the Jaw)

- trauma → necrosis in the devitalized bone
- frequent after extraction
- 6-10 %
- pathological fracture, fistule formation



BISPHOSPHONATES



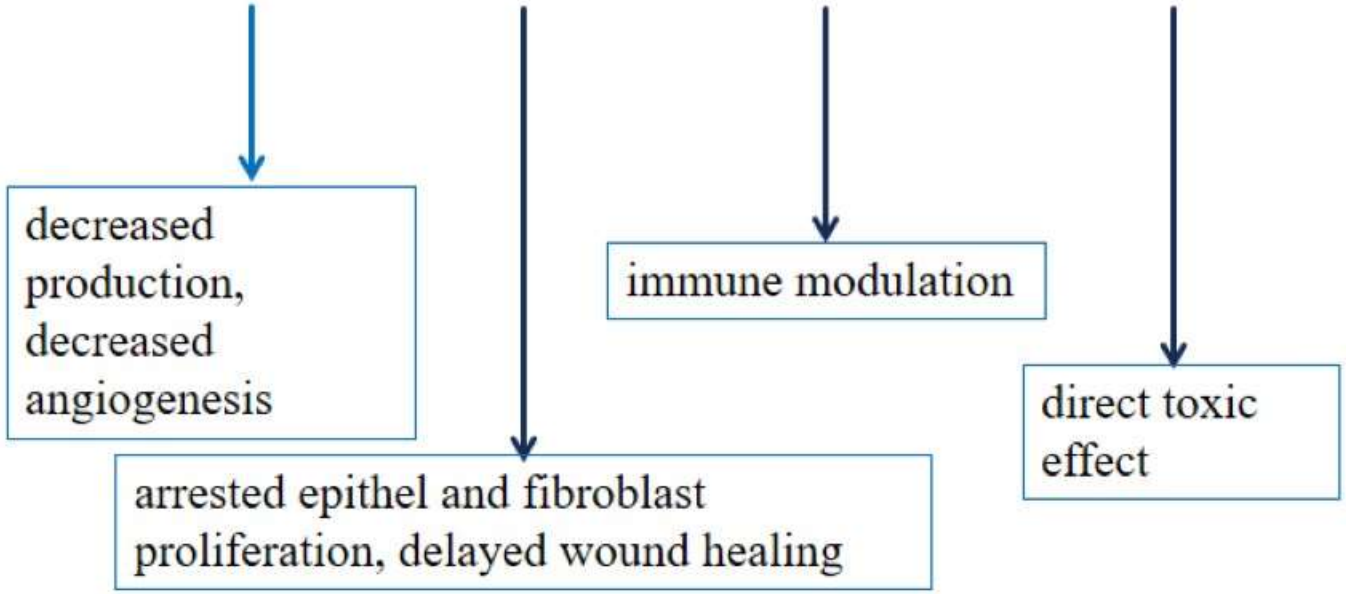
P – C – P basic structure

Applications:

Diseases with bone resorption

- malignant tumors with lytic bone met.
- Plasma cell myeloma (multiple myeloma)
- osteoporosis

BISPHOSPHONATE MECHANISM



Absorption with oral administration: ~ 3 %

Half-life: can be many decades! (low rate metabolism)

Osteoclasts:
Early cell death, decrease of VEGF-production

Osteoblasts:
Deregulation of apoptosis, increase of precursor cells

Tumor cells:
Increased apoptotic rate, inhibition of cell division

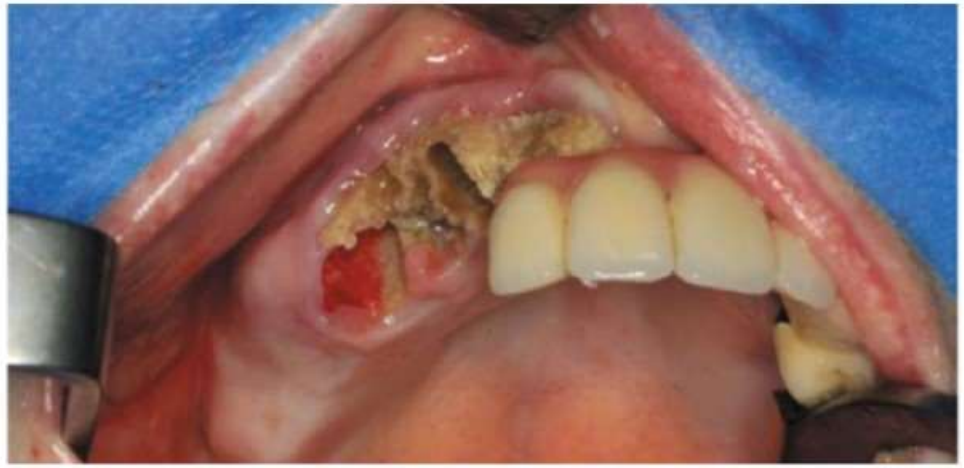
BRONJ – Bisphosphonat-related osteonecrosis of the jaw

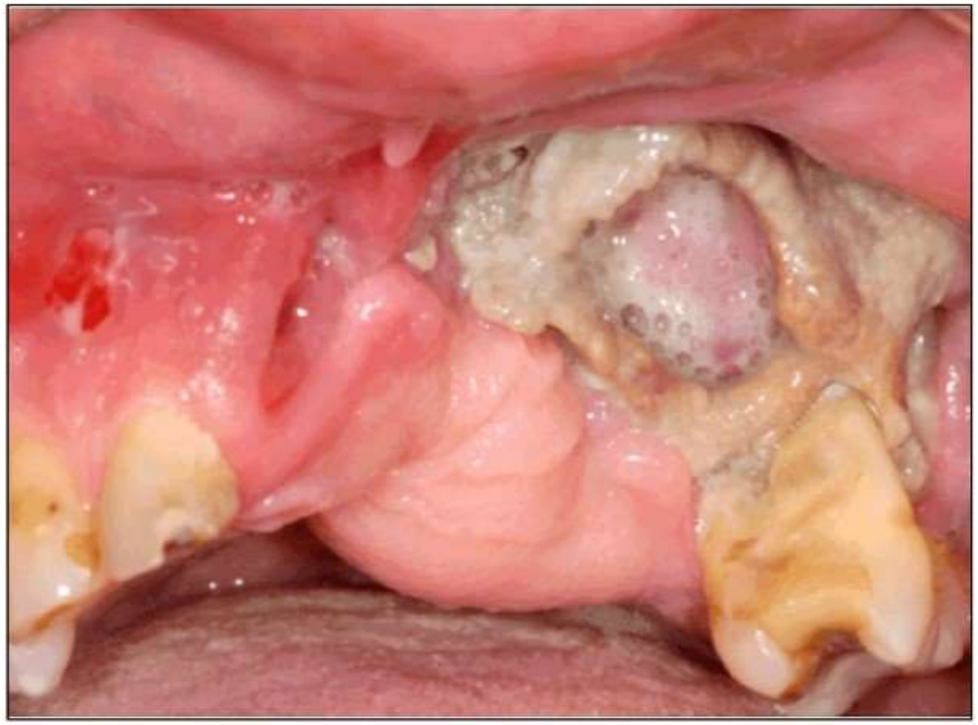
More frequent in malignant diseases than in osteoporosis
Mandible: 70%, maxilla: 30 %
Most frequently the molar region is involved
Predisposing local factors:
- extraction
- implant
- periapical focus
- continuous pressure from protesis

75% painful (visible signs of inflammation)

Histology:
- necrosis, inflammatory cells, Actinomyces
- exclude metastasis!

PATIENT Hx !!!

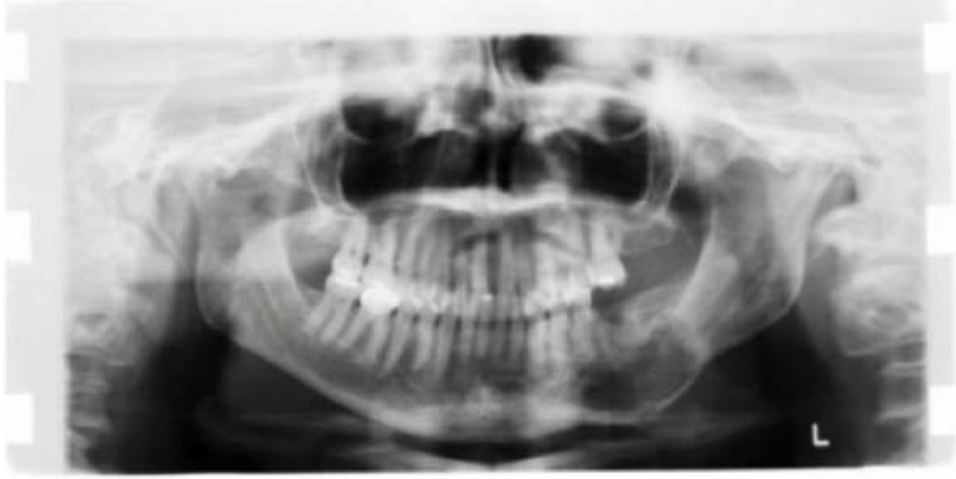




MRONJ – Medication-related osteonecrosis of the jaw

Required characteristics for diagnosis of medication-related osteonecrosis of the jaw (MRONJ):

- Current or previous treatment with antiresorptive or antiangiogenic agent
- Exposed bone in maxillofacial region for longer than 8 weeks
- No history of radiation therapy or obvious metastatic disease to the jaws

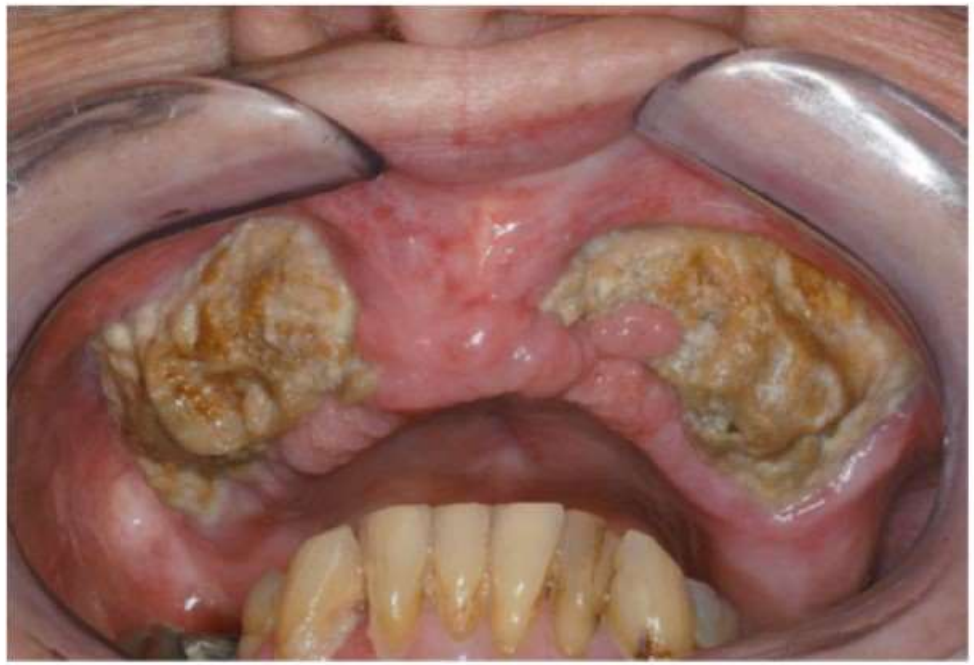


Tyrosine kinase inhibitors:

- Sunitinib (Sutent)
- Sorafenib (NexAVAR)

Monoclonal antibody inhibiting VEGF:

- Bevacizumab (Avastin)



PATIENT Hx !!!

NEOPLASTIC LESIONS OF THE JAW

NEOPLASTIC LESIONS OF THE JAW

Rare

Ossifying fibroma

- circumscribed, usually encapsulated

(ddg.: fibrous dysplasia)

Hemangioma

Chondroma

Osteosarcoma

Chrondrosarcoma

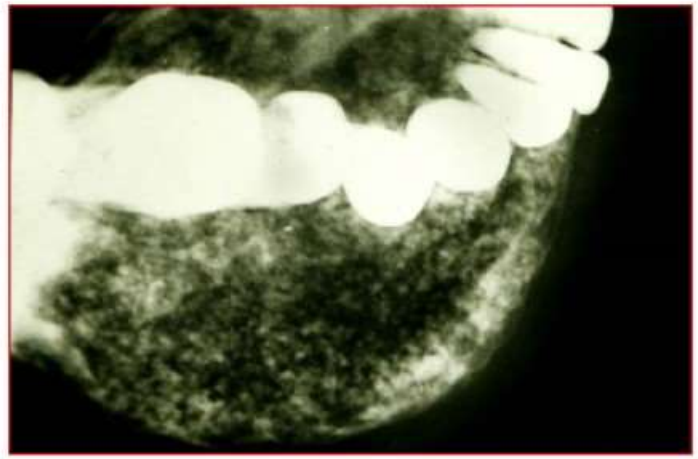
Plasmocytoma

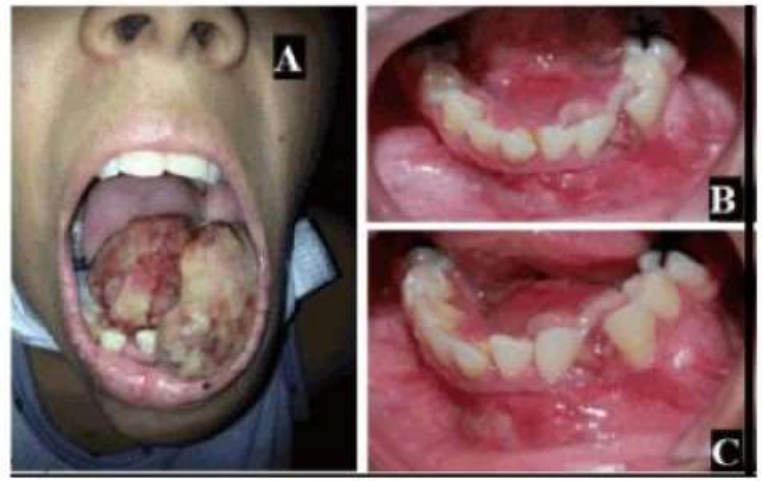
Langerhans-cell histiocytosis

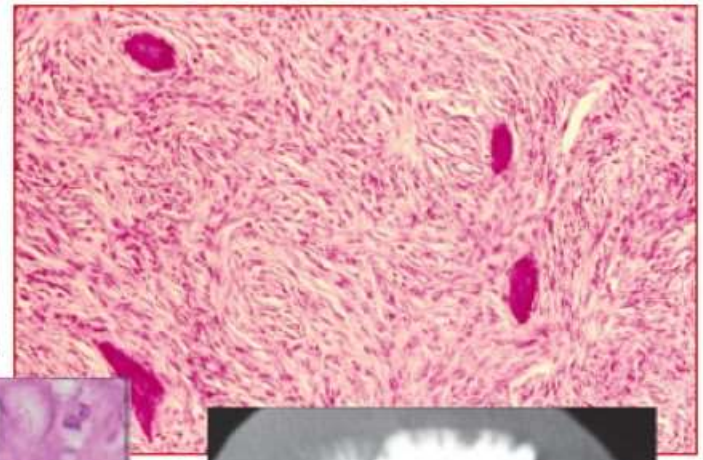
Metastatic tumors (1% of malignant tumors)

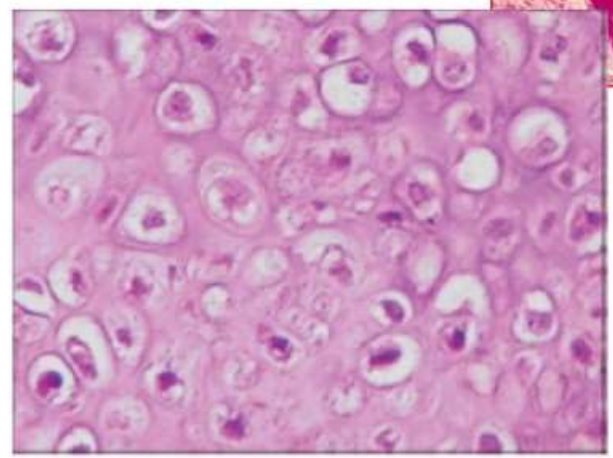
breast, lung, kidney

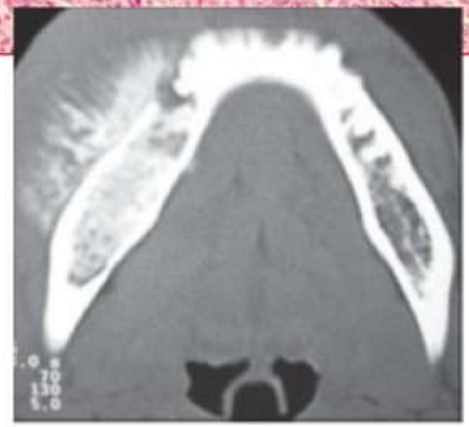
osteolytic, osteoblastic, mixed







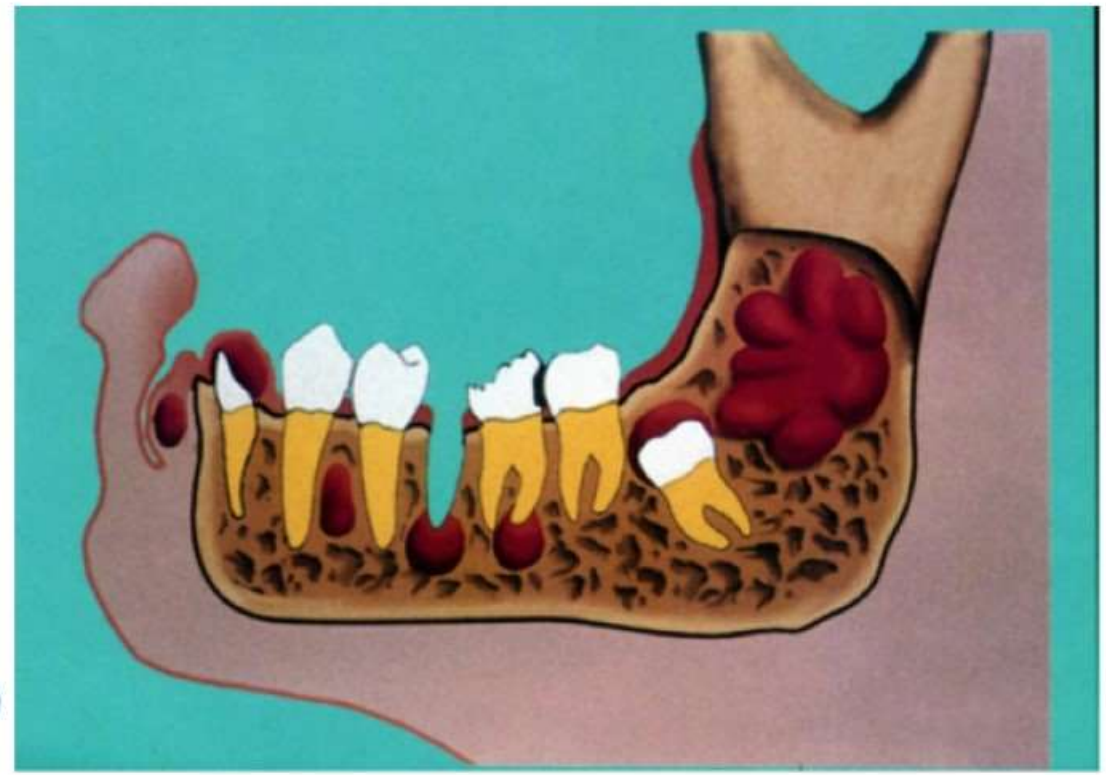




CYSTIC LESIONS OF THE JAW

MANDIBULAR (JAW) CYSTS

- Odontogenic (90%)
  - Inflammatory (60-70%)
  - Developmental
- Non-Odontogenic (10%)
  - Nasolabial (nasoalveolar)
  - Aneurysmal bone cyst
  - Nasopalatinal cyst (foramen incisivum)



ODONTOGENIC CYSTS

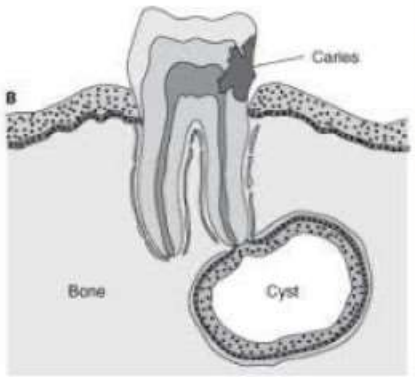
Developmental cysts
Orthokeratinised odontogenic keratocyst
Odontogenic keratocyst (previously tumor*)
Dentigerous (follicular) cyst
Gingival cyst of newborns
Gingival cyst of adults
Lateral periodontal cyst
Glandular odontogenic cyst
Eruption cyst
Calcifying odontogenic cyst

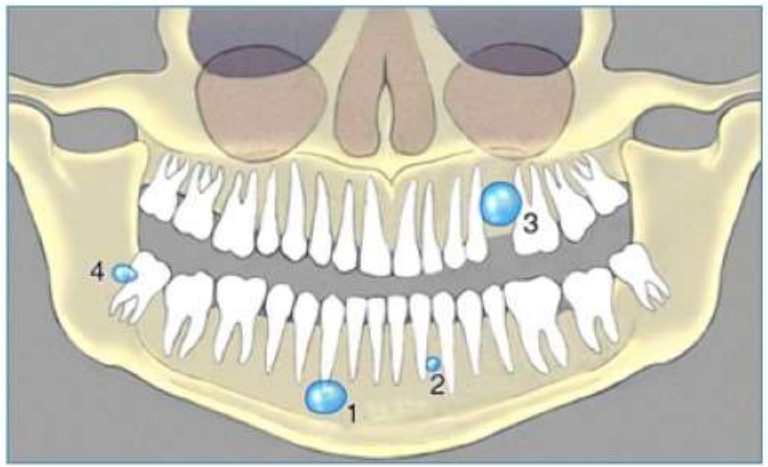
Inflammatory cysts
Paradental cyst
Radicular/periapical cyst
Residual cyst

Signs of inflammation:
Pain – Periapical cyst
Redness – Residual cyst
Proliferation – Paradental cyst

Cystic neoplasms
Unicystic ameloblastoma
Calcifying cystic odontogenic tumor

RADICULAR CYST





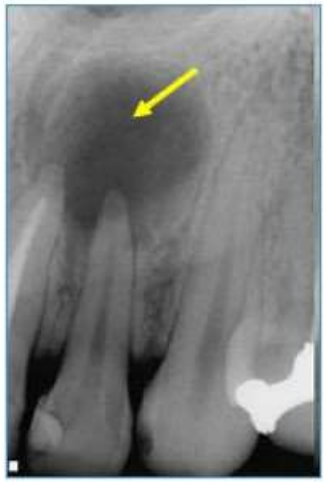
LOCALISATION:

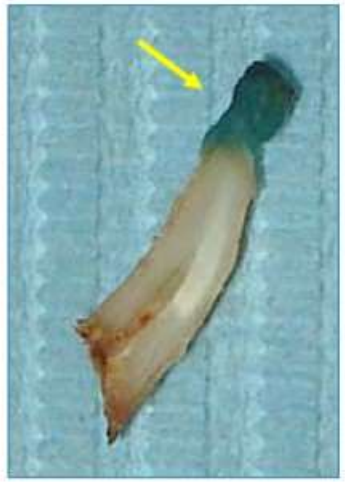
1 – apical

2 – lateral

3 – residual

4 – paradental (next to partially erupted wisdom tooth, associated with pericoronitis)





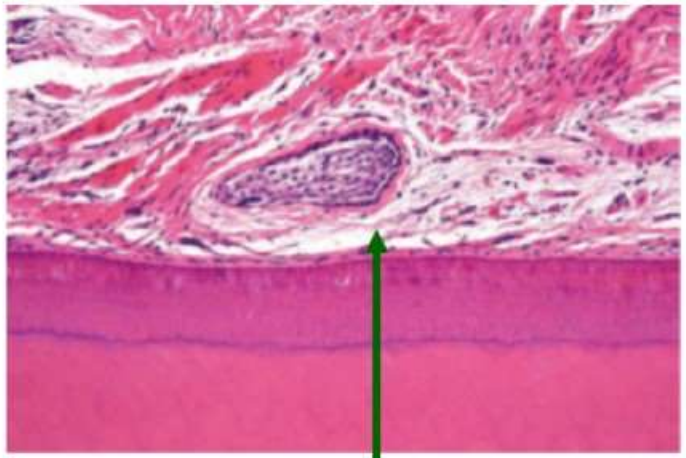
Around necrotised, non-vital tooth

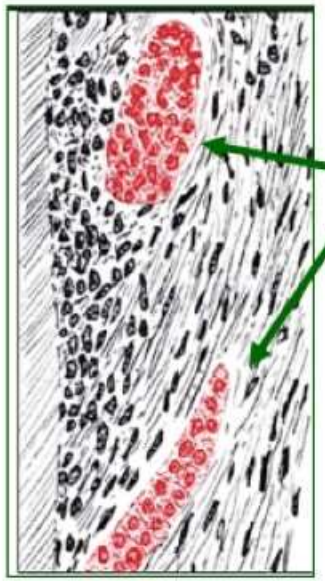
Periapical granuloma → cytokines, growth factors →

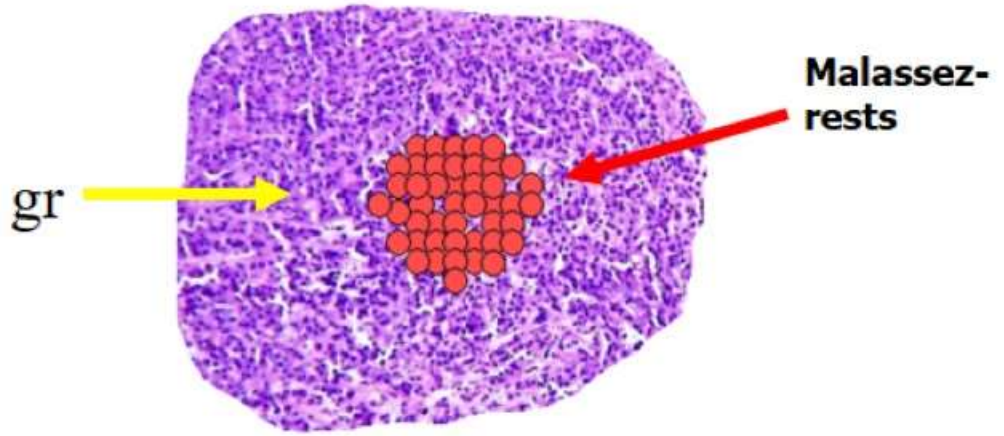
proliferation of rests of Malassez-f. → **cyst formation**

- Degeneration, death of the central cells, microcysts, confluent microcysts
- Infected root canal, bacteria, lytic effect

RADICULAR CYST

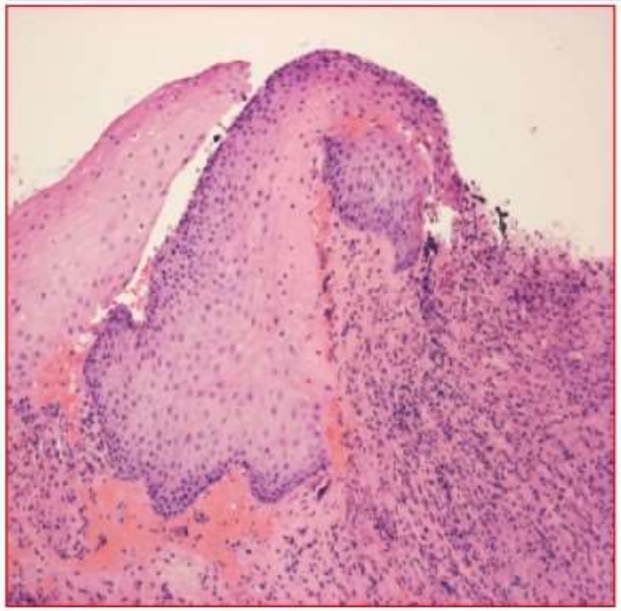






1. Periapical granuloma, bacterial endotoxins (mitogenic effect on the epithel cells + cytokines) - IL-1, IL-6, TNF, PDGF, TGFβ -
2. Center: hypoxic necrosis, high protein content
3. Osmotic fluid influx → more necrosis → more elevatad protein content → larger cavityüreg
4. Central cavitation becomes independent of the inflammation
5. May result in a bone resorption

RADICULAR CYST

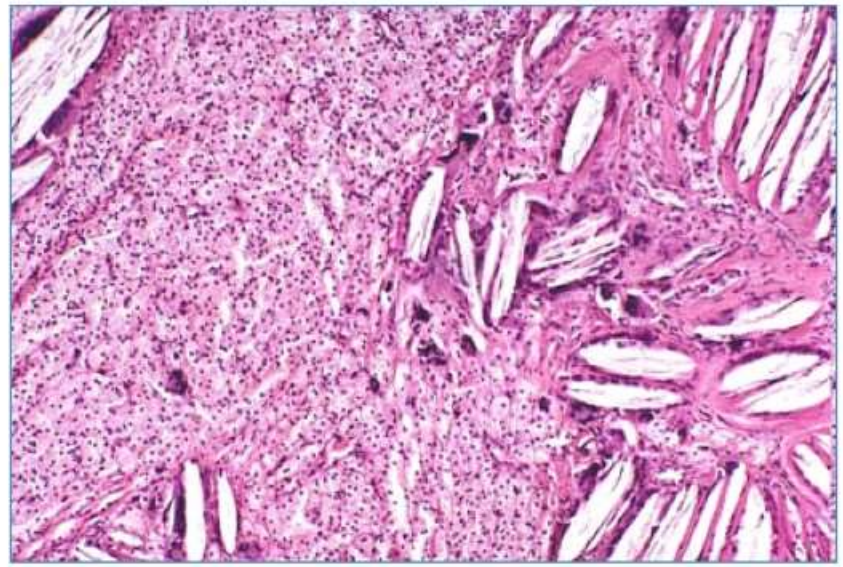


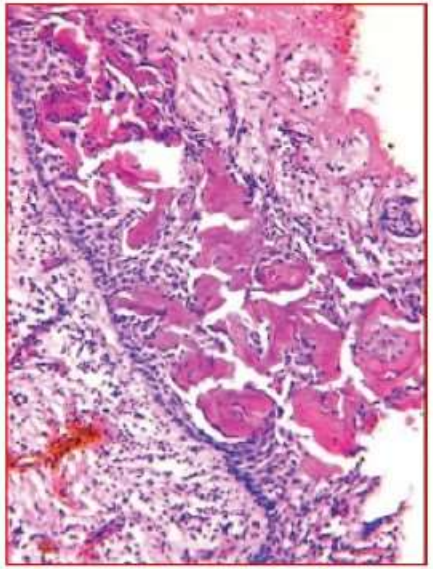
Hyperplastic, non-keratinizing squamous epithelium

Rushton-bodies (10 %)

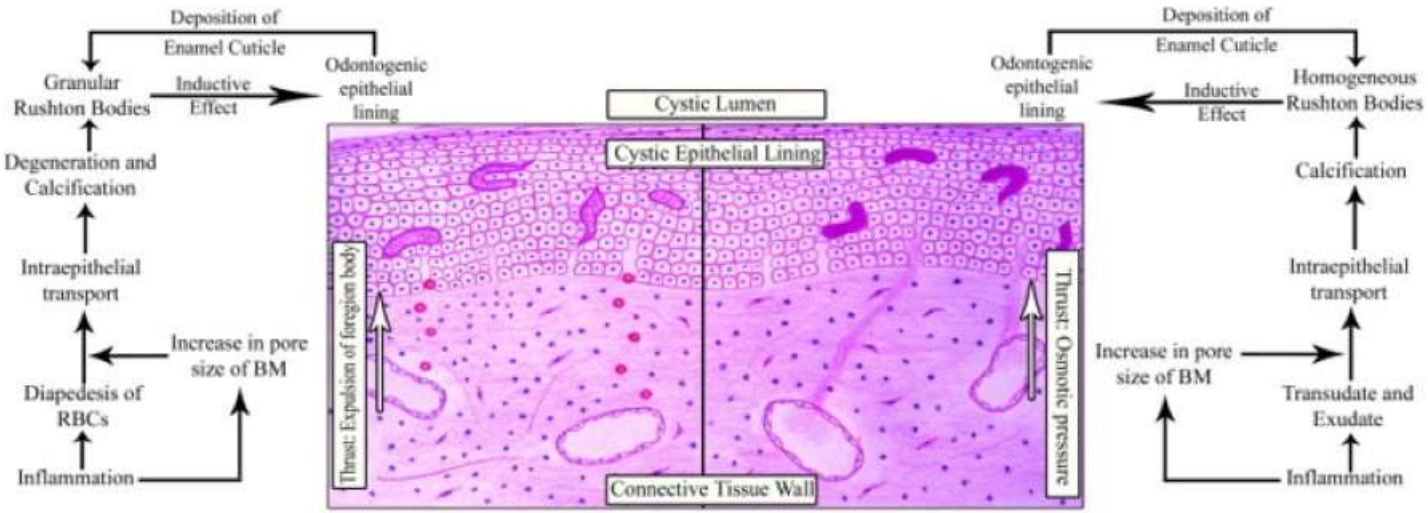
Cholesterin clefts

Chronic inflammatory stroma

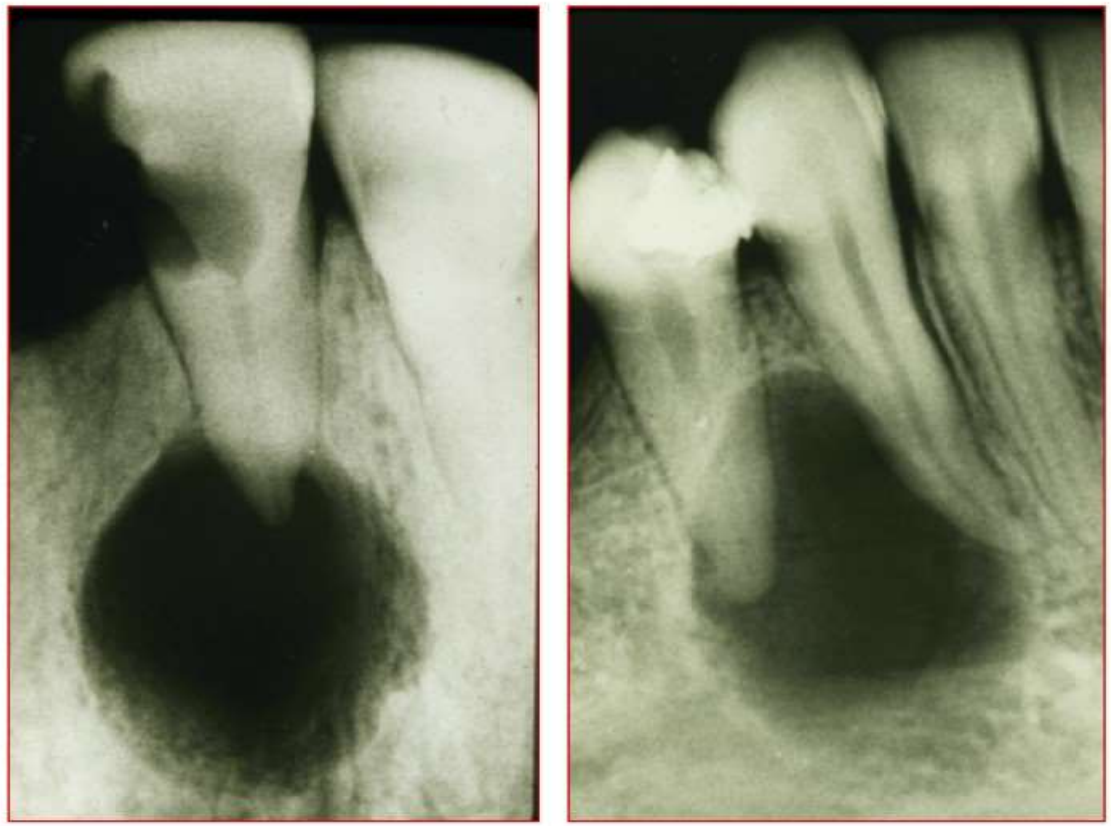




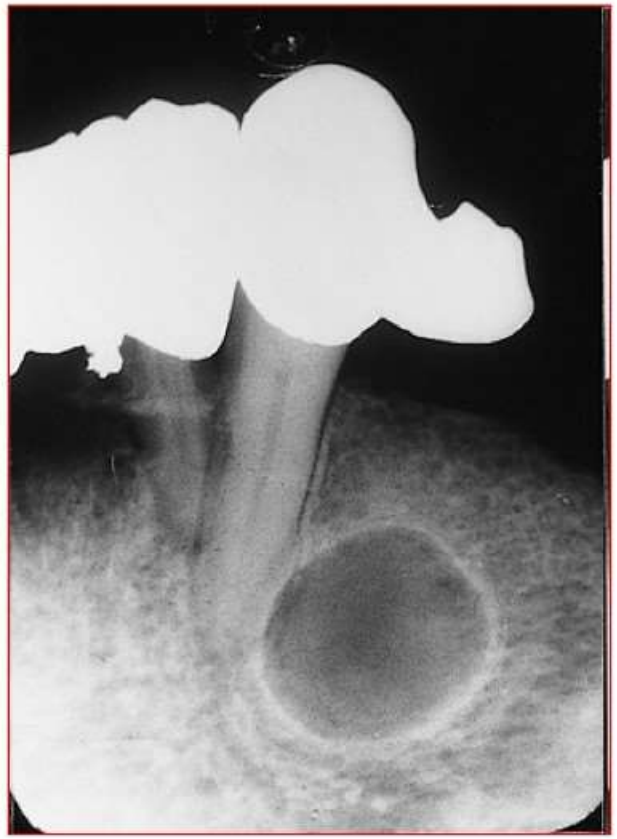
Development of Rushton bodies



RADICULAR CYST



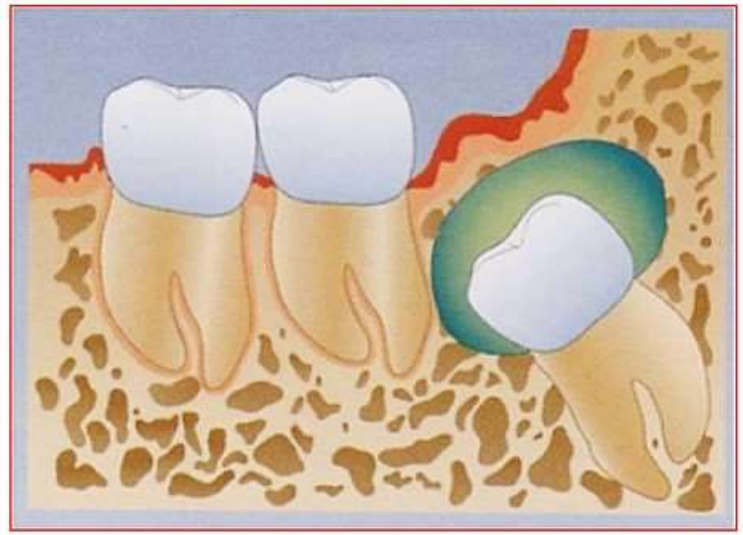
Periapical (radicular) cyst

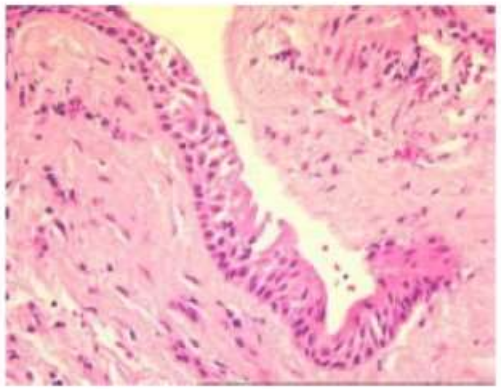


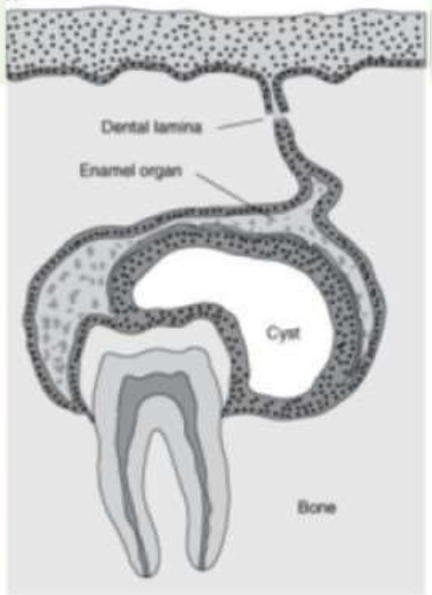
Residual periapical (radicular) cyst

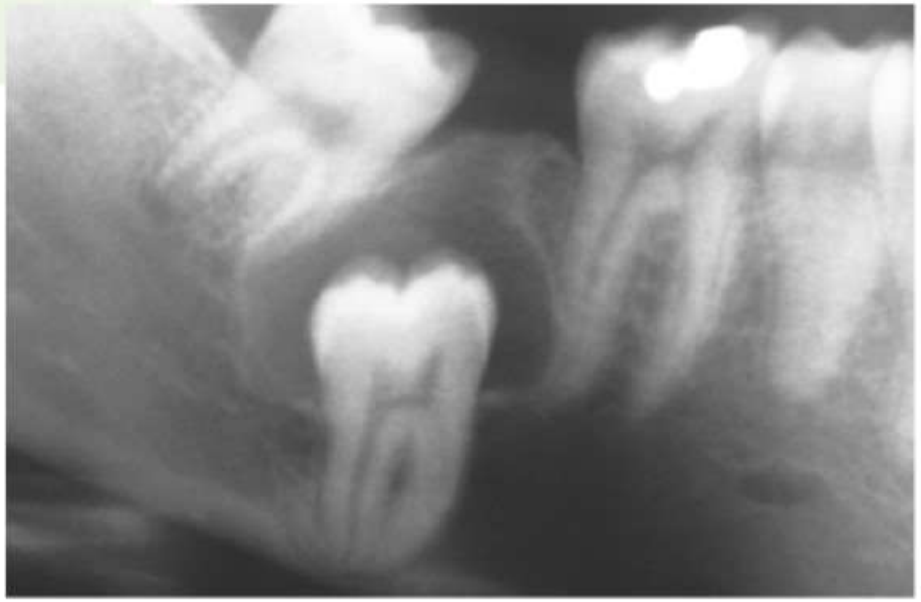
FOLLICULAR (DENTIGEROUS) CYST

- Encloses part of all of the crown of an unerupted tooth
- Mechanism is largely unknown
- Wide age distribution
- Painless
- Most frequent at the area of molar 3
- Unilocular
- 4-5 layers, non-keratinizing squamous epithelium (± mucinous metaplasia)
- Inflammation is usually absent







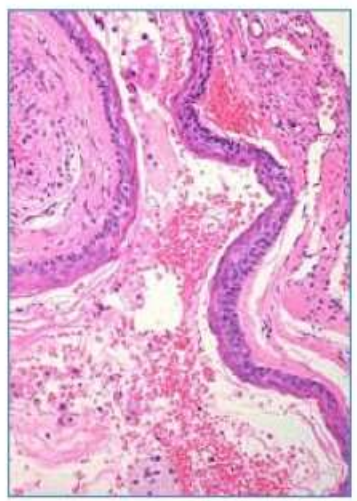


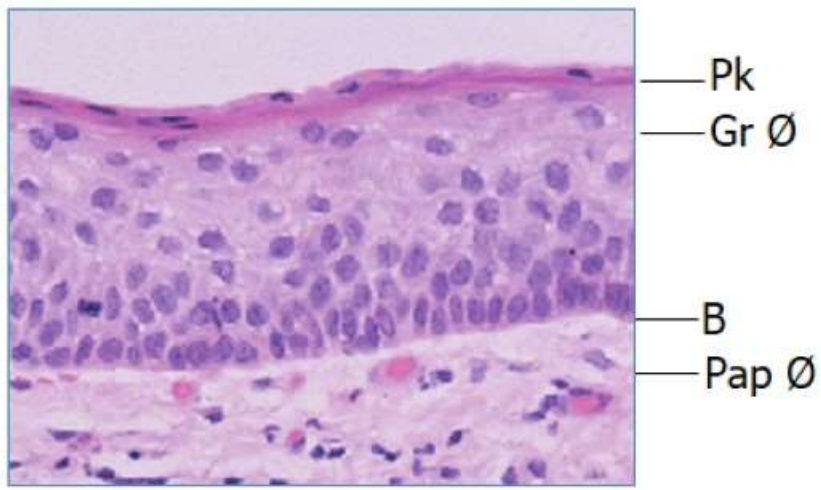
KERATOCYSTS

Odontogenic keratocyst (OKC)

(WHO: keratocystic odontogenic tumor (2005-17))
(now: cyst again)

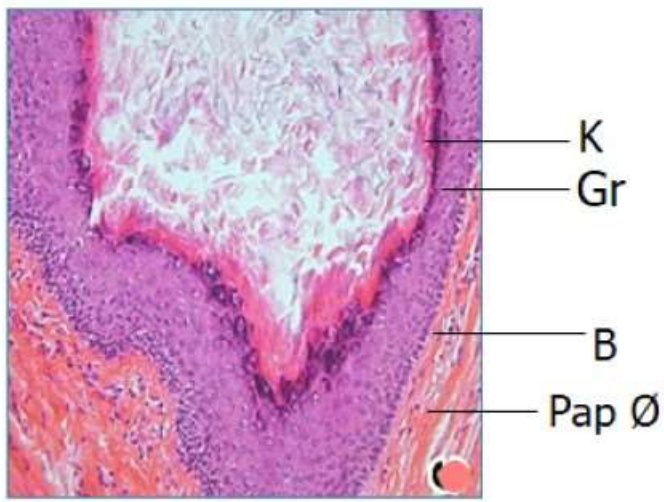
- Frequently more agressive than other cysts
- More frequent recurrance rate
- May be associated with nevoid basal cell cc syndr.
- 65-75% mandible (mainly molar)
- Young adults
- Unilateral, sclerotic rim
- May be secondarily inflamed

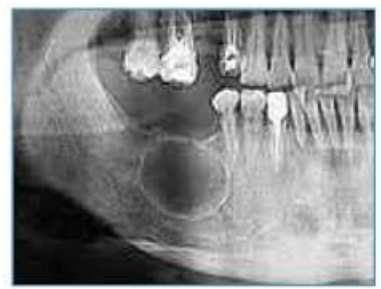




Orthokeratinized odontogenic keratocyst

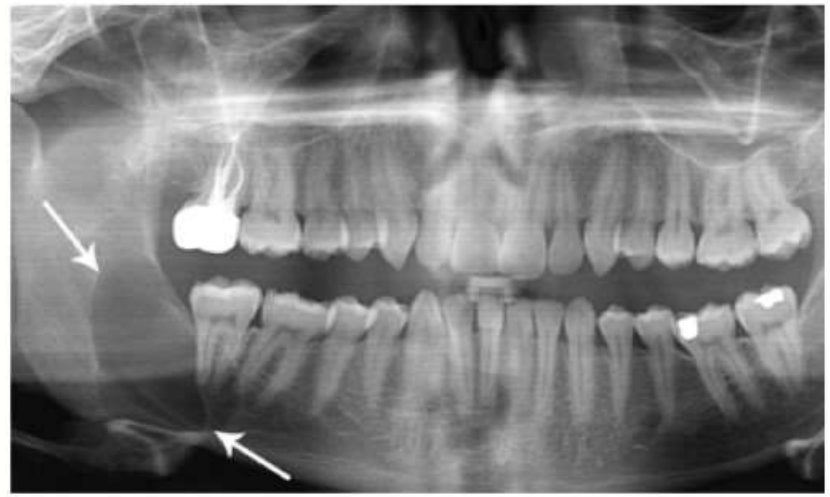
- Teenagers, young adults
- Male predominance (60-70%)
- Mainly in the posterior part of mandible
- 70% associated with impacted tooth
- Usually unilocular
- Rare recurrence rate (~ 3 %)
- No association with Gorlin-syndrome

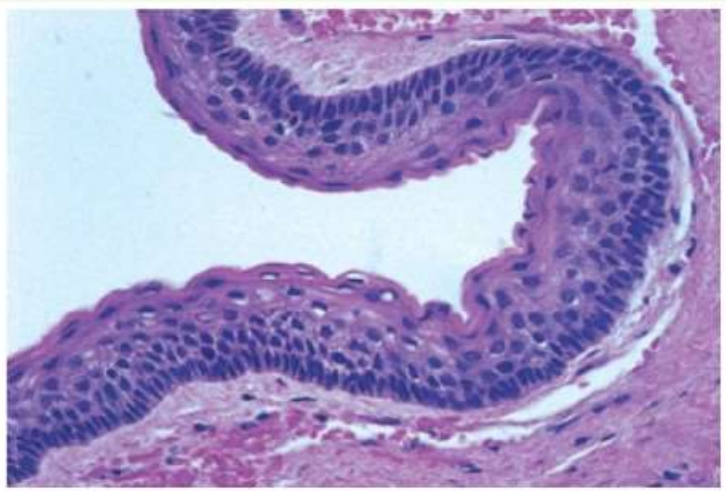


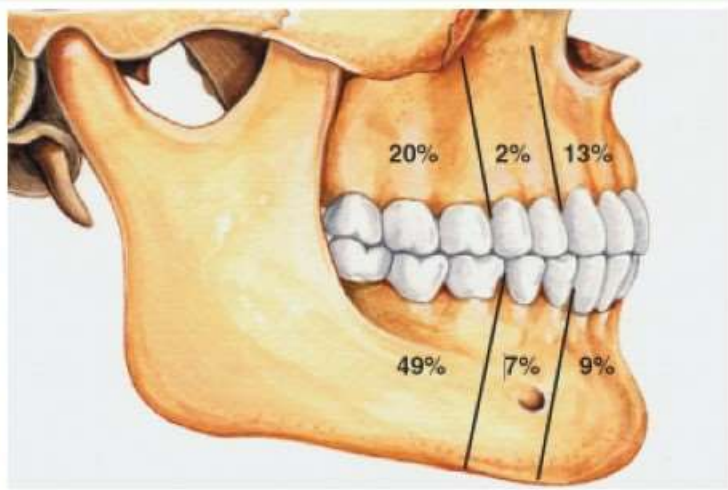


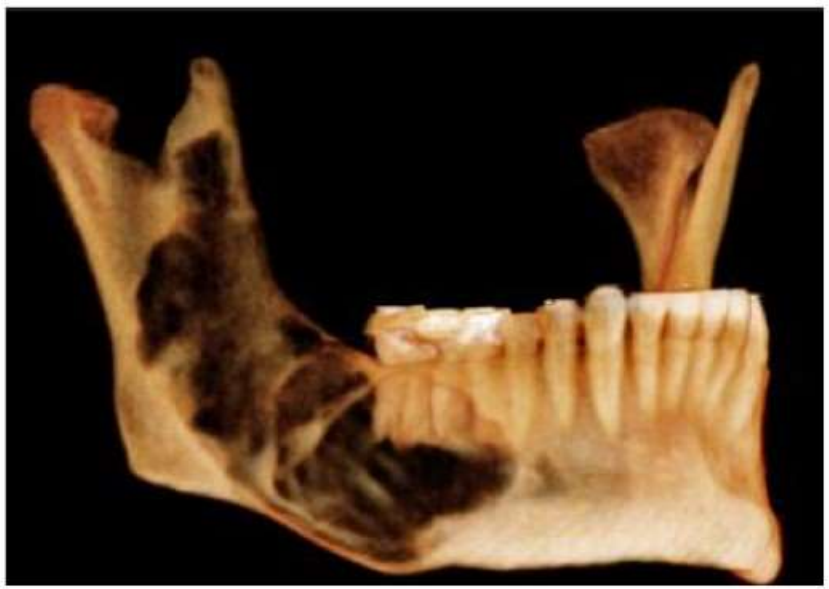
ODONTOGENIC KERATOCYST (OKC)

- the initial terminology for an odontogenic keratocyst (OKC) was "primordial cyst," as the origin of the lesion was thought to be the tooth primordium
- is known for its high recurrence rate, aggressive behavior, and its occasional association with the Gorlin-goltz syndrome
  (Gorlin-goltz sy = basal cell naevus syndrome BSCNS)
- Odontogenic keratocysts (OKCs) associated with Gorlin-Goltz syndrome have occasionally been reported to transform into aggressive neoplasms such as ameloblastomas and squamous cell carcinoma.

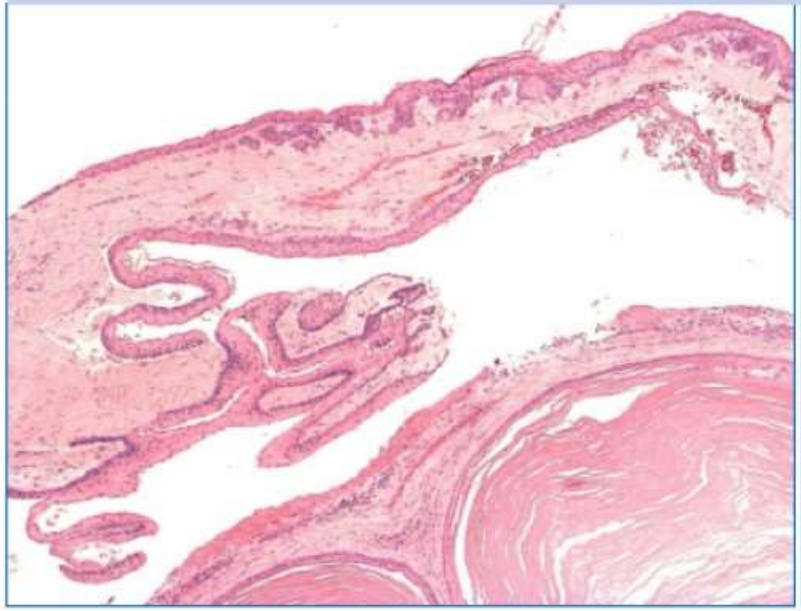


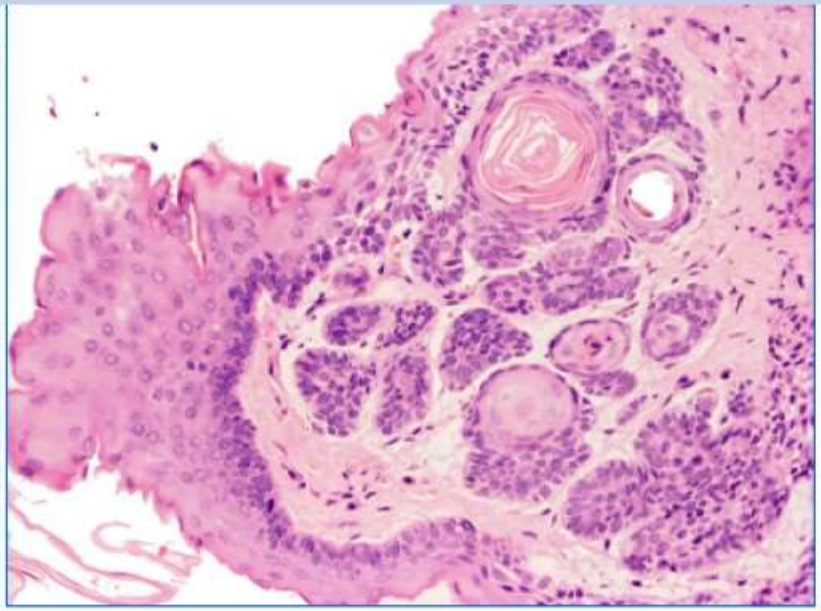






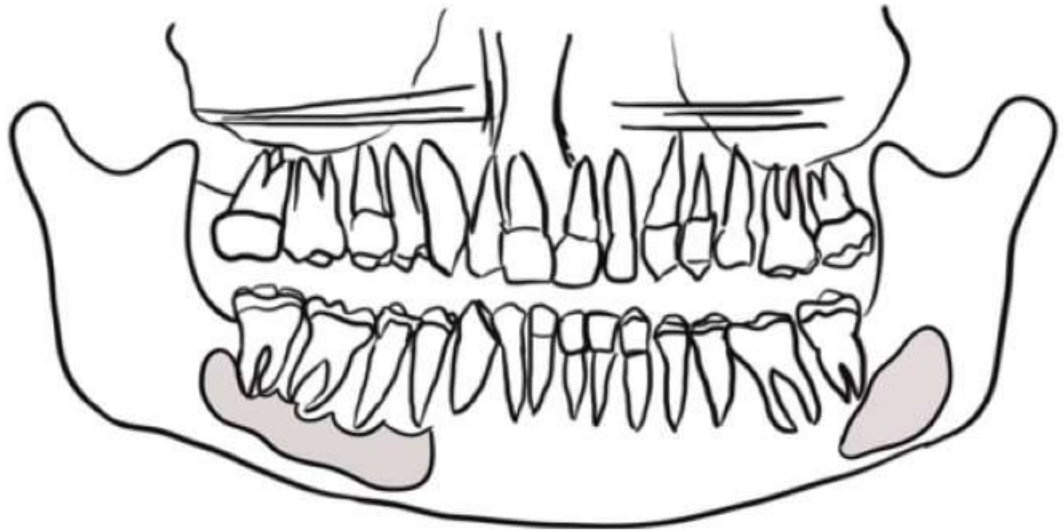
KERATOCYSTS

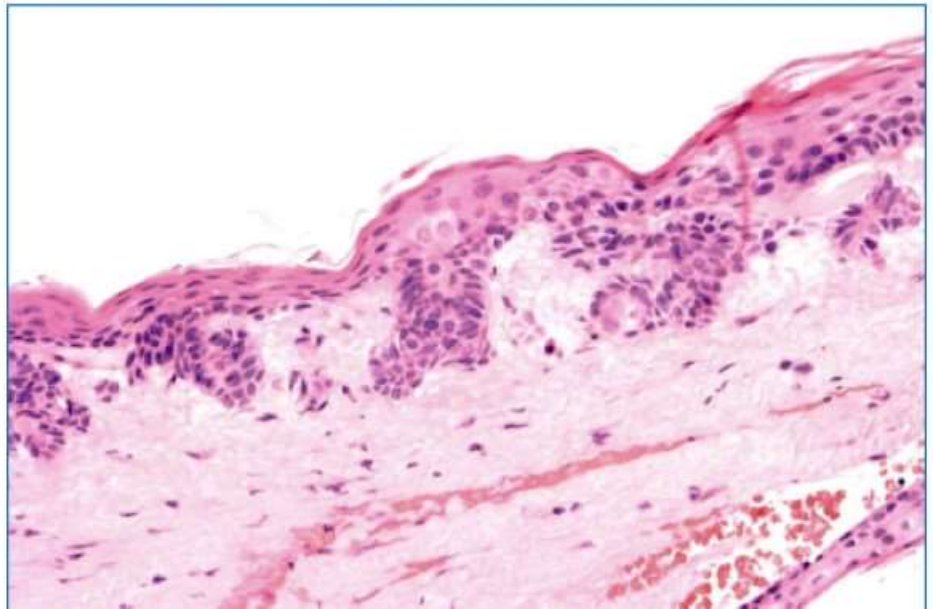




Radiographs are not diagnostic:

Differential:
Ameloblastoma
Unicystic ameloblastoma
Dentigerous cyst
Radicular cyst
Lateral periodontal cyst

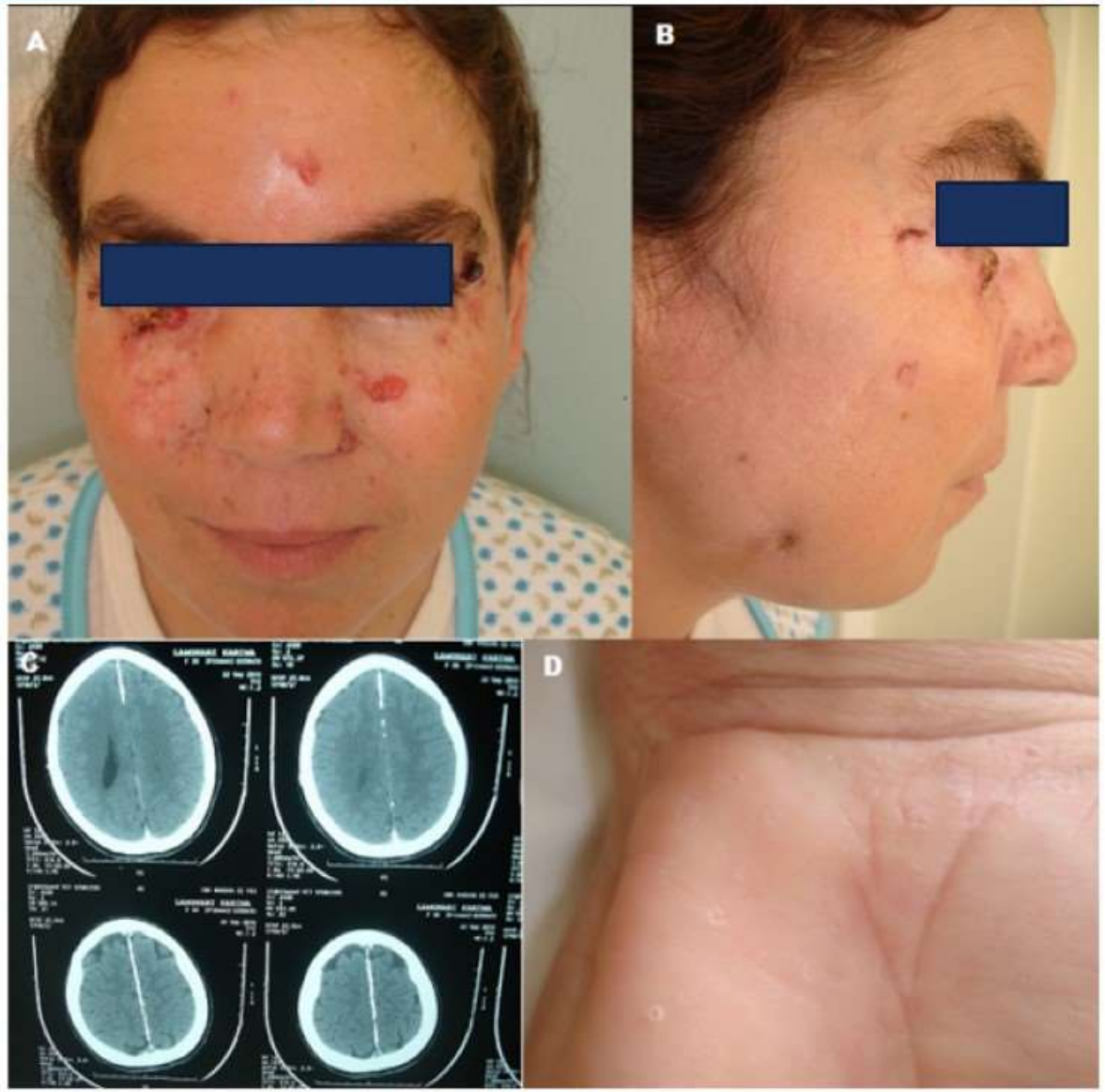




GORLIN-GOLTZ SYNDROME

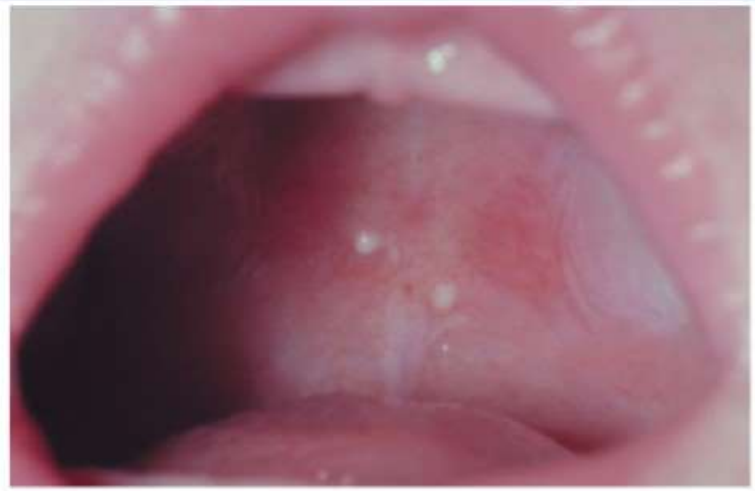
Gorlin-goltz syndrome:
ectomesodermal polydysplasia with numerous manifestations characterized most often by **cutaneous** abnormalities (basaliomas)

- **craniodentofacial anomalies**
  odontogenic keratocyst (OKC)
  Malocclusion
- **broad nasal bridge**, and increased head circumference;
- **skeletal anomalies**, including frontal and parietal bossing and mandibular prognathism,
- **costal anomalies**



PALATAL CYSTS OF THE NEWBORN (EPSTEIN'S PEARLS; BOHN'S NODULES)

Small developmental cysts are a common finding on the palate of newborn infants.

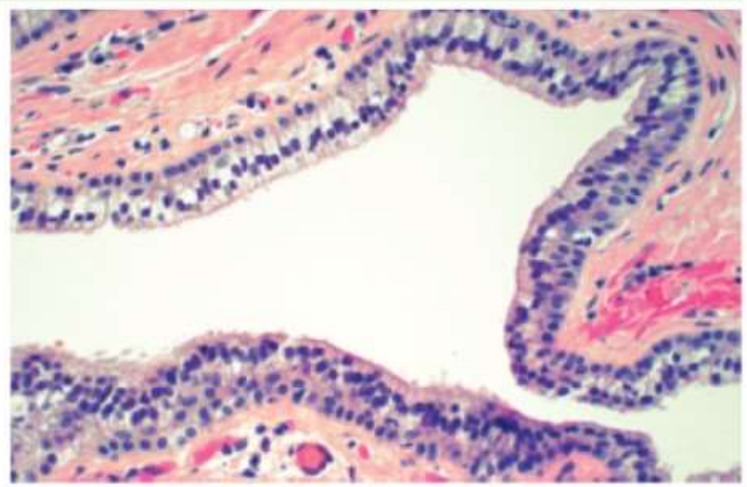


Histopathologic Features

- Microscopic examination reveals keratin-filled cysts that are lined by stratified squamous epithelium.
- Sometimes these cysts demonstrate a communication with the mucosal surface.

NASOLABIAL CYST

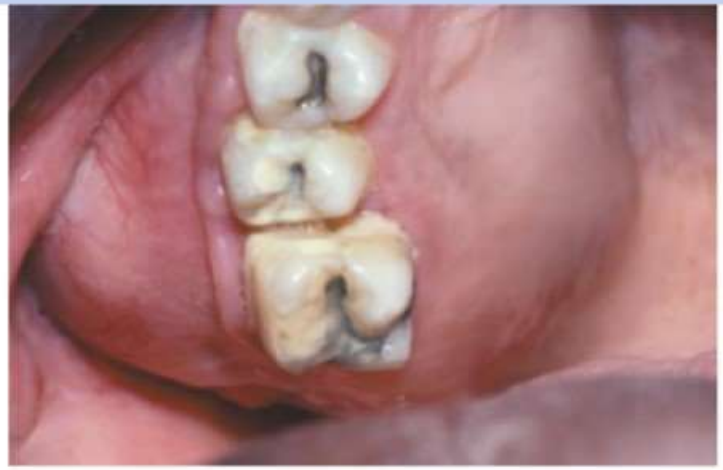
rare developmental cyst that occurs in the upper lip lateral to the midline. The pathogenesis is uncertain

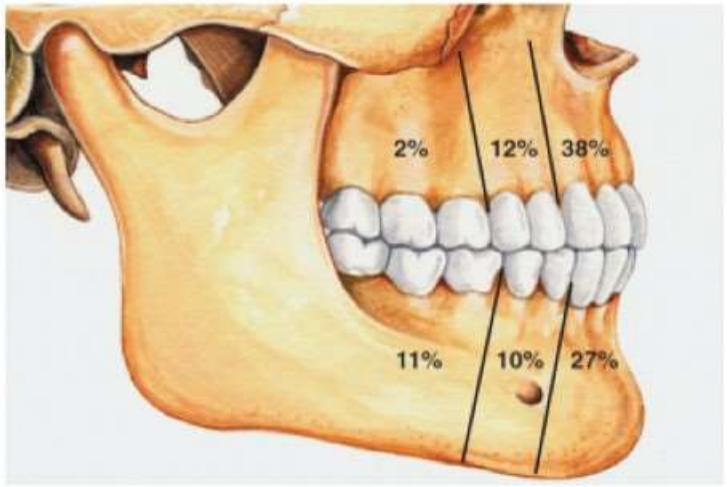


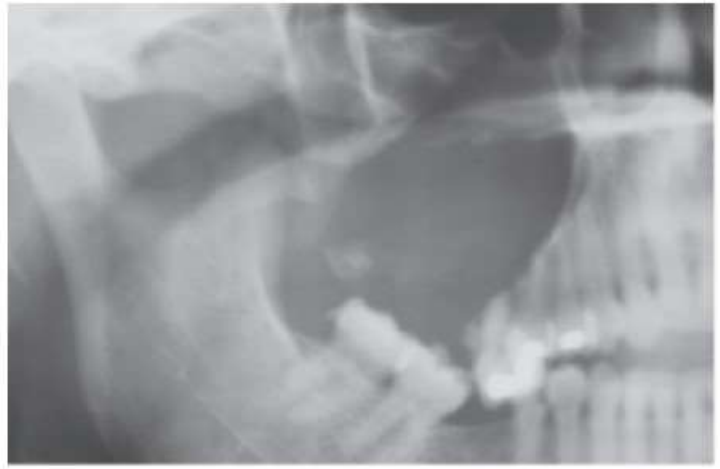
CALCIFYING ODONTOGENIC CYST

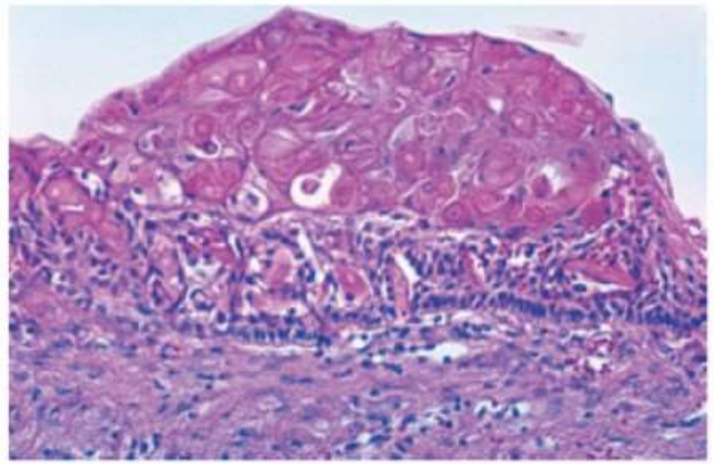
Intraosseous calcifying odontogenic cysts:

- Frequency: maxilla = mandible.
- About 65% of cases are found in the incisor and canine areas
- Mean age is 30 years
- The central calcifying odontogenic cyst is usually a unilocular
- well-defined radiolucency,





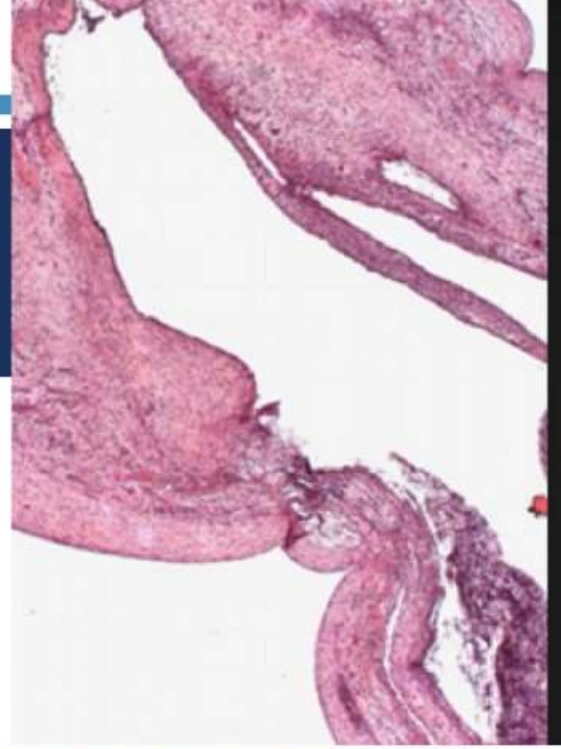


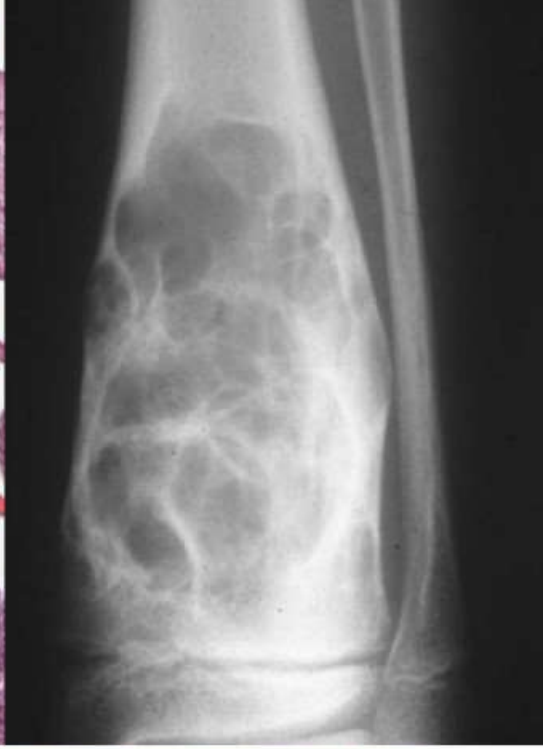


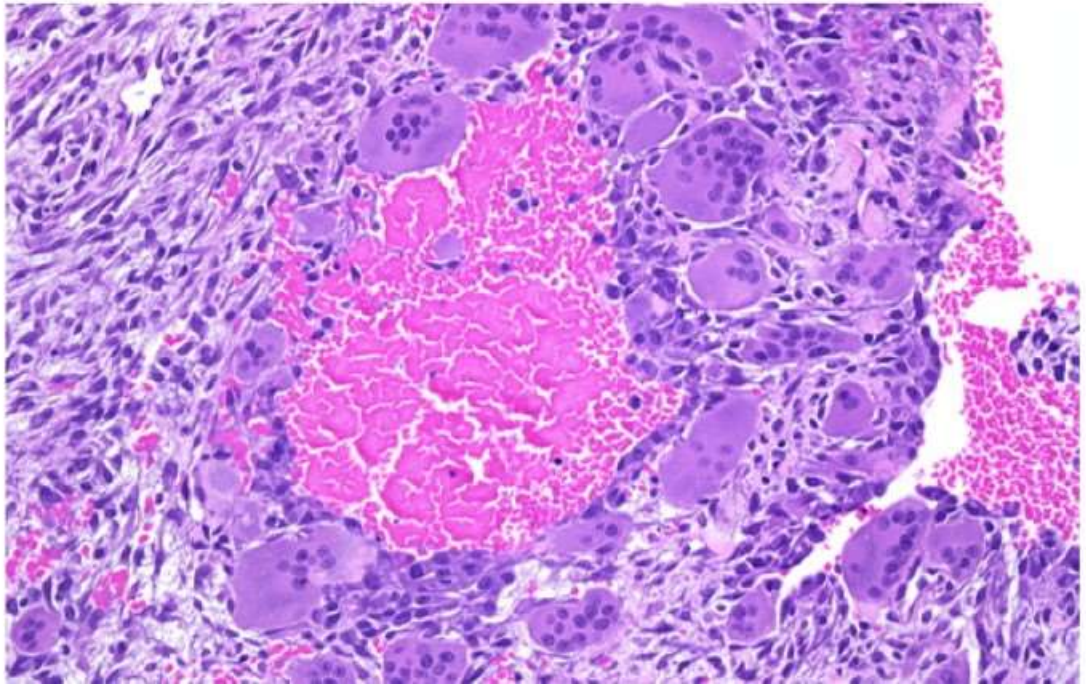
Histology:
Calcifying odontogenic cyst most commonly occurs as a well-defined cystic lesion with a fibrous capsule and a lining of odontogenic epithelium of four to ten cells in thickness

NONODONTOGENIC CYSTS: ANEURYSMAL BONE CYST

- Common bone lesion, but rare in the jaws
- It may arise as a **primary** or a **secondary** lesion (next to a preexsisting bone lesion)
- Mandible>maxilla
- May be uni- or multilocular
- May have a balloned-out appearance due to cortical expansion
- Unknown pathogenesis
- Genetics USP6 rearrangement
- Mikro:
  - Non endothelial lined blood filled cavities of varying sizes of cellular fibrous tissue
  - Multinucleated giant cells
  - Old and recent haemorhage







THANK YOU FOR YOUR ATTENTION!

Used literature (and pictures) from:
Pathologyoutlines.com,
Oral Pathology (Expert Consult) (Woo),
Oral and Maxillofacial Pathology (Neville)