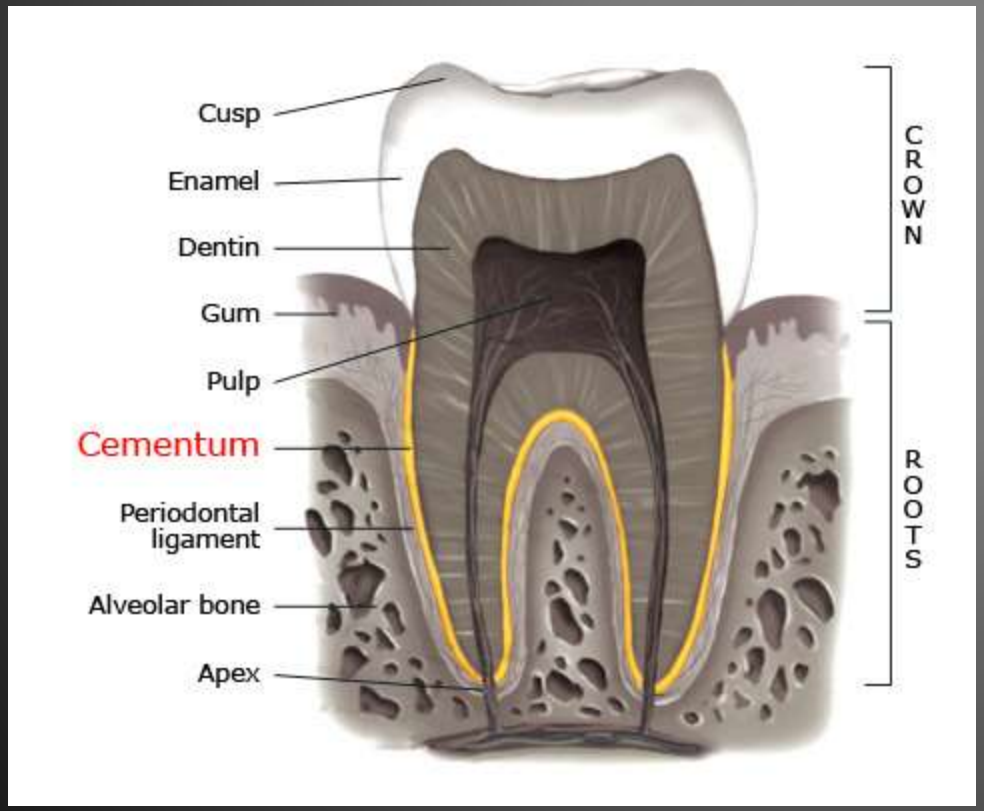
CEMENTUM & BONE

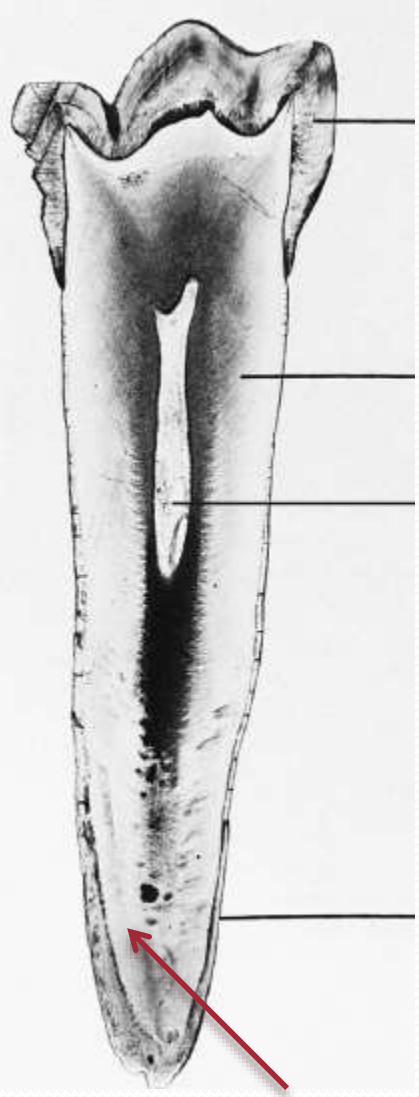


Contents:

- Cementum – properties & composition
- Cementogenesis
- Types of cementum
- CDJ & CEJ
- Functions
- Clinical considerations

Cementum:

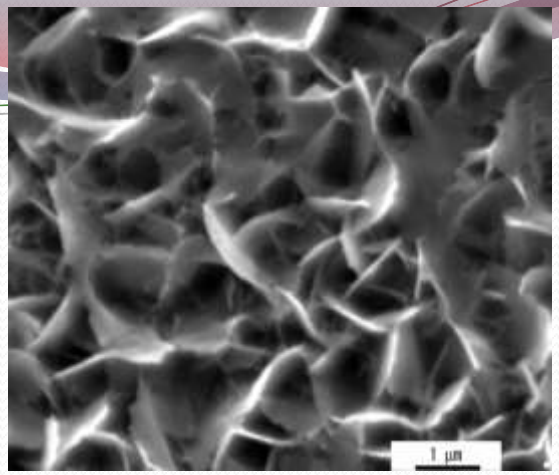
- Cementum is the mineralized dental tissue covering the anatomic roots of human teeth.
- 1st demonstrated microscopically in 1835 by two pupils of Purkinje.
- Begins at cervical portion of tooth at CEJ and continues to the apex.
- Specialized connective tissue.
- Avascular & Non innervated



Physical properties

- Hardness of fully mineralized cementum is less than that of dentin.
- Light yellow in color. Can be distinguished from enamel by its lack of luster and darker hue.
- Lighter in color than dentin.
- Thinnest at CEJ (20-50µm) and thickest towards apex(150-200 µm)

Chemical composition:



- 45-50 % inorganic substances
- 50-55 % organic material & water

- Inorganic content:

➢ Calcium & phosphate in form of hydroxyapatite

➢ Crystals are 55 nm wide and 8nm thick similar to bone.

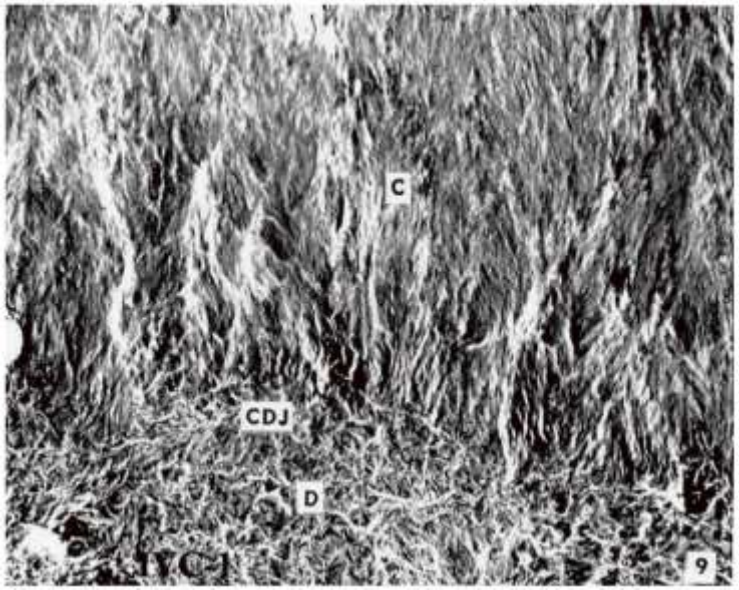
➢ Trace elements Mg, S, Cu, Zn.

➢ Cementum has highest fluoride content amongst dental tissues.

➢ Highest fluoride than any other calcified tissue

Organic contents

- Type I collagen mainly
- Other collagens – type III, V, VI, XII
- Proteoglycans – Chondroitin sulfate, Heparan sulfate, Hyaluronate



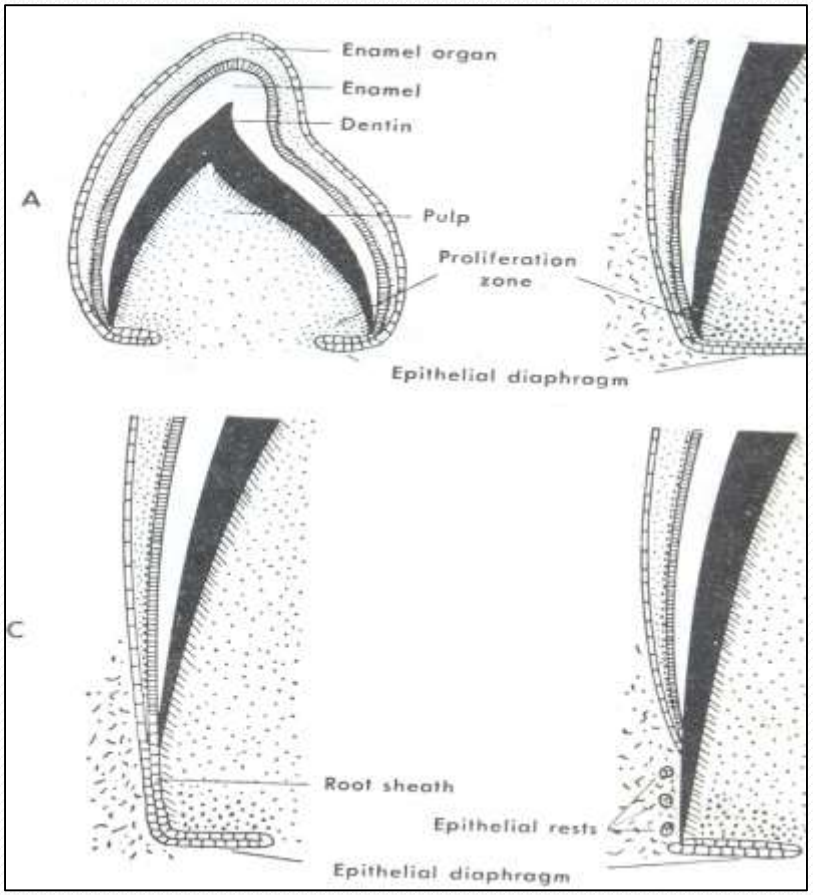
MOLECULE	ROLE IN CEMENTOGENESIS
1. GROWTH FACTORS: A) TGF-β superfamily including BMPs B) PDGF & IGF C) FGF	•Promote cell differentiation-cementogenesis •Alter cell cycle activities •Promote cell proliferation, migration & vasculogenesis
2. ADHESION MOLECULES: A) BSP- Bone Sialoprotein B) Osteopontin	•Promotes adhesion of selected cells to newly forming root & also mineralization •Regulates extent of crystal growth- inhibitor
3. EPITHELIAL / ENAMEL PROTEINS:	•Involved in promoting follicle cells along cementoblast pathway
4. Gla PROTEINS: (γ- carboxyglutamic acid) A) Matrix Gla proteins B) Bone Gla proteins	•Prevent abnormal ectopic calcification •Strong affinity for calcium- mineralization & regulation of crystal growth

MOLECULE	ROLE IN CEMENTOGENSIS
5.TRANSCRIPTION FACTORS (Osterix)	•Cementoblast differentiation
6. SIGNALING MOLECULES A) OPG- Osteoprotegerin B) RANK & RANKL	•Mediate bone & root resorption by cementoclasts

CEMENTOGENESIS

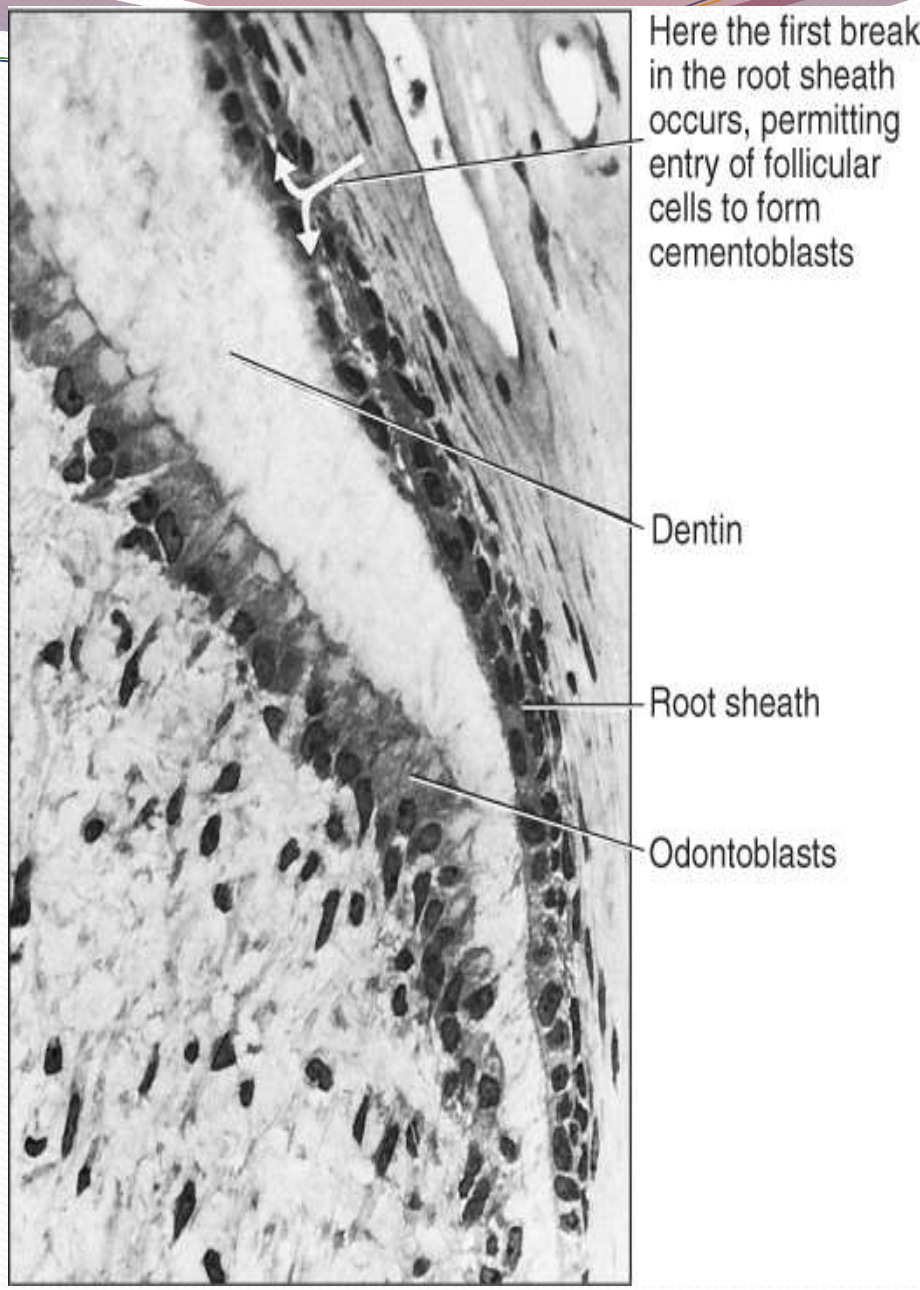
- Cementum formation in developing tooth is preceded by deposition of dentin along the inner aspect of HERS.

- Once dentin formation is under way, breaks occur in epithelial root sheath.



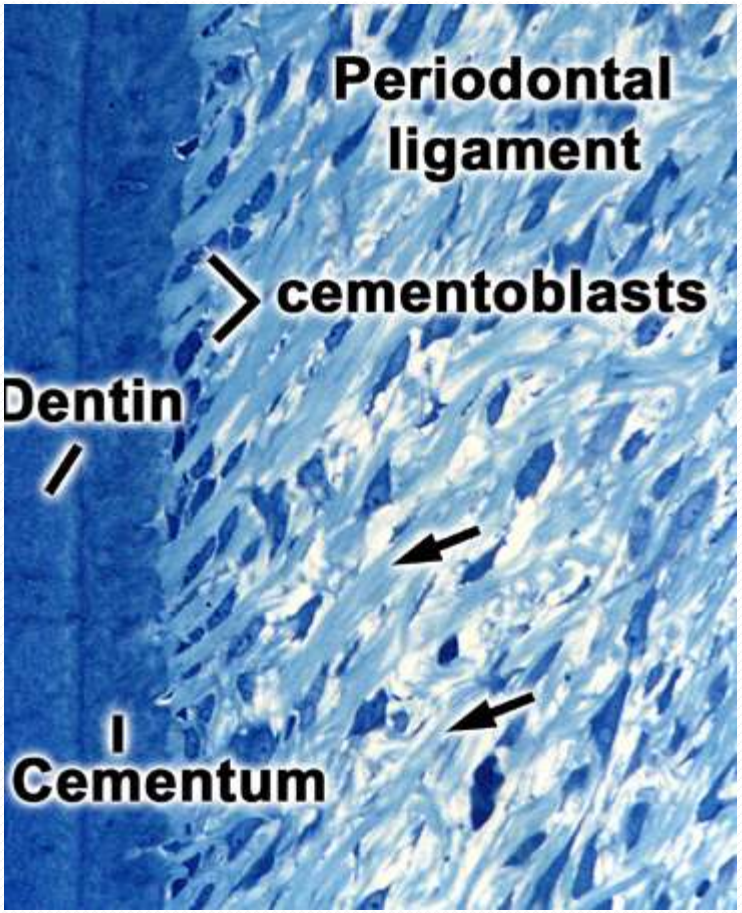
- The epithelium is moved away from the surface of the dentin so that connective tissue cells come into contact with the outer surface of the dentin and differentiate into

- *Cementoblasts* that deposit a layer of cementum onto the surface of the dentin.

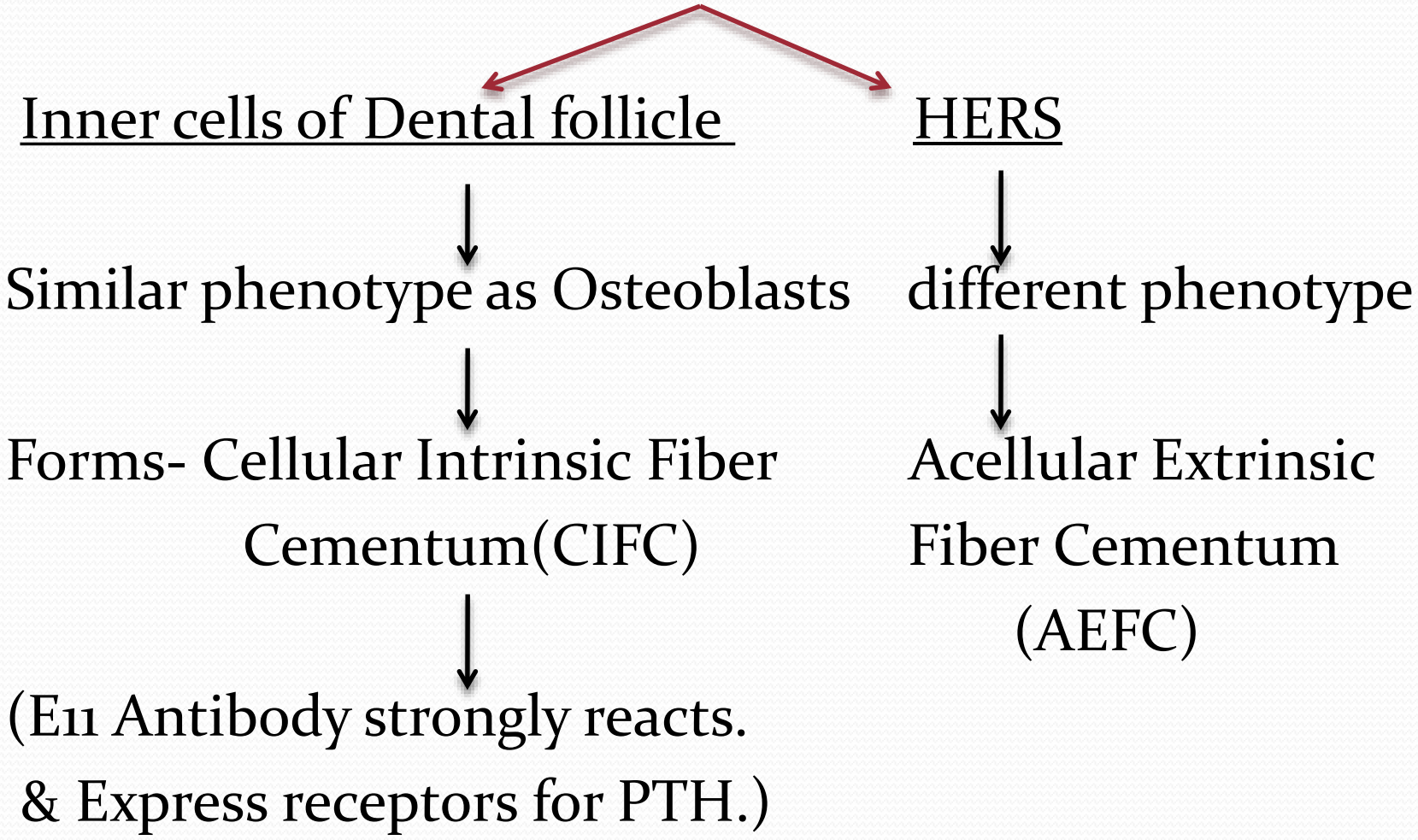


CEMENTOBLASTS

- Synthesize collagen and protein polysaccharides, which form the organic matrix of cementum.
- Cells have- numerous mitochondria, a well-formed Golgi apparatus & large amounts of granular ER.
- Cementoblasts are identified by 3H Thymidine labeling.



Cementoblasts derived from



Development of cellular cementum: (2 stages)

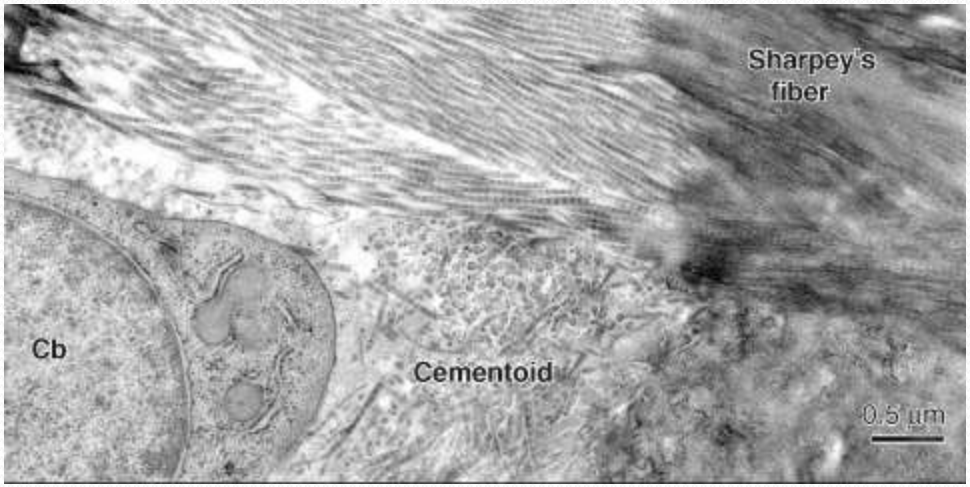
- Early stage- in which extrinic Sharpey's fibers are few & intrinsic fibers are randomly arranged.
- A later stage- in which Sharpey's fibers are thicker and intrinsic fibers are arranged to encircle them.
- Multipolar mode of matrix secretion & faster rate of formation → cementoblast entrapment in its own matrix(cementocytes) → cellular cementum

Formation of Acellular cementum:

- Associated with secretion of enamel matrix proteins (EMP) by HERS .
- HERS is also shown to secrete cementum related proteins like BSP, Osteopontin & fibrillar collagen.

CEMENTOID TISSUE

- After some matrix has been laid down, its mineralization begins.
- The uncalcified matrix is called – Cementoid.
- Growth of cementum- rhythmic process.
- New layer of cementoid formed, old one calcifies.
- Thin layer of cementoid usually found on cemental surface.



- Cementoid tissue is lined by cementoblasts.
- Connective tissue fibres from periodontal ligament pass between cementoblasts into cementum.
- Fibres are embedded into cementum and serve to attach the tooth to surrounding bone.
- Embedded portions are known as Sharpey's fibers.
- Cementoid tissue not observed in AEFC

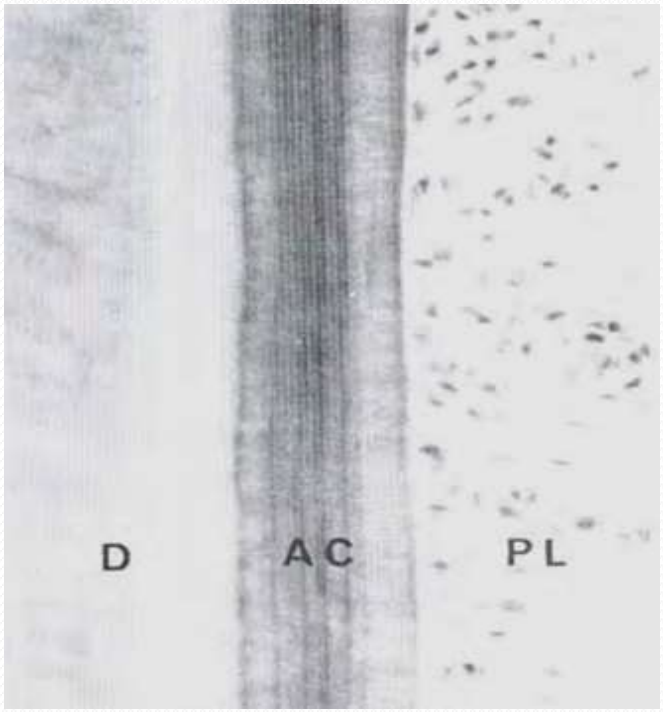
Incremental lines of Salter:

- Cementogenesis proceeds continuously with cyclic activity outward in to PDL, resulting in successive layers of cementum.
- Cyclic activity----- Incremental lines of Salter
- Appear as narrow lines following contour of the root.
- Thus, the fine lines represent periods between intervals of cementogenic activity.

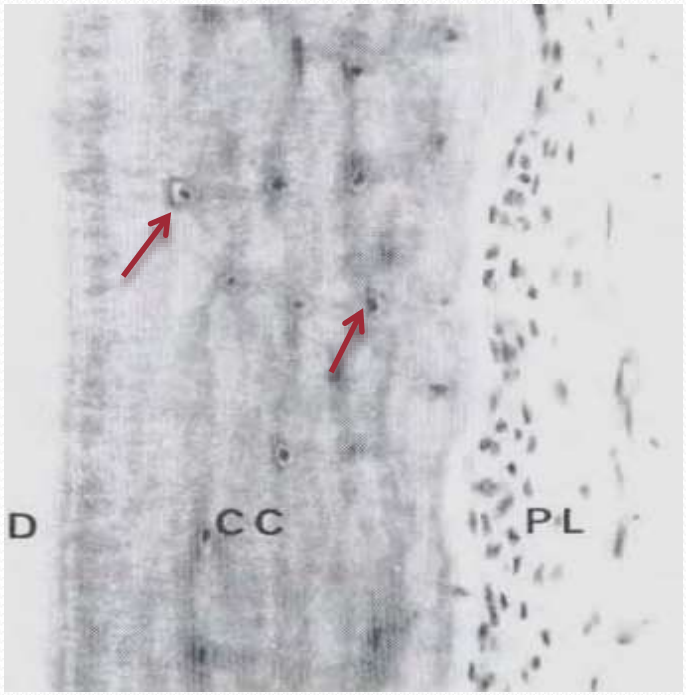
CLASSIFICATION

Based on the presence or absence of cementocytes : (Gottlieb B,1942)

- Acellular (primary) cementum



- Cellular (secondary) cementum.



Can also be classified on the basis of:

- Types of fibers- intrinsic/ extrinsic fibres
- Presence / absence- afibrillar cementum

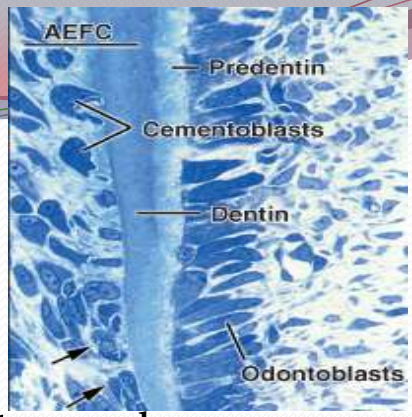
- Intrinsic fibres ↓ produced by cementoblasts (1-2 microns dia) ↓ Oriented parallel to surface

Extrinsic fibres ↓ PDL fibroblasts (5-7 microns dia) ↓ perpendicular

Different types of cementum

- Acellular Extrinsic Fibre Cementum (AEFC)
- Cellular Intrinsic Fibre Cementum (CIFC)
- Acellular Afibrillar Cementum (AAC)
- Acellular Intrinsic Fibre Cementum (AIFC)
- Cellular & Acellular Mixed Fibre Cementum
- Cellular Mixed Stratified Cementum

Acellular extrinsic fiber cementum:



- AEFC extends from cervical margin to apical 1/3rd.
- Only type of cementum in single rooted teeth.
- Extrinsic fibers are seen perpendicular to surface of cementum.
- Known as Sharpey's fibers- mineralized except their inner core.
- This type of cementum forms slowly & regularly → so incremental lines are placed parallel to surface & closer together.
- Main function---- Anchorage

Cellular cementum:

- Secondary cementum

- 2 types:

a) Cellular mixed fiber cementum: apical interradicular regions

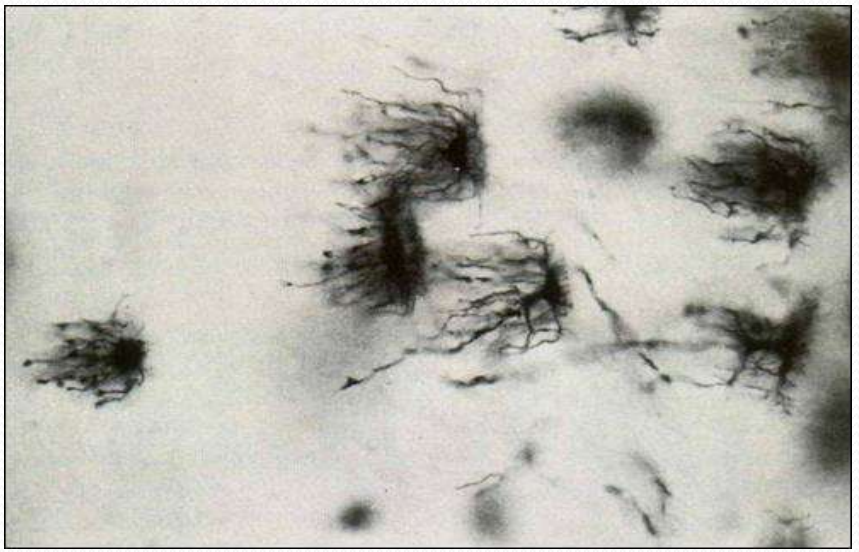
b) CIFC: middle & apical 3rd.

- Function: Adaptation & repair of cementum.
- Cells incorporated in matrix- Cementocytes.

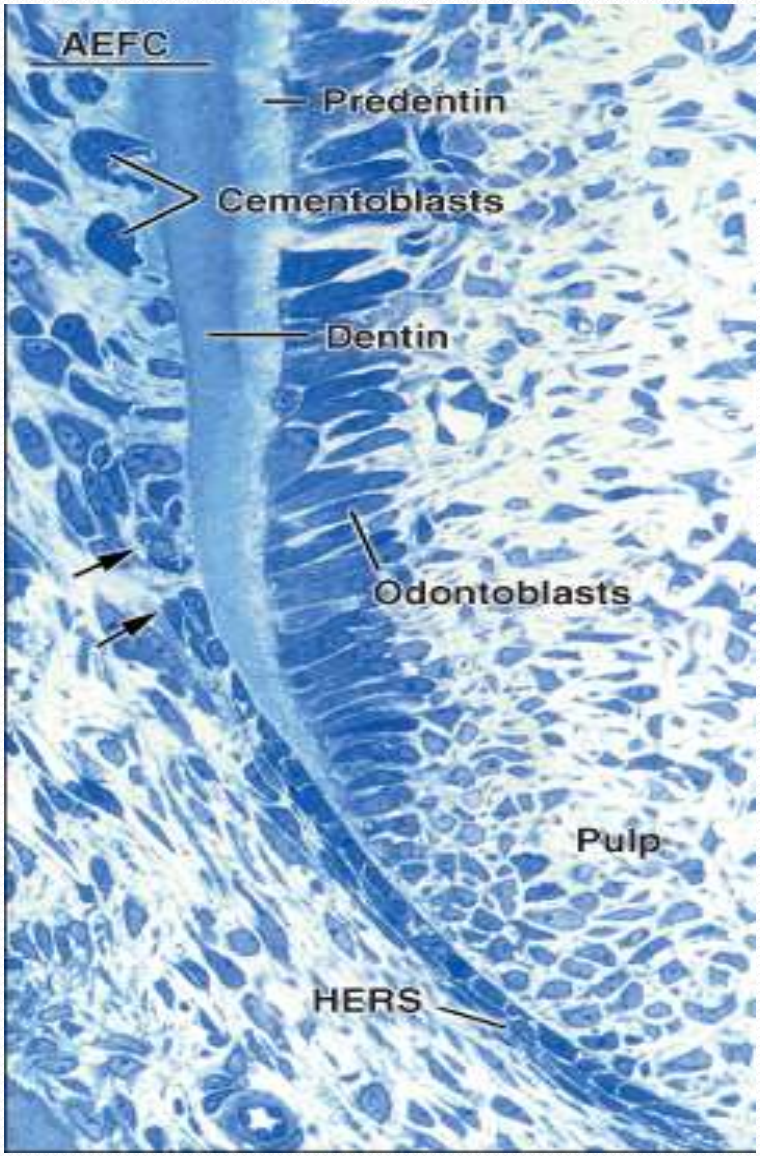
Differences between cementocytes & osteocytes:

- Lacunae of cementocytes varies from being ovoid to tubular but, Osteocytic lacunae are oval.
- The canaliculi less complicated & facing PDL but, Osteocytes have radiating canaliculi arranged in complex network.
- Immunocytochemical studies --- cementocytes immuno+ve for- Fibromodulin & Lumican

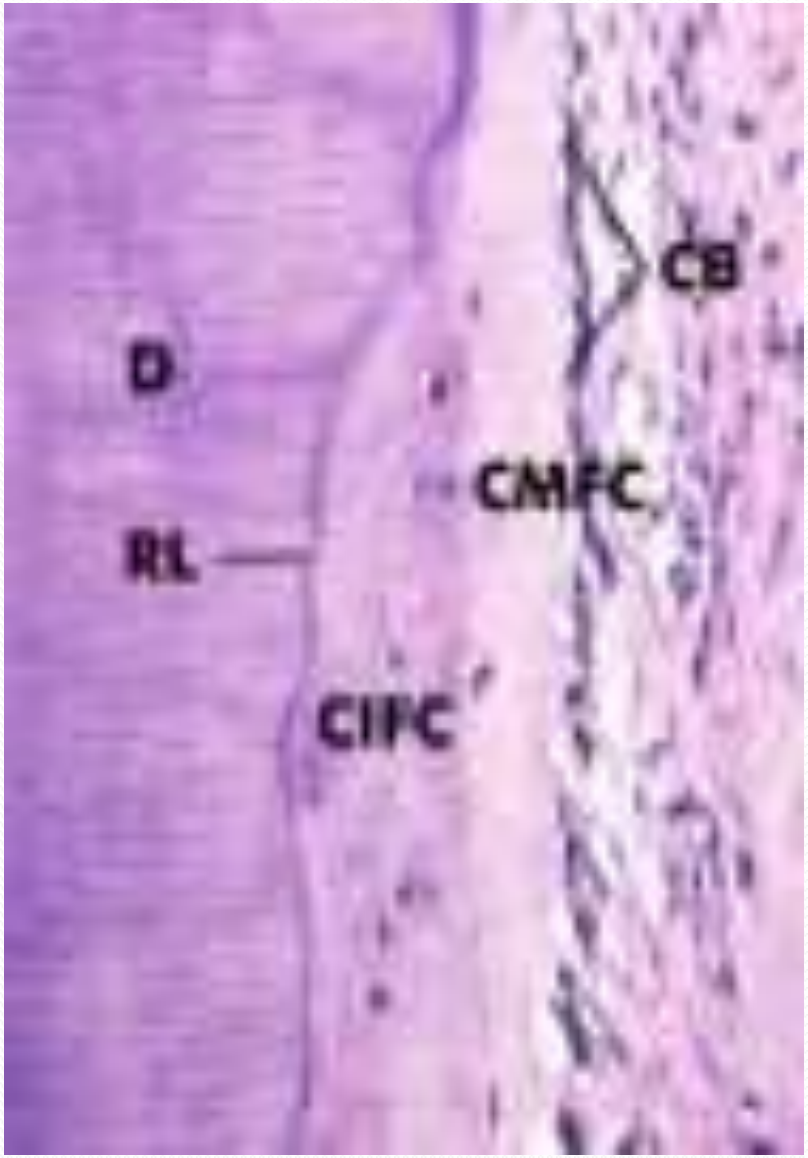
  but, not osteocytes.



AEFC

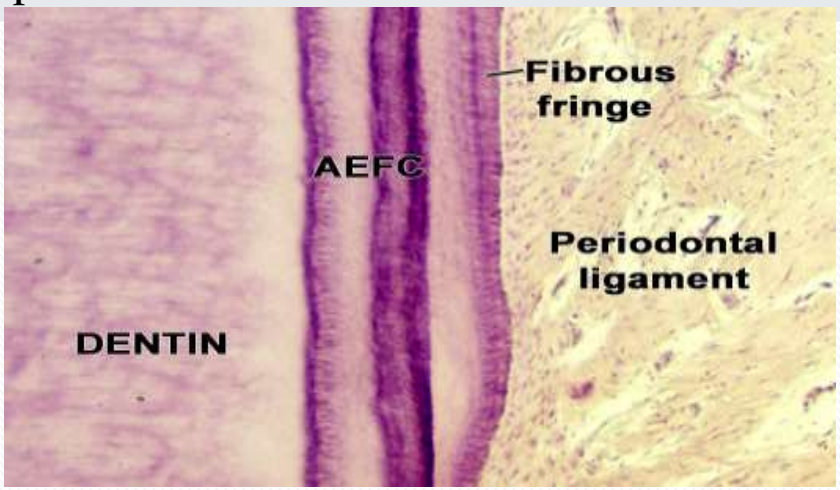

AEFC
Predentin
Cementoblasts
Dentin
Odontoblasts
Pulp
HERS

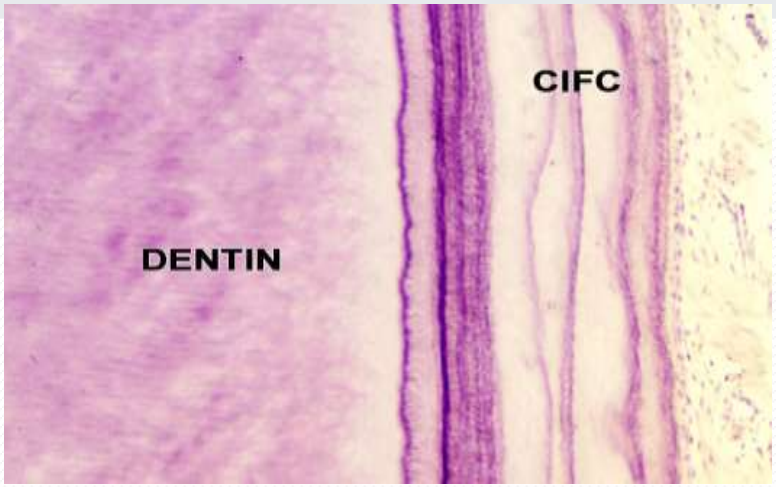
CIFC


CB
D
CMFC
RL
CIFC

ACELLULAR EXTRINSIC FIBRE CEMENTUM	CELLULAR INTRINSIC FIBRE CEMENTUM
1. Located from cervical to apical third	Apical third and furcations
2. Formed earlier- Primary cementum	Formed later & during repair - Secondary cementum
3. Noncollagenous proteins- Tenascin, Fibronectin, Osteocalcin absent	Non collagenous proteins are present.
4. Growth factors TGFβ & IGF not seen	Growth factors are seen.
5. Proteoglycans, Versican, Decorin, Lumican not identified in matrix	These proteoglycans are seen in matrix.
6. Cementoid is usually absent.	Cementoid seen on the surface
7. Contains extrinsic fibers produced by PDL fibroblasts	Contains intrinsic fibers produced by cementoblasts
8. Probably the only type of cementum seen in single rooted teeth	May be absent in single rooted teeth

ACELLULAR EXTRINSIC FIBRE CEMENTUM	CELLULAR INTRINSIC FIBRE CEMENTUM
9. Main function is anchorage.	Main function is adaptation and repair.
10. Slow formation	Rapid formation
11. Incremental lines therefore are closer together.	Incremental lines further apart
12. Cementocytes not seen	Cementocytes are seen
13. Cementoblasts derived from HERS	Cementoblasts derived from cells of dental follicle
14. Cementoblasts do not express PTH receptor.	Cementoblasts express PTH receptor





Cellular mixed stratified cementum:

- Towards the root apex and in the furcation areas of multi-rooted teeth.

- The acellular extrinsic fibre cementum & cellular intrinsic fibre cementum commonly may be present in alternating layers known as ------ cellular mixed stratified cementum.

Mixed fibre cementum:

- Collagen fibres are derived from both- extrinsic fibres (PDL) & intrinsic fibres (cementoblasts).

- Intrinsic & extrinsic fibres can be distinguished :

1. Intrinsic fibres run between extrinsic fibers in different orientation.
2. Fiber bundles are of different sizes:

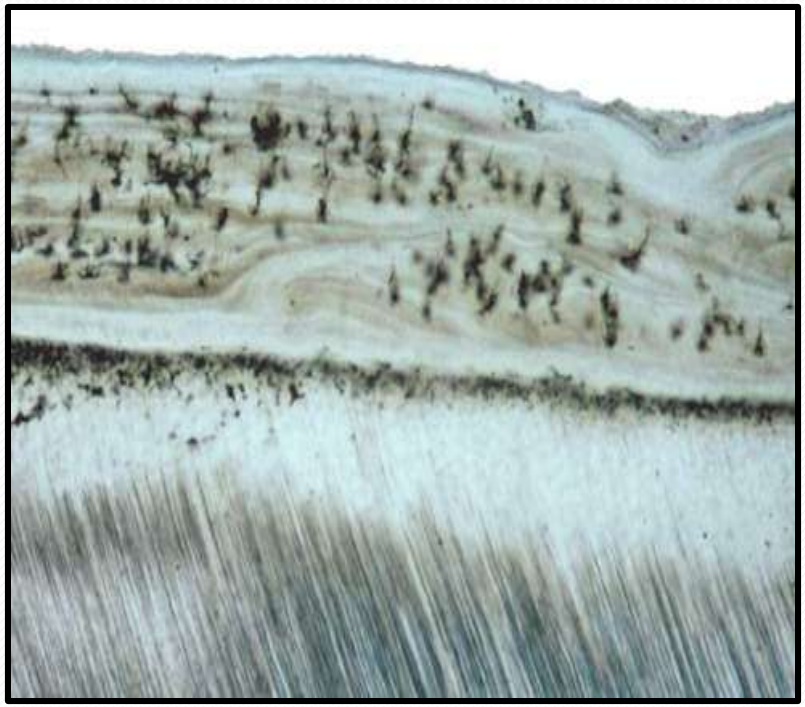
   - extrinsic fibre bundles: ovoid-round , 5-7 µm dia.
   - intrinsic fibre bundles: 1-2 µm in dia.

- Can be acellular / cellular mixed fibre cementum

Afibrillar cementum:

- Contains no collagen fibres
- Sparsely distributed & contains well mineralized ground substance
- Thin, acellular, which covers the cervical enamel or intervenes between fibrillar cementum & dentin
- Afibrillar cementum is thought to be formed at this site following the loss of reduced enamel epithelium.

CEMENTO-DENTINAL JUNCTION



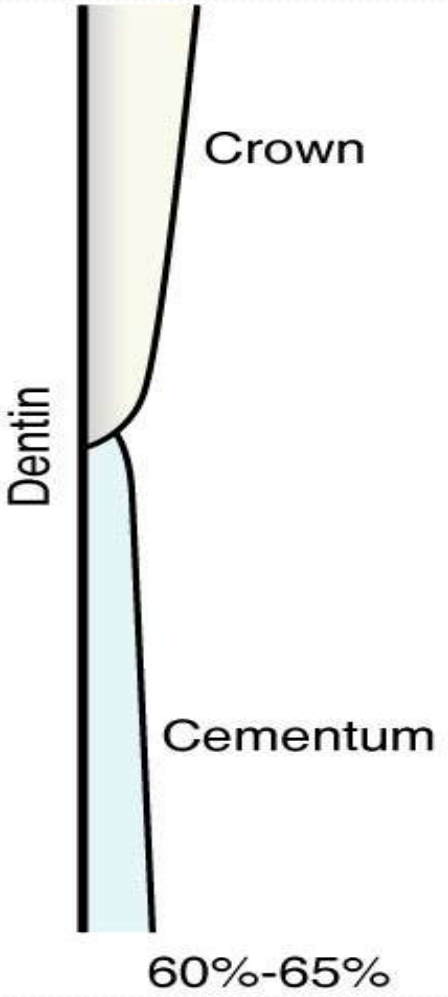
- Relatively smooth in permanent teeth, scalloped in deciduous teeth
- Attachment is quite firm.
- CDJ consists of wide zone containing large quantities of collagen associated with Glycosaminoglycans like Chondroitin sulfate- stiffness

- Cemental fibers intermingle with dentinal fibers at CD junction. This aids in attachment of cementum to dentin.
- But, the presence of proteoglycans is the major factor in this attachment.

- **Intermediate cementum layer/ Hyaline layer:**
- Apical thirds of roots of molars & premolars
- Represents the areas where cells of HERS become trapped in rapidly deposited dentin or cementum matrix
- Considered to be of dentinal origin

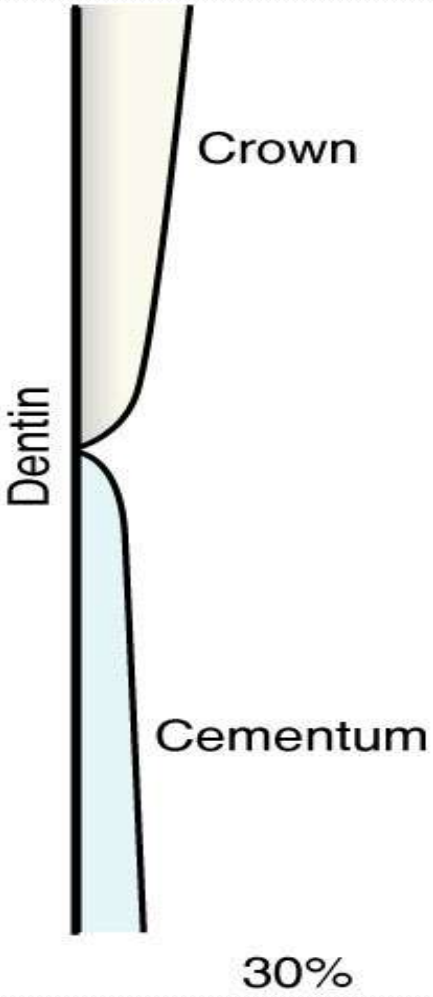
CEMENTO- ENAMEL JUNCTION

Overlap junction



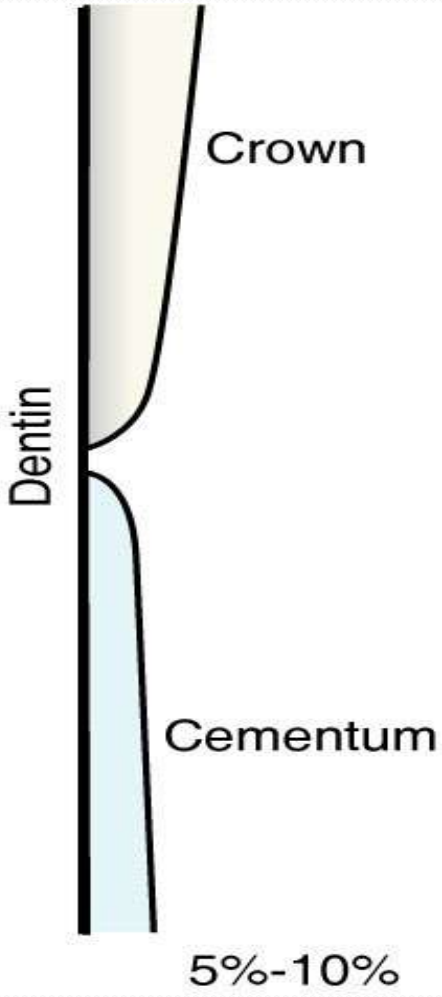
60%-65%

Butt joint



30%

Gap junction



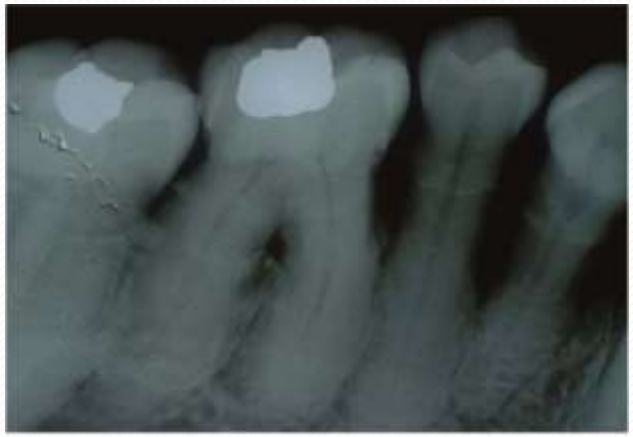
5%-10%

FUNCTIONS

- Anchorage- furnish a medium for attachment of collagen fibres that bind tooth to alveolar bone.
- Adaptation- deposition of cementum in apical area can compensate for tooth substance due to occlusal wear.
- Repair – damage to roots such as fractures & resorption can be repaired by deposition of new cementum.

CLINICAL CONSIDERATIONS

- **HYPERCEMENTOSIS**
- Abnormal thickening of cementum
- Non-neoplastic condition in which excessive cementum is deposited in continuation with normal radicular cementum.
- Secondary cementum deposition in entire root/apex.

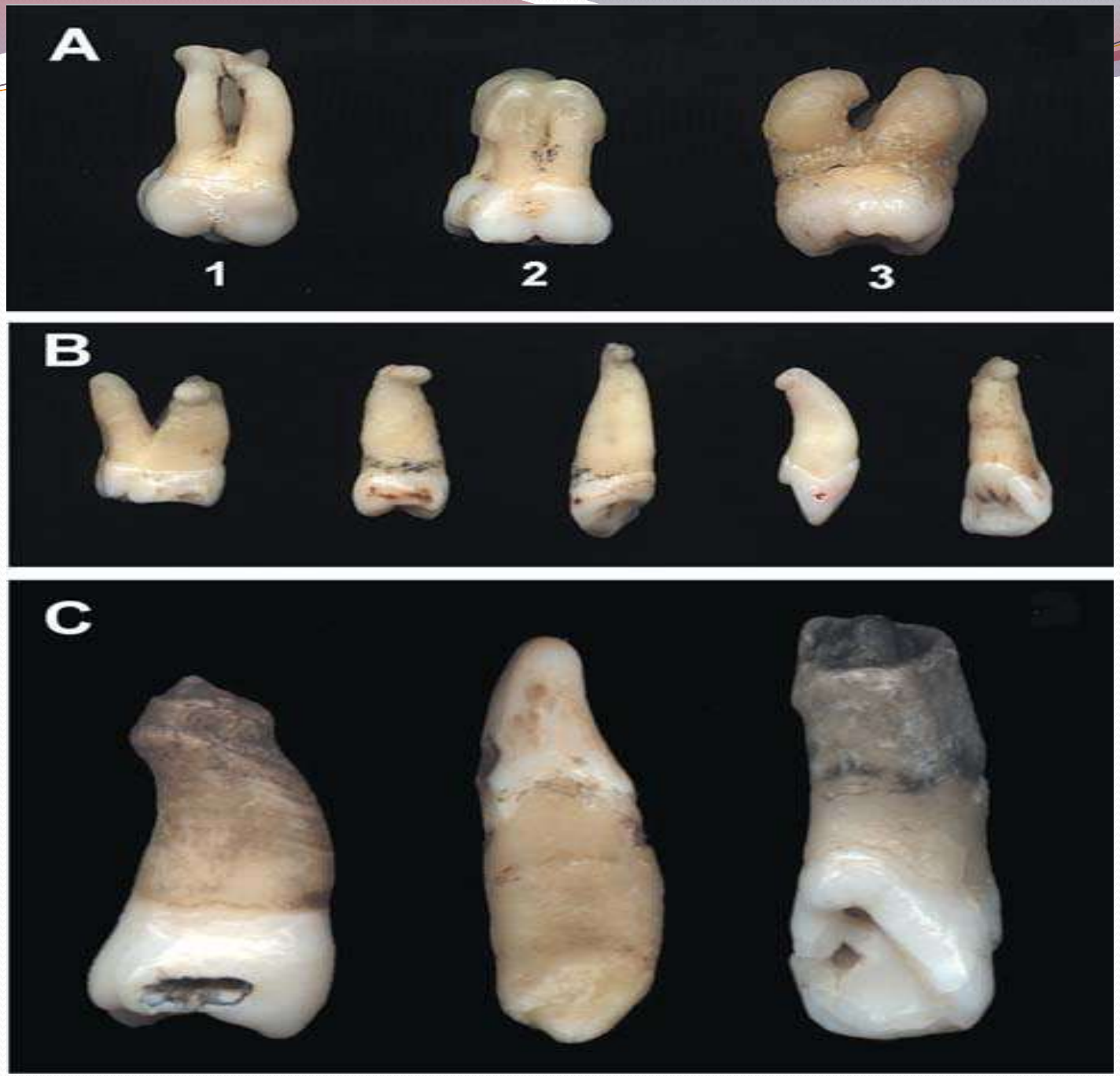


Localised hypertrophy:

- A spur or prong like extension of cementum is formed.
- Seen in teeth that are exposed to great stress.
- The prong-like extension of cementum provides larger surface area for attaching fibers ---- firmer anchorage assured.

Hyperplastic:

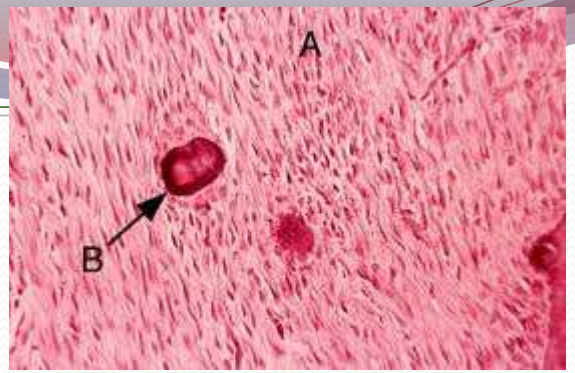
- Seen in areas where enamel drops have developed over dentin
- Hyperplastic cementum covering the enamel drops are irregular & sometimes contain round bodies that may be calcified epithelial rests.
- These calcified bodies found on localised areas of hyperplastic cementum--- Excementoses


A
1
2
3
B
C

- **Etiology:**
- Accelerated root elongation
- Inflammation about the root
- Tooth repair / Trauma from occlusion (TFO)
- Paget's disease

- **Histopathology:**
- Cellular cementum over a thin layer of acellular cementum
- Secondary cementum termed as- Osteocementum: cellular nature – resemblance to bone

CEMENTICLES



- Foci of calcified tissue, not necessarily cementum , which lie free in PDL of lateral & apical root areas.
- Dystrophic calcification – regressive change

- Formation:
- 1. Calcification of epithelial rests in PDL
- 2. Focal calcification of C.T between Sharpey's bundles
- 3. Cemental tears- if detached
- 4. Calcification of thrombosed capillaries in PDL

ANATOMIC & FUNCTIONAL REPAIR:

- Trauma/ Excessive forces: cementum resorption
- Severe cases ---- up to dentin

- Damage repaired either by formation of acellular or cellular cementum or by alternate formation of both.

- In most cases there is tendency to re-establish the former outline of the root surface.
- This is called **Anatomic repair.**

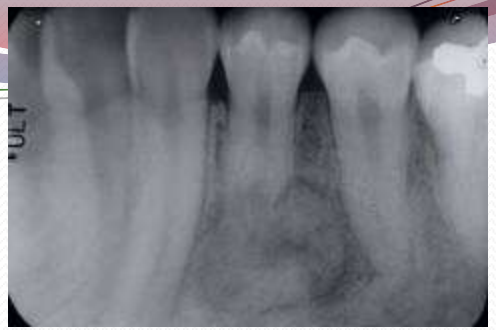
- However, if only a thin layer is deposited on the surface of deep resorption, the root outline is not reconstructed and a baylike recess remains.....

- In such areas sometimes PDL space is restored to its normal width by a bony projection ⟶ so that proper functional relationship will result.

- The outline of the alv. bone in these cases follows that of the root surface.

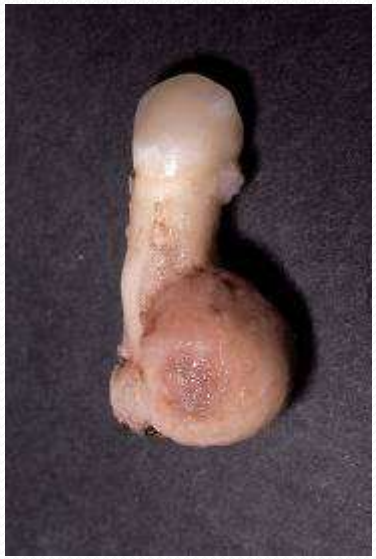
- This change is called **Functional repair.**

CEMENTOBLASTOMA



- Benign cementoblastoma is a true neoplasm of functional cementoblasts which form a large mass of cementum or cementum like tissue on the root.

- Mandi. 1st molar
- H/p: sheets of cementum like tissue
- Reversal lines scattered throughout
- Cemental trabeculae lined by cementoblasts



HYPOPHOSPHATASIA

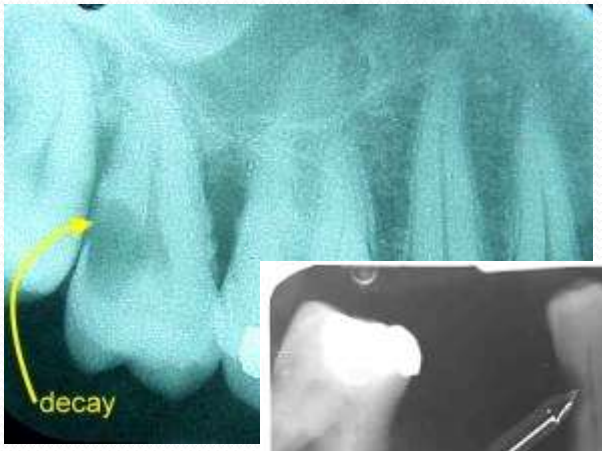
- Rare inherited metabolic disease of decreased tissue nonspecific alkaline phosphatase &
- Defective bone mineralization
- Loosening and premature loss of teeth
- Failure of cementogenesis ---- No sound functional attachment of tooth to bone by PDL.

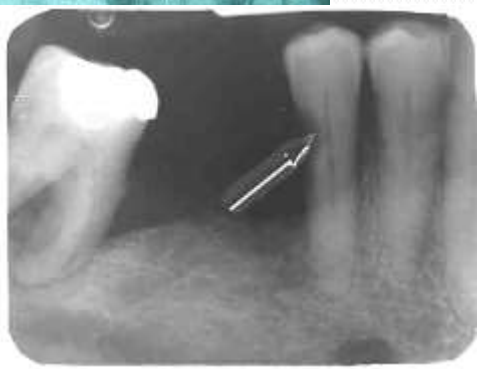
CEMENTAL CARIES

•“Soft ,progressive lesion that is found anywhere on root surface that has lost the connective tissue attachment & is exposed to the oral environment”

•Root caries is usually saucer shaped. Root caries does not occur in areas covered by a well attached gingiva.

•Microorganisms invade cementum along Sharpey’s fibres or between bundles of fibres.





AGE CHANGES IN CEMENTUM:

- Permeability of cementum decreases with age.
- Cellular proliferative activity of cementum decreases with age.
- Cementum surface becomes irregular with age i.e., an irregular surface into which the sharpey's fibers are inserted.
- Cementum is deposited through out the life of an individual.

REFERENCES

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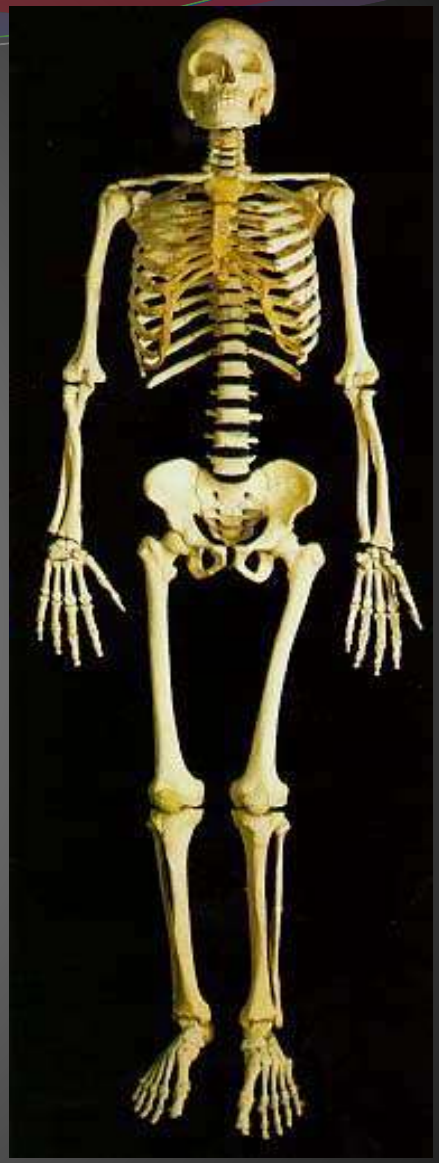
- A SCANNING ELECTRON MICROSCOPIC STUDY OF HYPERCEMENTOSIS -J Appl Oral Sci. *2008;16(6):380-4*
- INTERNET

THANK YOU

HISTOLOGY OF BONE

Bone is a special dense connective tissue wherein the cells and fibres are embedded in a calcified matrix.



FUNCTIONS OF BONE:

1. Give shape and support to the body.
2. Provide surface for the attachment of muscles, tendons, ligaments.
3. The skull, vertebral column & thoracic cage protect brain, spinal cord and thoracic viscera, respectively.
4. It manufactures blood cells.
5. It stores 97% of the body calcium and a very large part of body phosphorous.
6. Helps in immunity.

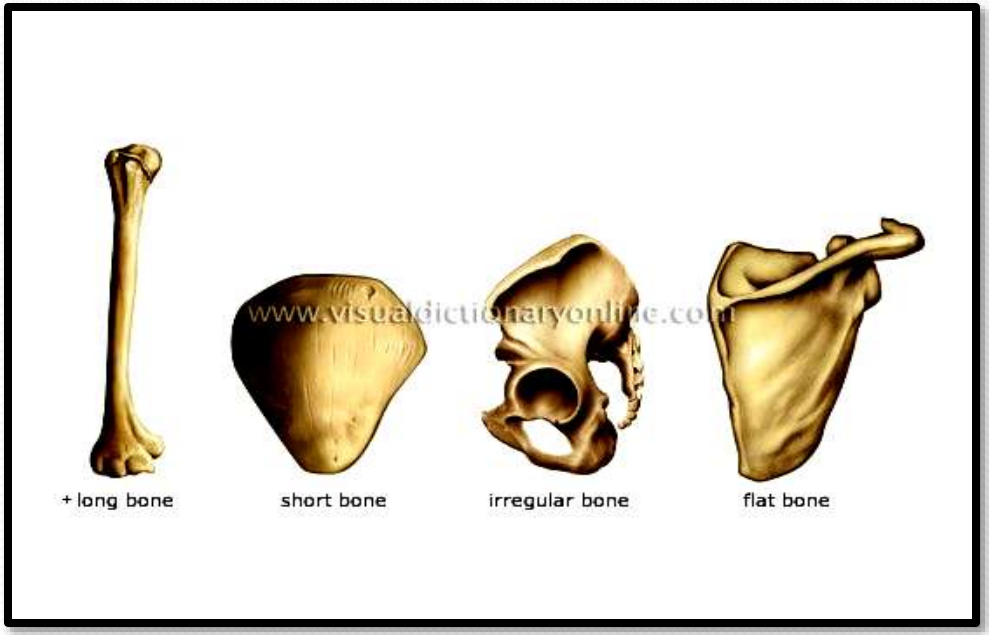
CLASSIFICATION

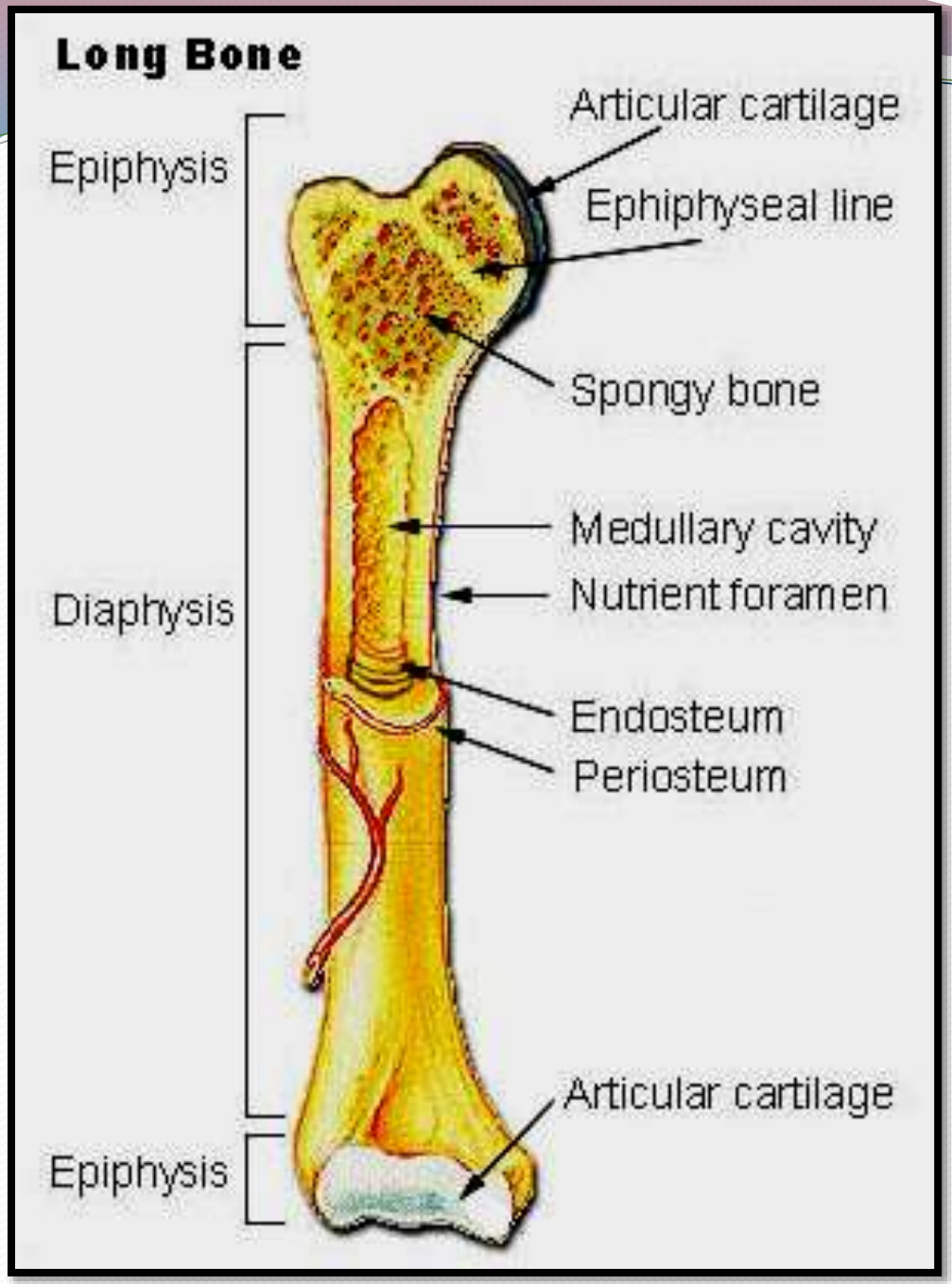
Based on location

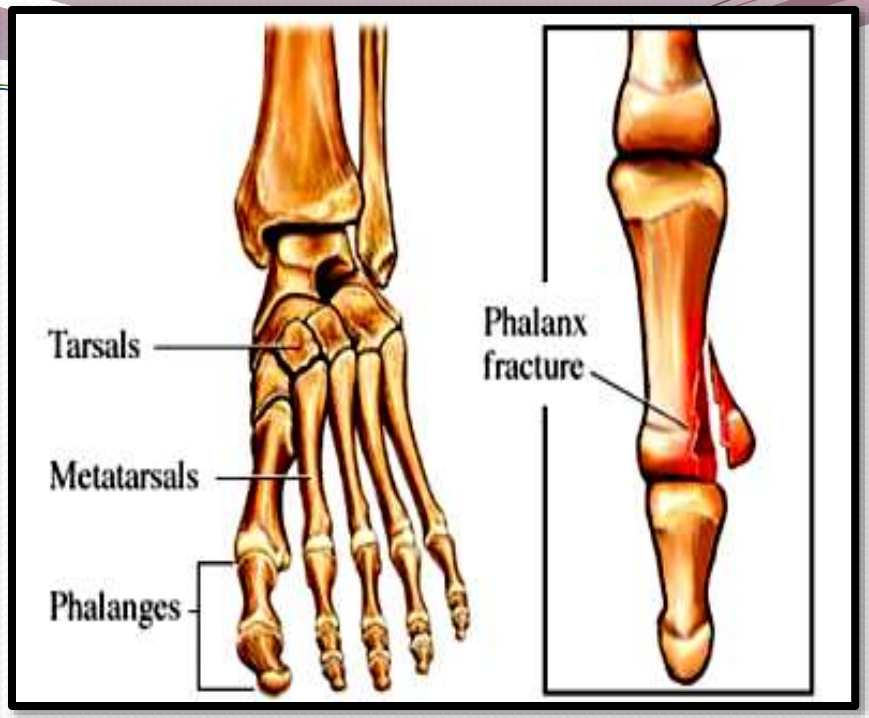
- Axial skeleton - skull, vertebral column
- Appendicular skeleton - etrimities

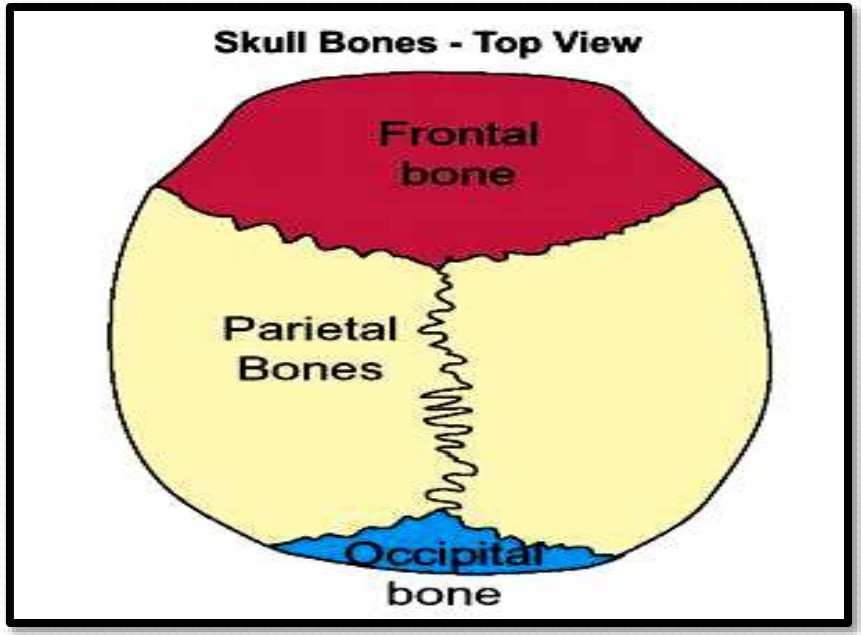
Based on shape

- Long bones- humerous
- Short bones- carpals
- Flat - skull
- Irregular - Face
- Sesamoid - patella




Long Bone
Articular cartilage
Epiphysis
Ephiphyseal line
Spongy bone
Medullary cavity
Diaphysis
Nutrient foramen
Endosteum
Periosteum
Articular cartilage
Epiphysis


Tarsals
Metatarsals
Phalanges
Phalanx fracture


Skull Bones - Top View
Frontal bone
Parietal Bones
Occipital bone

Based on microscopic structure:

- Lamellar bone/ mature bone: compact/ cancellous
- Woven bone

Based on Maturity

- Immature bone
- Mature bone

Based on developmental origin

- Intramembraneous– facial flat bones, mandible, clavicle
- Intracartilagenous – bones of trunk and extremities

COMPOSITION OF BONE

- 67% inorganic
  - hydroxyapatite
- 33% organic
  - 28% collagen type I
  - 5% noncollagen protein
    - osteocalcin
    - sialoprotein
    - phosphoprotein
    - osteonectin
    - bone specific protein
    - BMPs

Inorganic Mineral:

- Consist of calcium phosphate salt in form of hydroxyapatite
- Shape – rhombic prism
- Hydroxyapatite crystallite – 100 x 200 x 50 x 50 Å
- Ions like Mg, F, Al, Na are also present.

Organic contents:

- Collagen Type I & also Type III, V, XII
- Ground substance

Non collagenous proteins

- **1. Osteocalcin-**
- 15% of non collagenous proteins
- Bone gla protein- γ carboxy glutamic acid
- Carboxy terminal segment of osteocalcin acts as chemoattractant for osteoclasts. Role in bone resorption
- Also, it has role in bone calcification- as it is a calcium binding protein

- 2. Bone Sialoprotein (BSP)
- Initiation of mineral crystal formation

- 3.Osteopontin:
- Inhibitor of hydroxyappetite crystal growth
- Enriched at cell matrix interface where it mediates attachment of cells including osteoclasts

- 4. Osteonectin:
- It is bound to hydroxyappetite crystals
- It is a secreted calcium binding glycoprotein.
- Role- regulation of cell adhesion & proliferation

- 5. Proteoglycans:
- Chondroitin sulfate, Biglycan, Decorin
- Bind to TGF-β & extracellular macromolecules including collagen → regulate fibrillogenesis

- 6. Lysyl oxidase:
- Critical enzyme for collagen cross linking

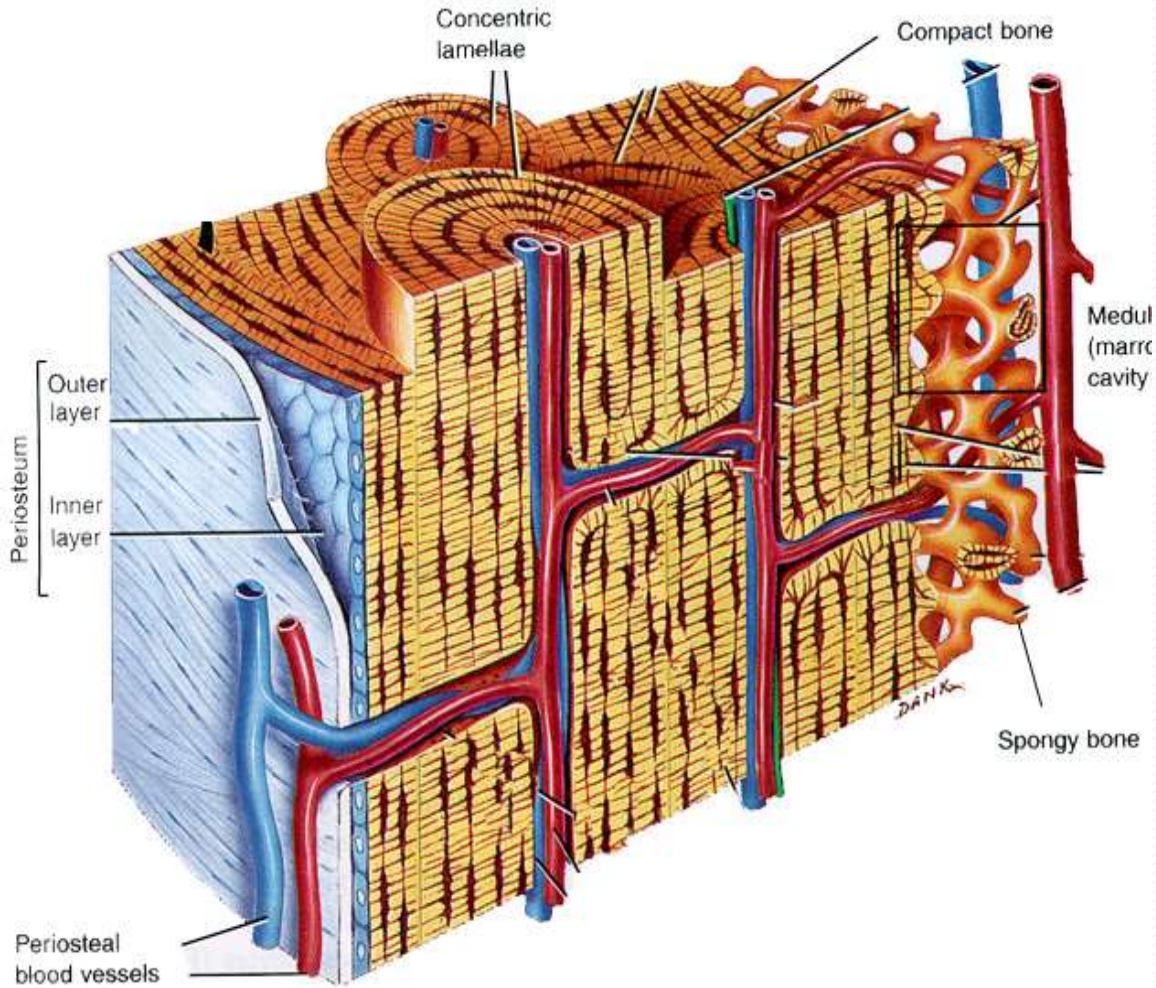
- 7. Matrix gla proteins:
- Prevent mineralization in vascular tissues & cartilage

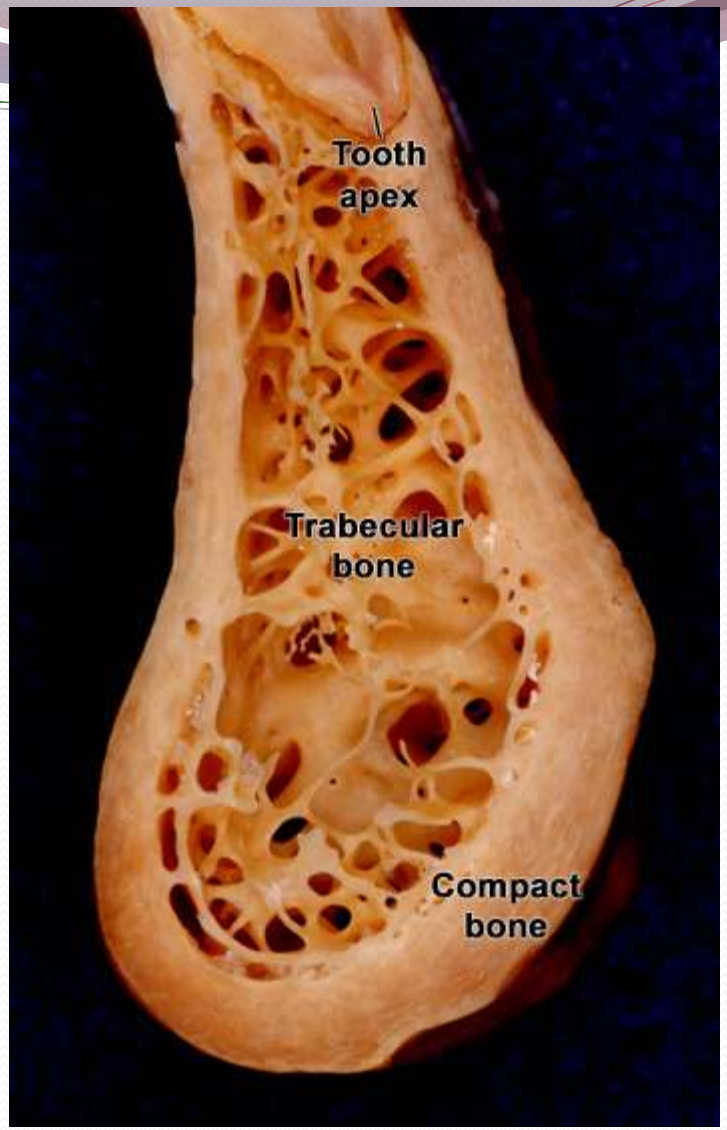
- **Cytokines :**

- Bone morphogenetic proteins (BMP)
- Platelet derived growth factors (PDGF)
- Insulin like growth factors (IGF)
- Fibroblast growth factors (FGF)
- Transforming growth factor (TGF)

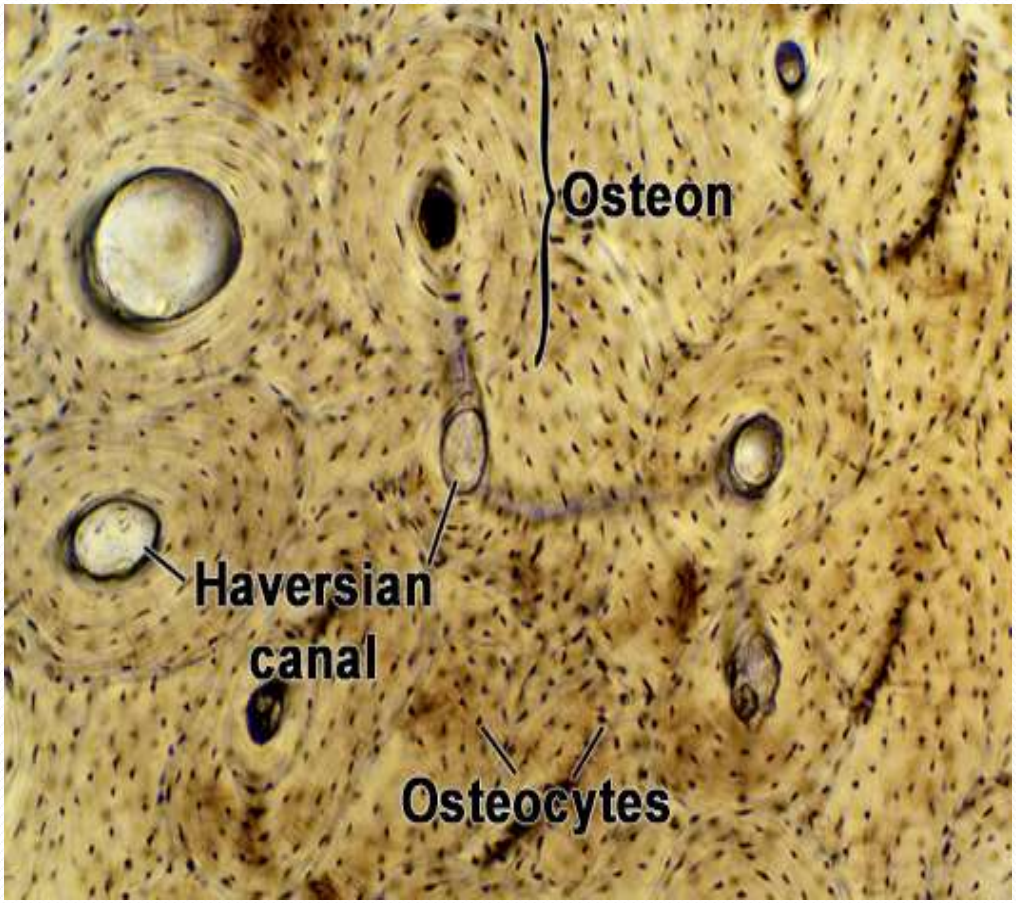
THE CYTOKINES INCREASE RAPIDITY OF BONE FORMATION & REPAIR

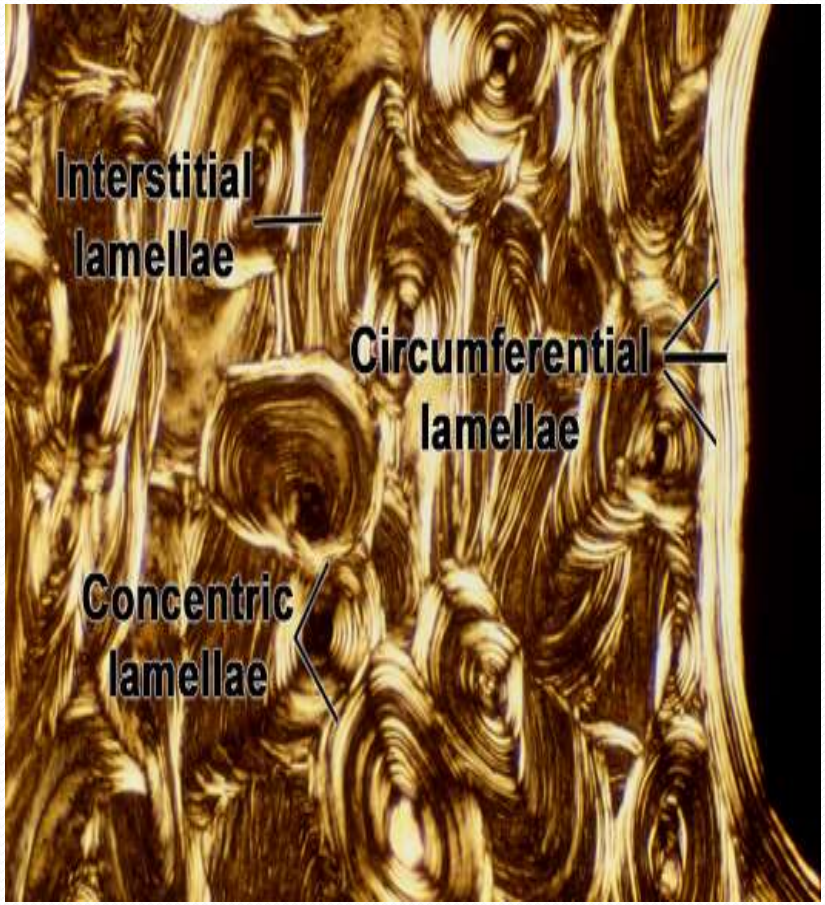
BONE HISTOLOGY



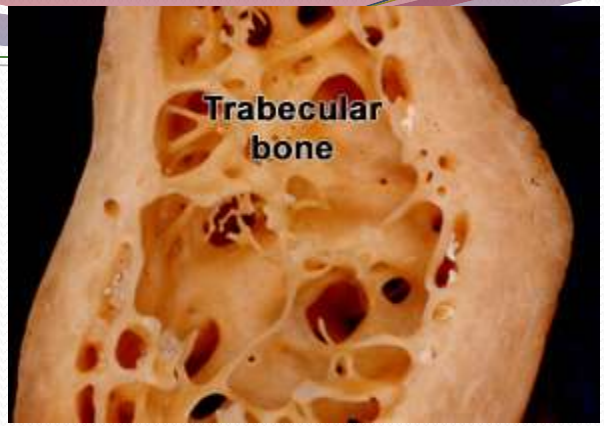


HISTOLOGY OF BONE





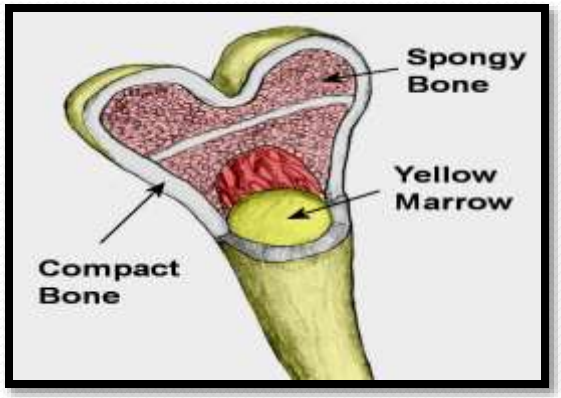
SPONGY BONE



- Trabecular/ Cancellous bone
- Same cells and intercellular matrix as compact bone but, differ in arrangement of components

- Large slender spicules – trabeculae
- Oriented along lines of stress to withstand the forces applied to bone
- Marrow spaces are large
- Trabeculae derive nutrition from marrow

Hemopoietic tissue in bones:



- Red marrow- young bones
- Yellow marrow- old bones

- Red marrow seen in- the cavities of spongy bone
- In newborn infants- medullary cavities & spongy bone contains red marrow.

- Red marrow – mesenchymal cells/ blood cell lineage

- Yellow marrow- loss of hemopoietic potential.

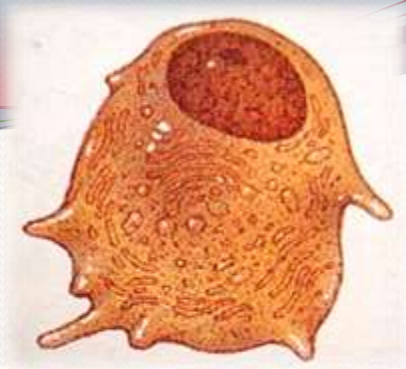
BONE CELLS:

Two cell lineages are present in bone:

1. Osteogenic cells, which form and maintain bone, and
2. Osteoclasts, which resorb bone.

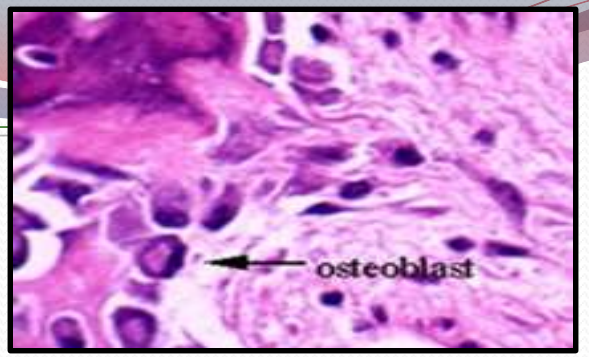
Osteogenic cells include osteoprogenitors, preosteoblasts, osteoblasts, osteocytes, and bone-lining cells.

OSTEOBLASTS



- Mononucleated cells responsible for the synthesis & secretion of macromolecular organic constituents of bone matrix.
- Derived from: osteoprogenitor cells of mesenchymal origin in bone marrow & other C.T
- PERIOSTEUM also imp reservior- during childhood growth, after skeletal fractures

Morphology:



- Basophilic, plump cuboidal or slightly elongated cells
- Exhibit abundant & well developed protein synthetic organelles.
- Intense cytoplasmic basophilia- abundance of RER
- RER- Procollagen & organic bone matrix → transfer vesicles → Golgi complex → secretory granules ↓
- Granules release their contents along the cell surface opposed to forming bone which, assemble as fibrils to form osteoid.

Formation of osteoblasts

Undifferentiated pluripotent stem cells

↓

Inducible osteo-progenitor cells (IOPC)

↓ BMP's, Growth factors

Determined osteo-progenitor cells(DOPC)

↓ Bone derived growth factors

osteoblasts

Functions:

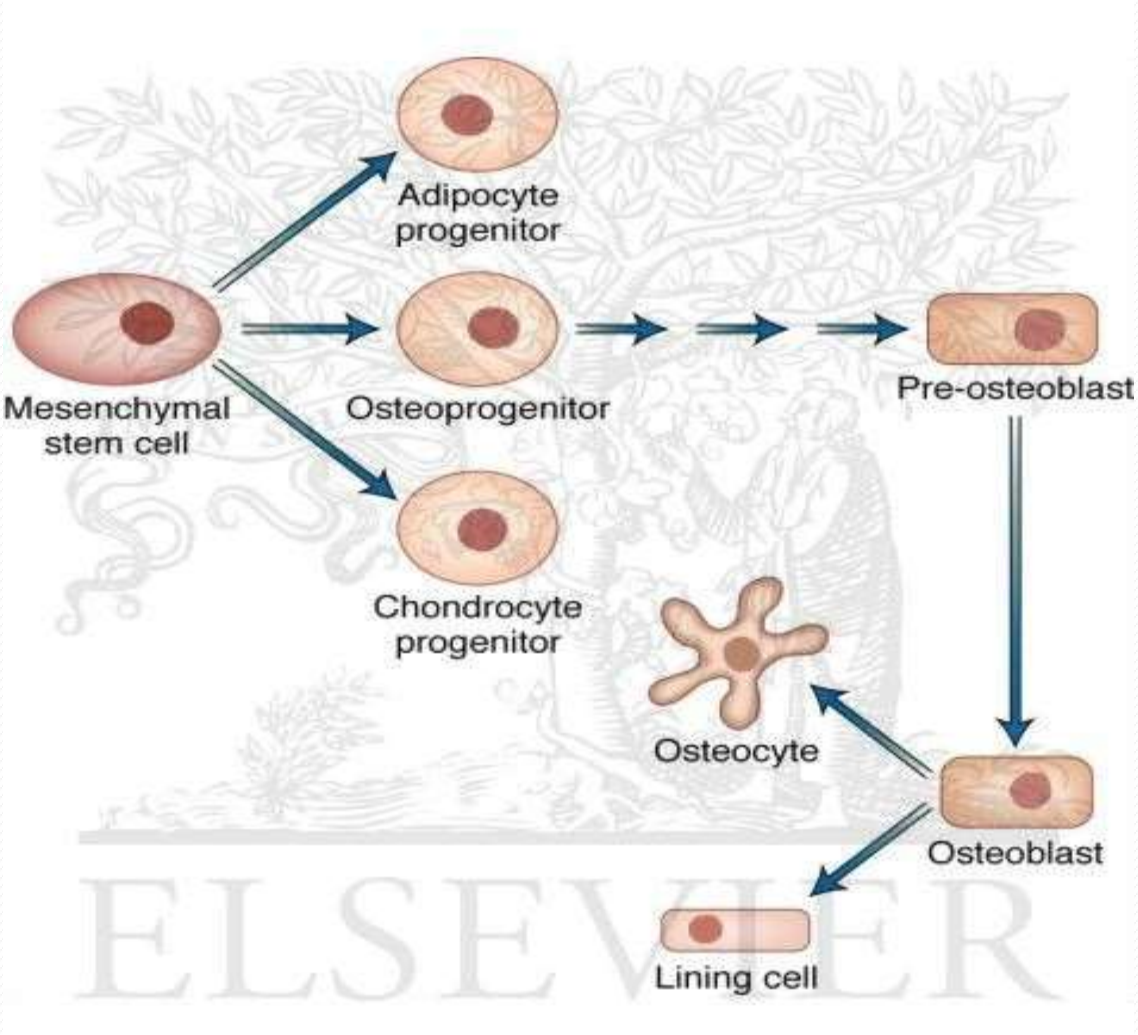
- Formation of new bone via synthesis of proteins & polysaccharides
- Regulation of bone remodeling & mineral metabolism
- Mineralization of the osteoid

- Osteoblasts secret RANKL, Cbfa-1 (osteoblast specific transcription factor)
- RANKL: membrane bound TNF- Osteoclast differentiation
- Cbfa-1 : regulates expession of OPG – potent inhibitor of osteoclast formation

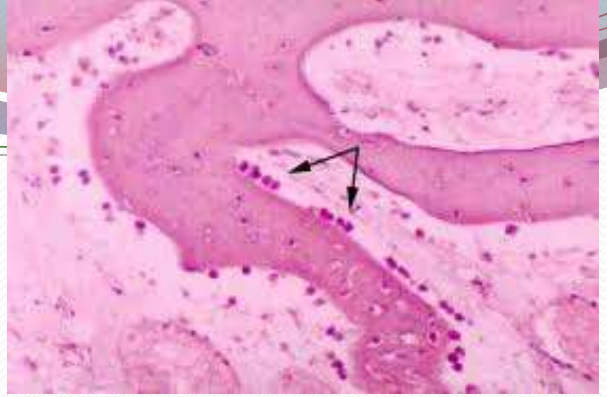
Regulation of osteoblast activity:

- Role of PTH: Hypocalcemia ⟶ release of calcium from bone ⟶ PTH receptors on osteoblasts ⟶ bone resorption
- Vitamin D3: Bone resorption

  Also essential for bone growth & Ca absorption from intestine
- Growth hormone: attaining normal bone mass
- Insulin: IGF-1 ⟶ matrix formation & mineralization
- BMPs: differentiation of mesenchymal cells to osteogenic cells
- FGF, PDGF: osteogenic differentiation & osteogenesis


Adipocyte progenitor
Mesenchymal stem cell
Osteoprogenitor
Pre-osteoblast
Chondrocyte progenitor
Osteocyte
Osteoblast
Lining cell

Bone lining cells:

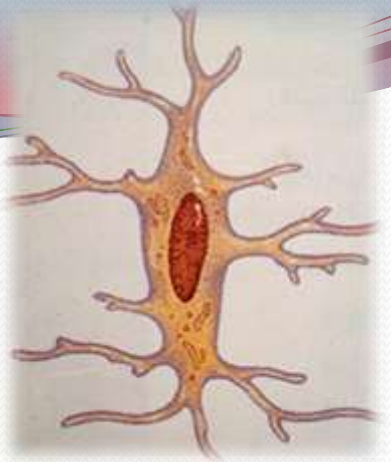


- Once osteoblasts have completed their function, they are either entrapped in bone matrix and become osteocytes or remain on the surface as lining cells.

- Osteoblasts flatten & extend along the bone surface
- Very few organelles but retain gap junctions with osteocytes

- Apoptosis: TNF Antiapoptotic- TGF-β & IL-6

OSTEOCYTES:



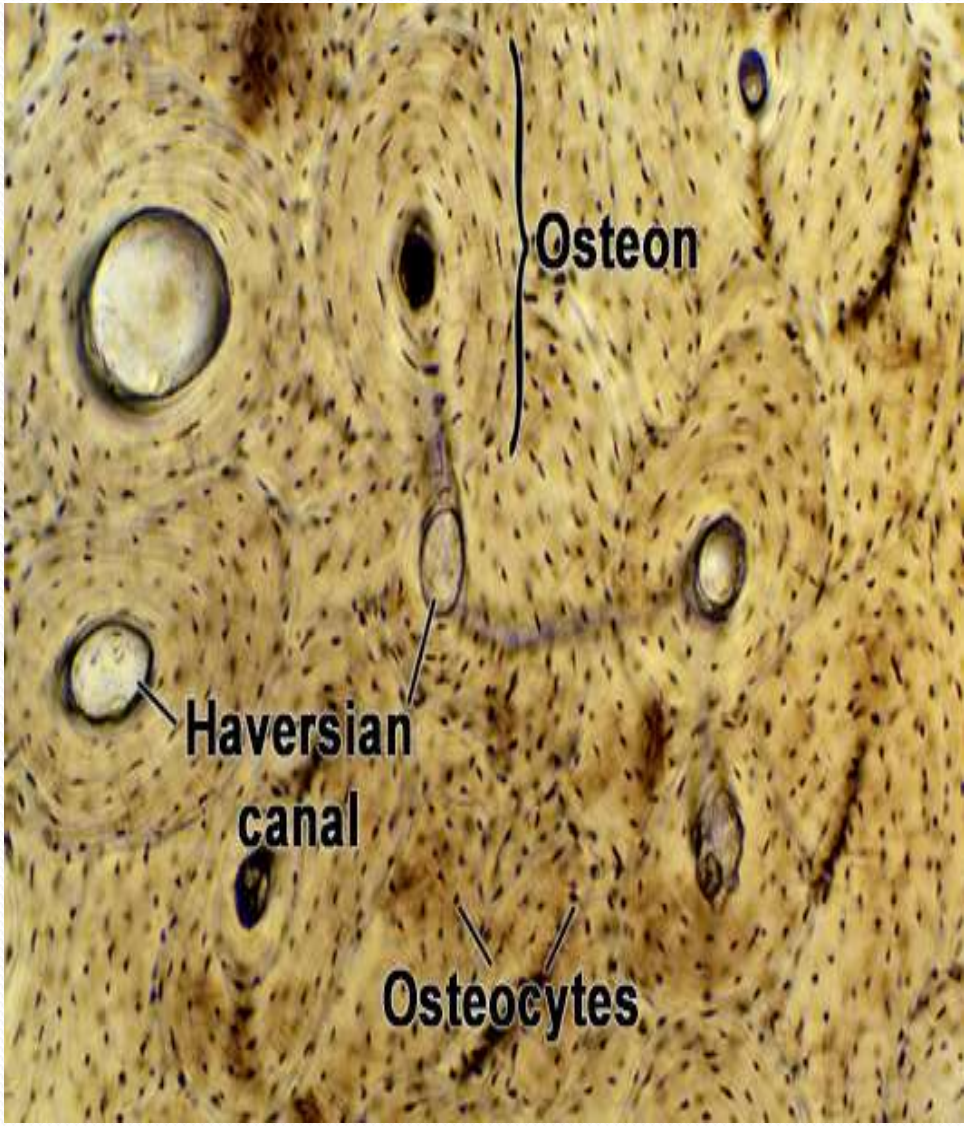
- Osteoblasts entrapped within the matrix
- No. of osteocytes depends on the rapidity of bone formation. Embryonic woven bone has more osteocytes than lamellar bone
- Osteocytic lacuna
- Narrow extensions of these lacunae form channels – Canaliculi
- Canaliculi contain osteocytic processes
- Canaliculi penetrate the bone matrix & permit diffusion of nutrients, gases & waste products between osteocytes & blood vessels.

- Functions:

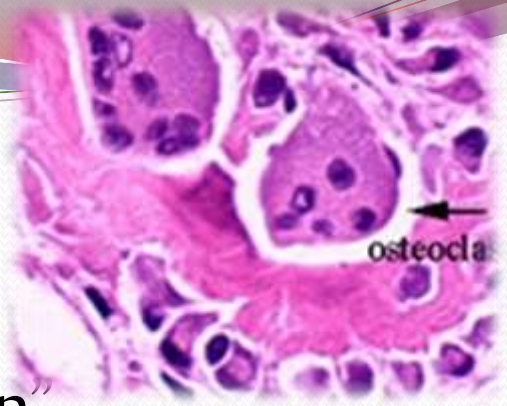
1. Maintain bone matrix and

2. Release calcium ions from bone matrix when calcium demands increase.

3. Also sense the changes in environment & sends signals that affect response of other cells in remodelling

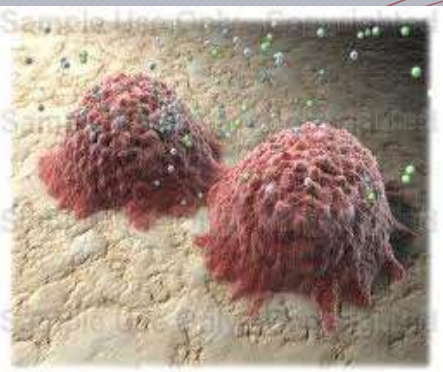


OSTEOCLASTS:

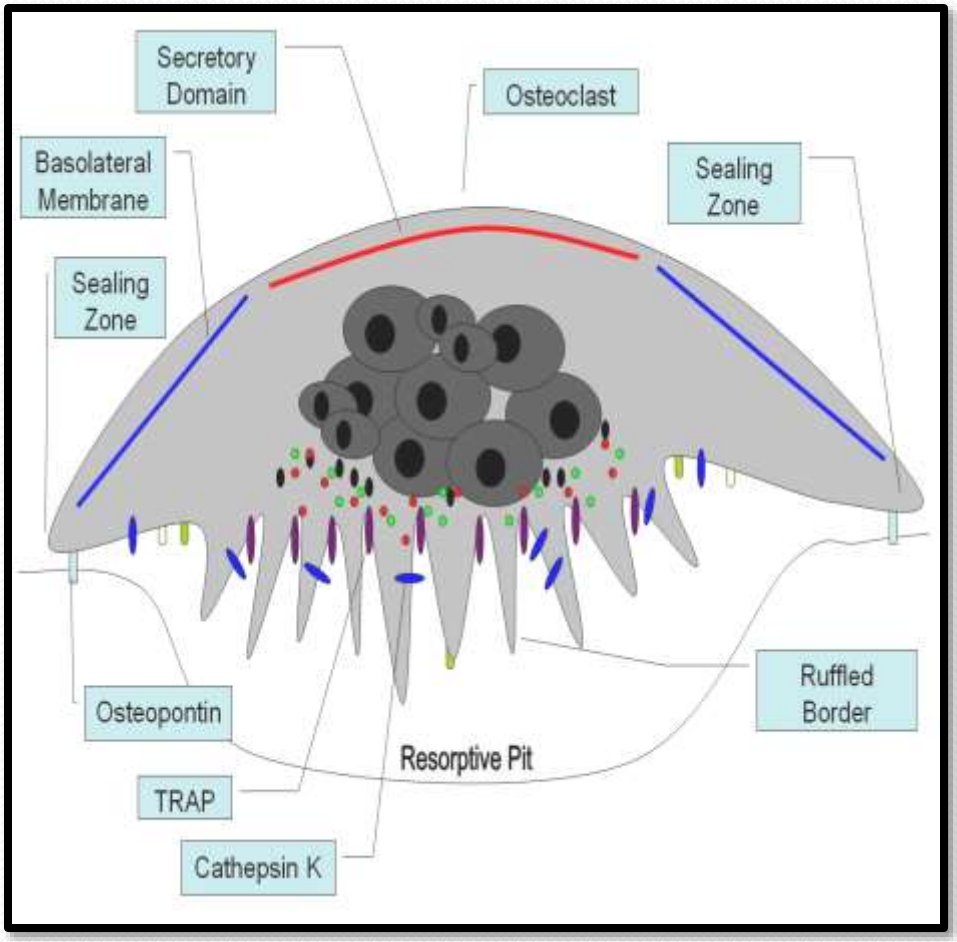


- Osteoclast- Greek word : "bone & broken"
- Type of bone cell that removes the bone tissue by removing the mineralized matrix of bone.
- 40-100 µm in diameter with 15 to 20 closely packed nuclei.
- Cytoplasm shows acid phosphatase containing vesicles and vacuoles- distinguishes osteoclast from other multinucleated giant cells
- Lie in resorption bays called as HOWSHIP's LACUNAE.

Morphology of Osteoclasts:



- Extensive mitochondria – except below ruffled border
- Golgi complex- extensive
- Cathepsin containing vesicles- close to ruffled border indicating resorptive activity of cells



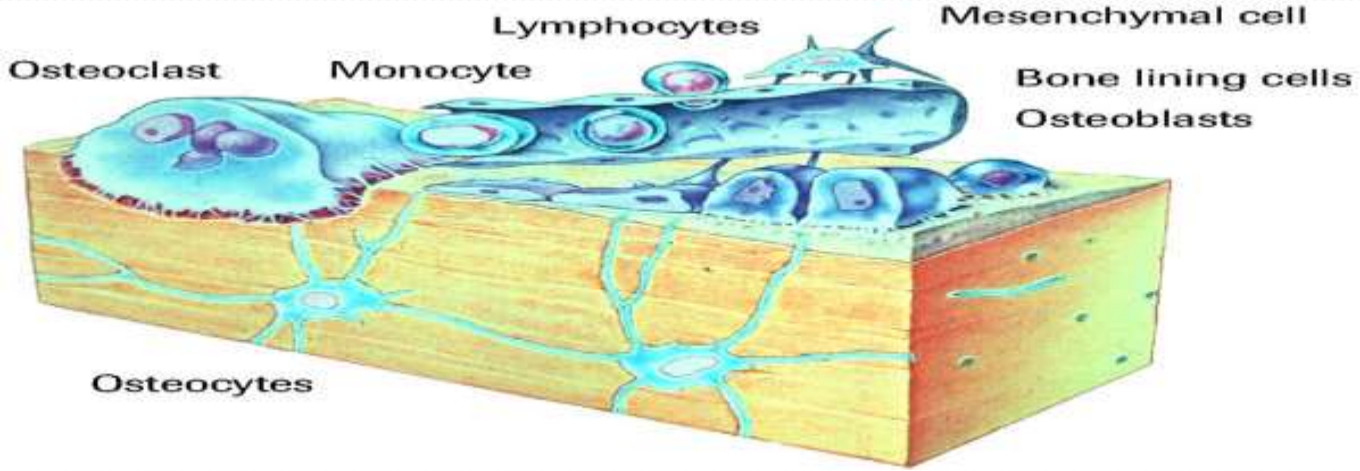
Formation:

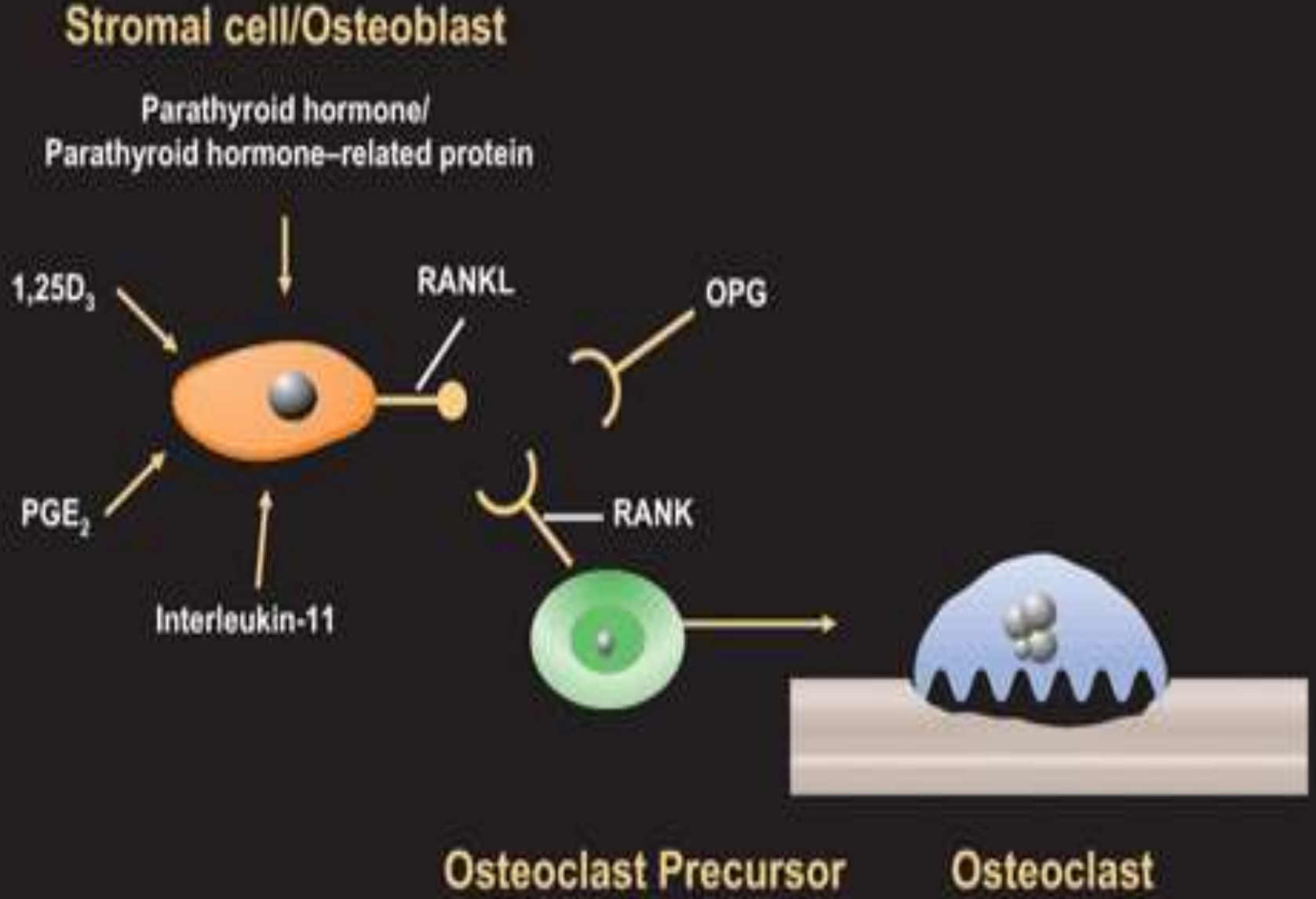
Hemopoietic stem cells of
monocyte-macrophage lineage

cell cell interaction → ← RANKL, M-CSF

↓

osteoclast




Stromal cell/Osteoblast
Parathyroid hormone/
Parathyroid hormone–related protein
1,25D3
RANKL
OPG
PGE2
RANK
Interleukin-11
Osteoclast Precursor
Osteoclast

Regulation of Osteoclast activity:

- OPG(Osteoprotegerin): member of TNF receptor family ⟶ natural RANKL antagonist
- Estrogen: supresses production of bone resorbing cytokines- IL-1 & IL-6
  ↑ es TGF-β ⟶ APOPTOSIS of osteoclast
- Vit D3 & PTH: Stimulate bone resorption through osteoclasts
- Calcitonin: Inhibitor of osteoclast activity

BONE FORMATION

- Intramembranous ossification
- Endochondral bone formation

Intramembranous ossification:

- Direct formation of bone within highly vascular sheets of condensed primitive mesenchyme.
- Occurs in the flat bones of the skull and clavicles.
- Begins towards the end of second month of gestation.

- Process involves the following steps:

1. Formation of bone matrix within the fibrous membrane.
2. Formation of woven bone.
3. Appositional growth.
4. Formation of osteon.

Formation of bone matrix within the fibrous membrane.

Loose mesenchyme at bone development site.

↓ centre of osteogenesis develops

Proliferation & condensation of mesenchyme to form compact nodules.

↓

Center cells differentiate to OSTEOBLASTS.

↓

Forms organic bone matrix which later calcifies to irregular bony spicules.

Formation of woven bone

Bony spicules gradually lengthen into longer and anastomosing structures called trabeculae.

↓

Trabeculae grow in radial pattern to enclose blood vessels

This early membrane bone- **Woven bone**.

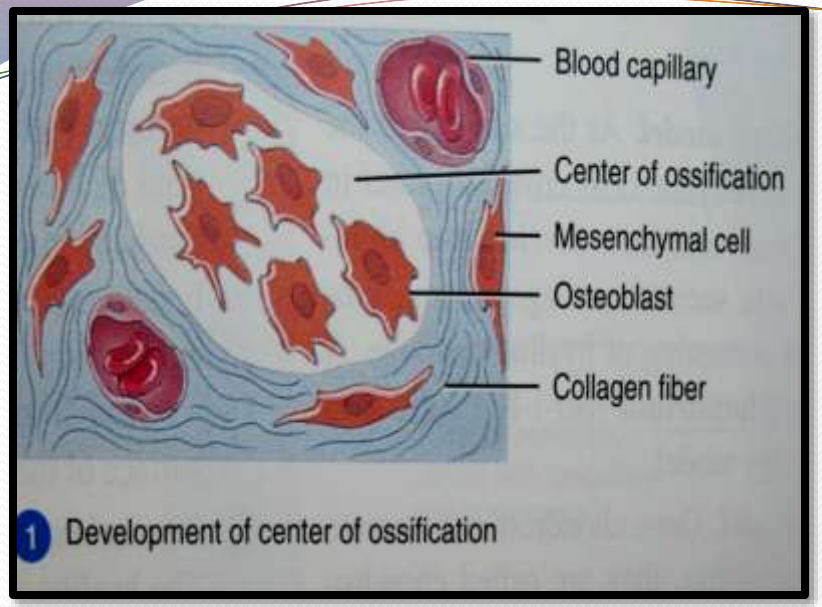
↓

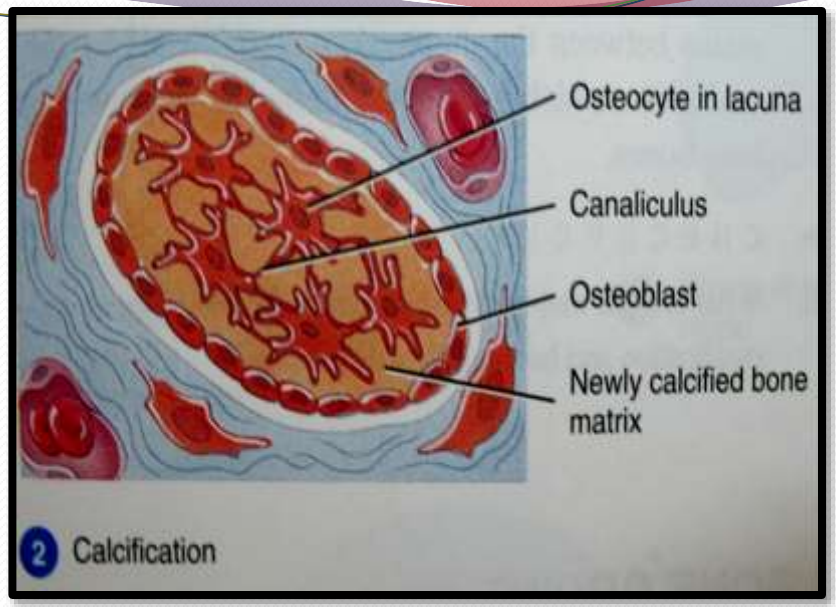
External to the woven bone, there is condensation of vascular mesenchyme to form **Periosteum**.

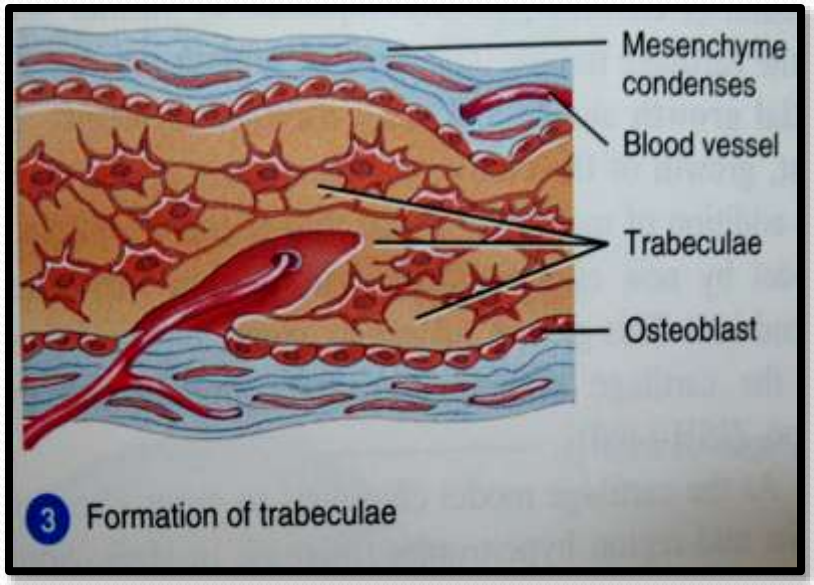
Appositional growth & formation of compact bone

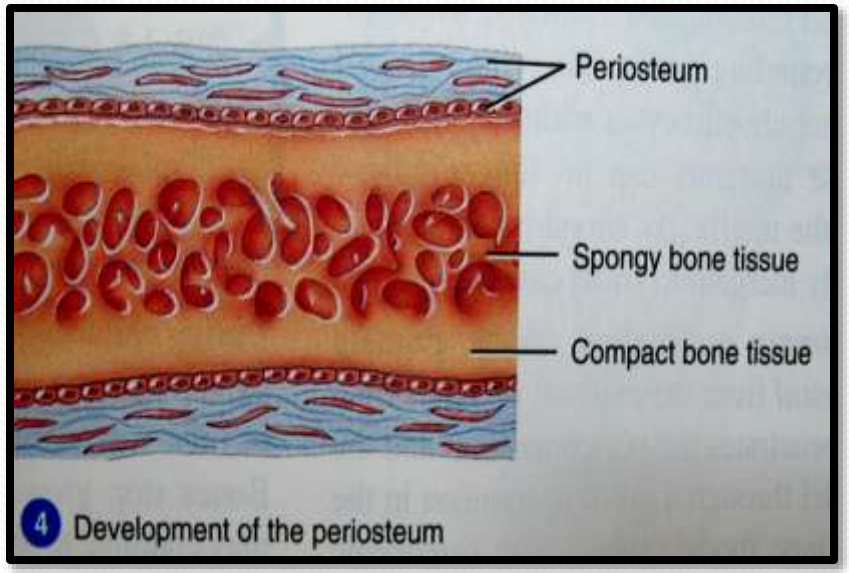
- Osteoblasts & osteogenic cells cover the spicules & trabaculae of bone.
- These osteogenic cells proliferate in richly vasclarised environment & give rise to osteoblasts that
- deposit new layer of bone matrix on preexisting bone surfaces.
- This is appositional growth – build up of bone tissue one layer at a time.

Cbfa1 and BMP's are required for the process to take place









INTRAMEMBRANOUS OSSIFICATION

Difference between mature & woven bone

Features	Mature bone	Woven bone
Orientation of collagen fibres	Collagen fibres in one lamella lies at right angles to other lamella	Collagen fibres oriented in different directions
Interfibrillar space Mineral density	Space less more	Space is more less
Deposition and mineralization	Slow than woven bone, osteocytes lesser in number	Faster, more number of osteocytes are present
Resorption	Portion of lamellar matrix is resorbed at one time	Woven bone can be entirely removed
H & E staining	Eosinophilic	Basophilic (higher proteoglycan content)

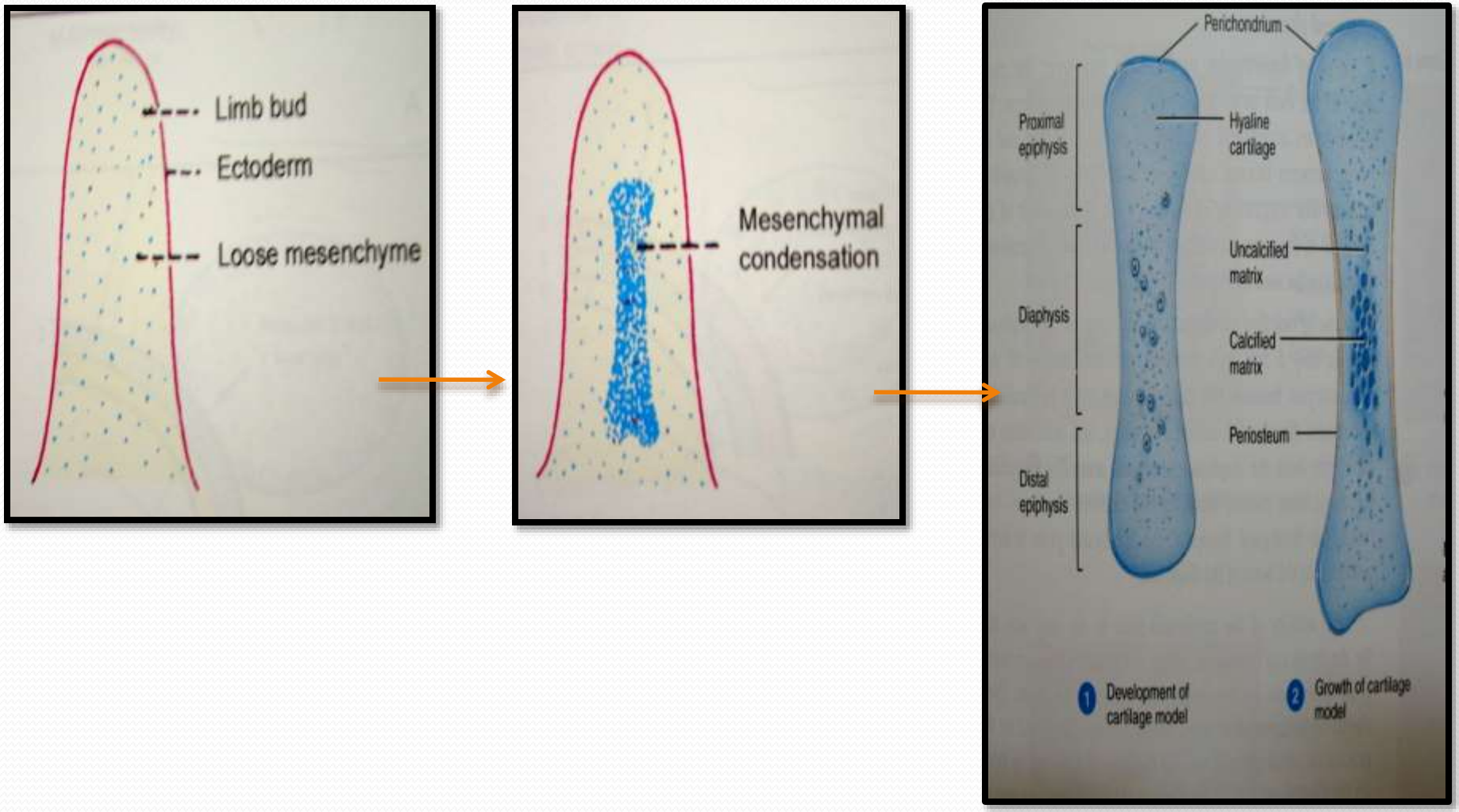
Endochondral ossification:

1. Replacement of a cartilaginous model by bone.
2. Occurs at the extremities of all long bones, vertebrae, ribs, articular extremity of the mandible and base of the skull.

The process involves the following steps:

1. Formation of a **cartilaginous model**.
2. Formation of **bone collar**.
3. Formation of **periosteal bud**.
4. Formation of **medullary cavity**.
5. Formation of **secondary ossification center**.
6. Mechanism of **calcification**.

FORMATION OF CARTILAGENOUS MODEL:

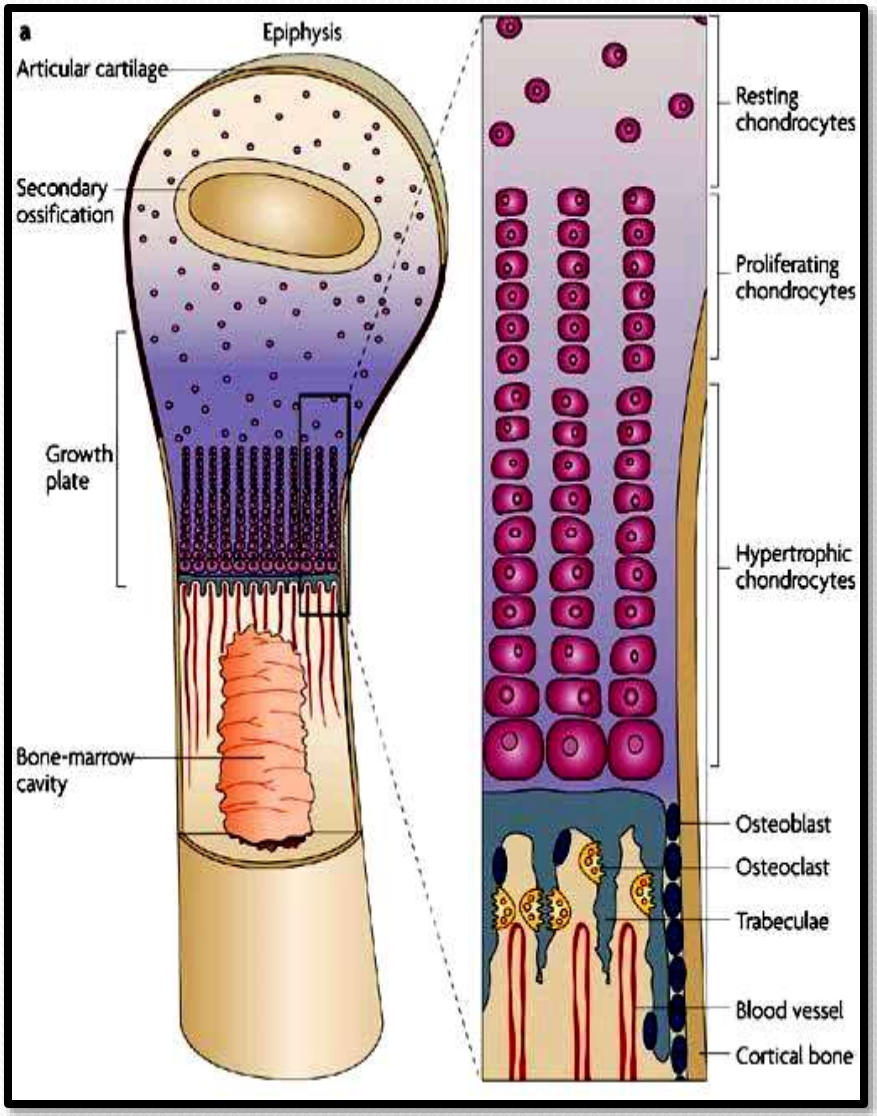


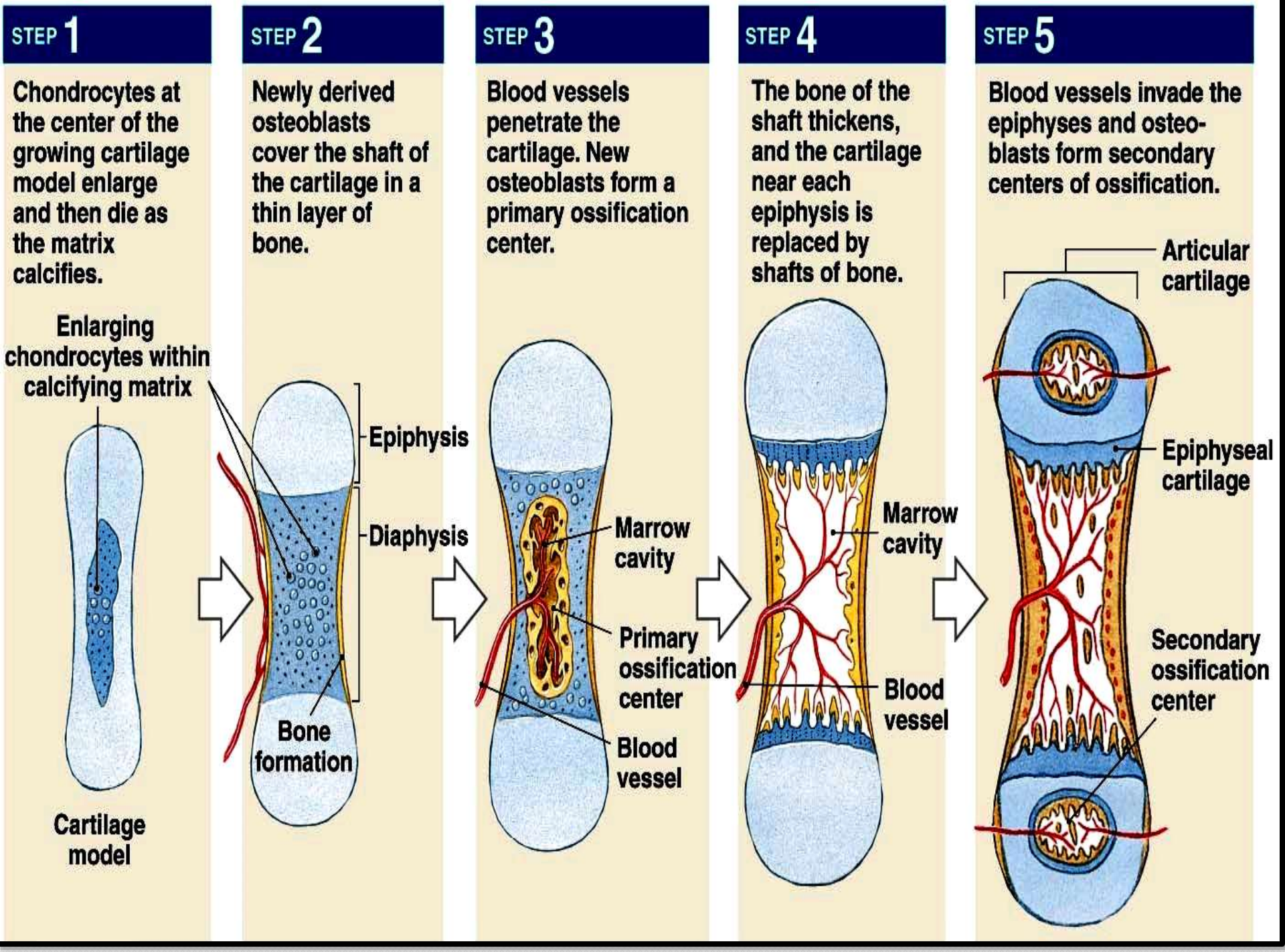
FORMATION OF A CARTILAGINOUS MODEL.

1. Zone of proliferation- small, flat cells.

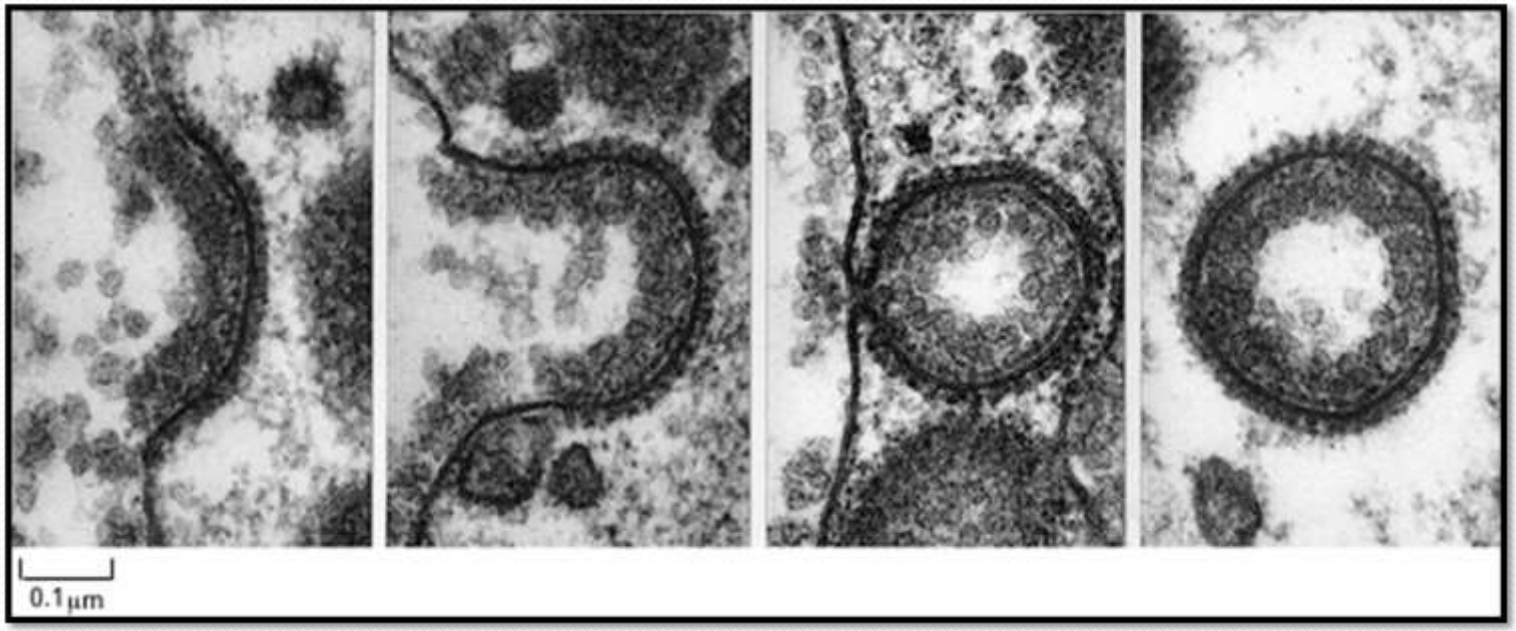
2. Zone of hypertrophy and maturation- secret collagen & non-collagenous proteins

3. Zone of provisional mineralization- begins mineralization




STEP 1
Chondrocytes at the center of the growing cartilage model enlarge and then die as the matrix calcifies.
Enlarging chondrocytes within calcifying matrix
Cartilage model
STEP 2
Newly derived osteoblasts cover the shaft of the cartilage in a thin layer of bone.
Epiphysis
Diaphysis
Bone formation
STEP 3
Blood vessels penetrate the cartilage. New osteoblasts form a primary ossification center.
Marrow cavity
Primary ossification center
Blood vessel
STEP 4
The bone of the shaft thickens, and the cartilage near each epiphysis is replaced by shafts of bone.
Marrow cavity
Blood vessel
STEP 5
Blood vessels invade the epiphyses and osteoblasts form secondary centers of ossification.
Articular cartilage
Epiphyseal cartilage
Secondary ossification center

Role of Matrix vesicles



PLAY A ROLE IN NUCLEATION

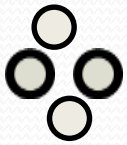
Pi ions are introduced into vesicular membrane by ALKALINE PHOSPHATASE

Initial ACP precipitated

Single crystals of HA appear

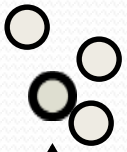
Crystals grow rapidly and rupture from the confines of the vesicles, spread as clusters of crystallites

Matrix vesicles accumulate Ca++ via a Ca++ pump(ATP driven)



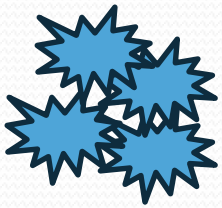
ALK. PHOSPHATASE

Pi



Ca++ ion pump

Ca++ Ca++ Ca++



- Alkaline phosphatase which is associated with the vesicle represents 2 distinct enzymatic activities:

1. Active against pyro-phosphatase which is an inhibitor of HA formation
2. Helps in growth of the crystal

- Vesicles show a high level of alkaline phosphatase

The mechanisms of mineralization and role of alkaline phosphatase in health and disease, Hideo Orimo, J of Nippon Med Sch, 2010

Theories of mineralization

- First theory -Nucleation-formation of crystals upon substrates acting as models or templates (eg.in collagenous tissue where crystallites are deposited along collagen fibrils)-**epitaxis**

- Second theory-mineral is initially deposited as an amorphous calcium phosphate. Subsequently becomes hydrolyzed to crystalline hydroxyapatite

- Third theory-neither a nucleation site nor an amorphous precursor is necessary and that tissues are supersaturated with respect to calcium and phosphorus & will precipitate crystals spontaneously.

Oral Histology- Inheritance and Development, Provenza, 2nd ed.

BONE RESORPTION:

- Removal of mineral and organic components of the ECM

- **SEQUENCE OF EVENTS**
- **Ist PHASE:** formation of osteoclast progenitors in the blood, followed by vascular dissemination & formation of osteoclasts.

- **IInd PHASE:** activation of osteoclasts and retraction of osteoblasts to expose minerals to osteoclasts.

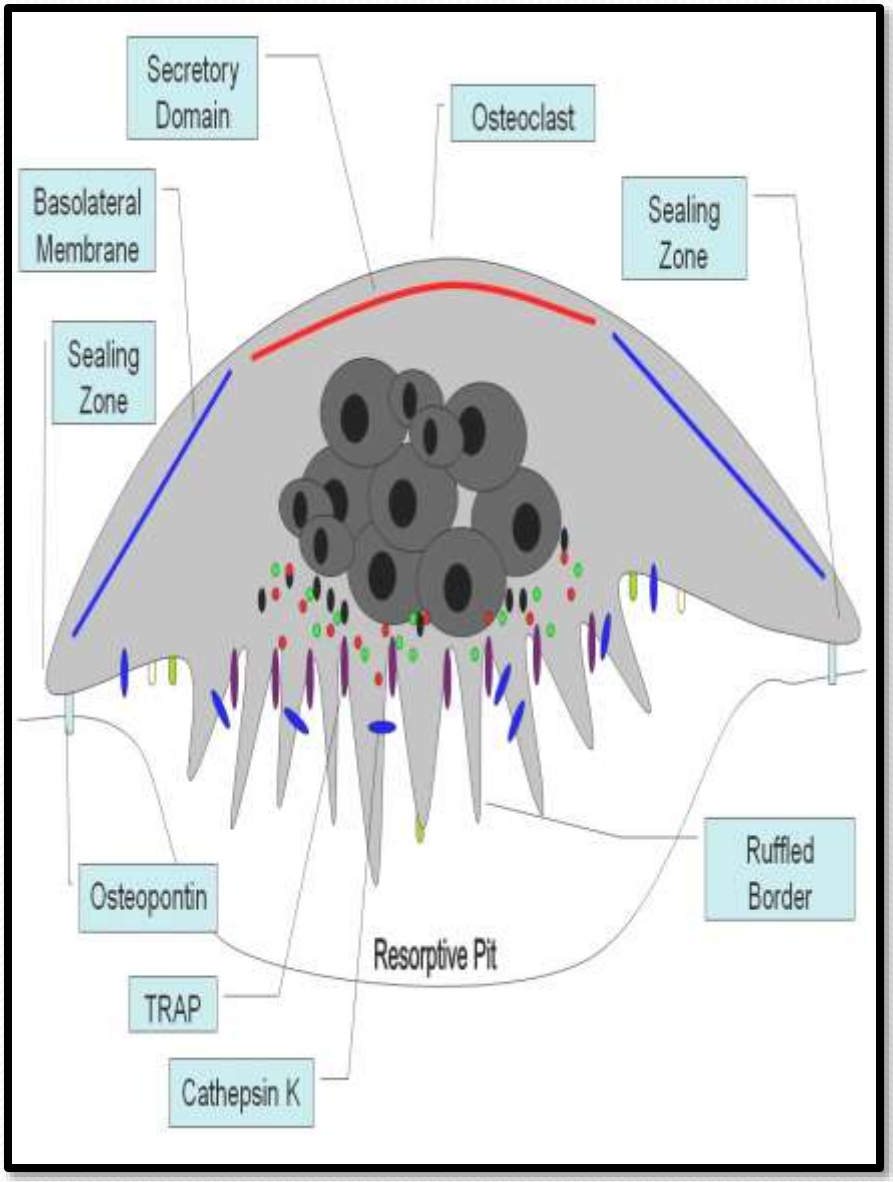
- **IIIrd PHASE:** activated osteoclasts resorbing bone.

- **ALTERATION IN OSTEOCLASTS:**

1. Formation of ruffled borders: extensive surface area

2. Clear (sealing) zone: attachment- through integrins

- Isolated microenvironment



- **REMOVAL OF HYDROXYAPATITE:**

1. Dissolution by HCL creating a pH of 2.5-3.
2. The protons for HCL arise from activity of Carbonic Anhydrase II synthesized by osteoclasts.

- **DEGRADATION OF ORGANIC MATRIX:**

1. Brought about by proteolytic enzymes CATHEPSIN-K, MMP-9

- **REMOVAL OF DEGRADATION PRODUCTS:**

1. Endocytosis and removal from FUNCTIONAL SECRETORY DOMAIN -FSDs (exocytosis).
2. Following resorption osteoclasts undergo APOPTOSIS. (TGF-β & Estrogen promote apoptosis)

Recently **TRAP (tartrate resistant acid phosphatase)** role is emphasized in regulation of bone resorption.

BONE REMODELING:

- Bone- highly dynamic connective tissue
- Process by which the overall size and shape of bone is established (**COUPLING of bone resorption & formation**)
- **Turnover rates**- 30%- 100% per year in rapidly growing children. Adults- slow

- **Function of remodeling:**
  - Prevent accumulation of damaged & fatigued bone by regenerating new bone
  - Allow bone to respond to changes to mechanical forces
  - To facilitate mineral homeostasis

- **SEQUENCE OF EVENTS:**

1. Osteoclasts tunnel into surface of bone- 3 wks.

2. Osteoclasts travel along the vessel and resorb haversian lamellae & part of circumferential lamellae & form a **"cutting cone".**

3. After sometime resorption ceases and osteoclasts are replaced by osteoblasts.

4. Osteoblasts lay down a new set of haversian lamellae. Entire area of active osteon formation-**"filling cone"**

ALVEOLAR BONE

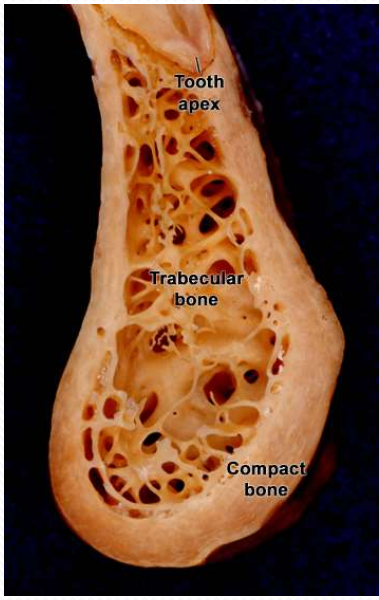
Defined as that part of maxilla and mandible that forms and supports the sockets of the teeth.

FUNCTIONS:

1. Houses the roots of teeth.
2. Anchors the roots of teeth to the alveoli- Sharpy's fibers in to bone
3. Helps to move the teeth for better occlusion.
4. Helps to absorb and distribute Occlusal forces.
5. Supplies vessels to PDL.
6. Organizes eruption of primary & permanent teeth.

STRUCTURE OF ALVEOLAR BONE:

1. ALVEOLAR BONE PROPER: thin lamella of bone that surrounds the root of tooth & gives attachment to the PDL
    a. Lamellated bone
    b. Bundle bone-



Bundle bone:

- Principle fibers of PDL are anchored.
- "bundle bone"- bundles of principle fibers
- Scarcity of fibrils
- Radiographically: lamina dura
- Radiopacity- thick bone without trabeculations

- Cribriform plate:
- Inner wall of the socket perforated by many openings that carry branches of interalveolar nerves & blood vessels in to PDL.
- Interdental septum:
- Bone between 2 teeth & composed entirely of cribriform plate

- The interdental & interradicular septa contain the perforating canals of *Zuckerkandl & Hirshfield (nutrient canal)* --- house the artries, veins, lymph vessels, nerves

2. SUPPORTING ALVEOLAR BONE:

a. Cortical plates

- Compact bone. Forms inner & outer plates of alveolar processes.

b. Spongy bone

Fills the area between the corticle plates & alv. bone proper

i. Type I- interdental & inter radicular trabeculae are regular & horizontal in ladderlike arrangement (MANDIBLE)

ii. Type II- shows irregularly arranged, numerous, delicate trabeculae. (MAXILLA)

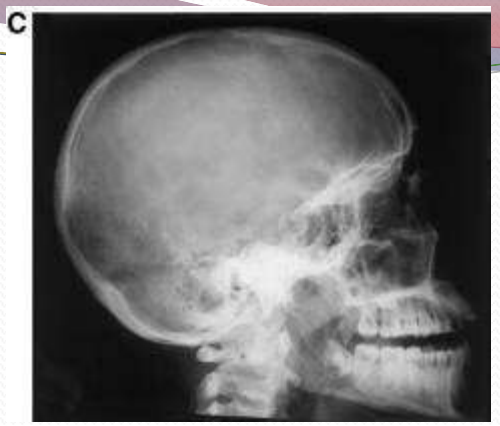
CLINICAL CONSIDERATIONS

Osteogenesis Imperfecta

- Brittle bones , Lobstein disease
- Abnormality in type-1 collagen ---- Mutation of COL1A1 (chromosome 17) or COL1A2 (7)
- Autosomal dominant

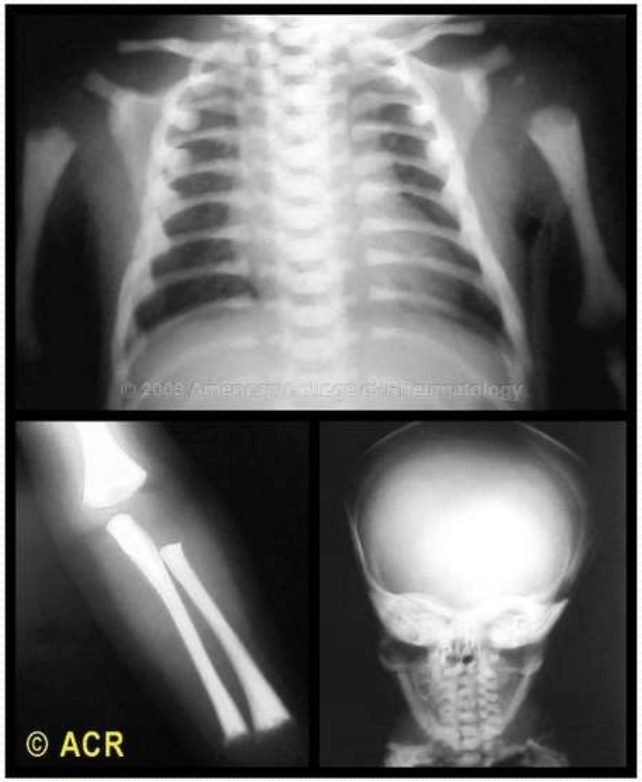
- 4 types: I, II, III, IV
- C/F: bone fragility, fractures, blue sclera
  a/w DI, short stature etc
- H/P: Thin, spongy bone, reduced osteoblast activity,
- Both- qualitative & quantitative defect of collagen

Oseopetrosis



- Marble Bone Disease / Albers-Schonberg disease

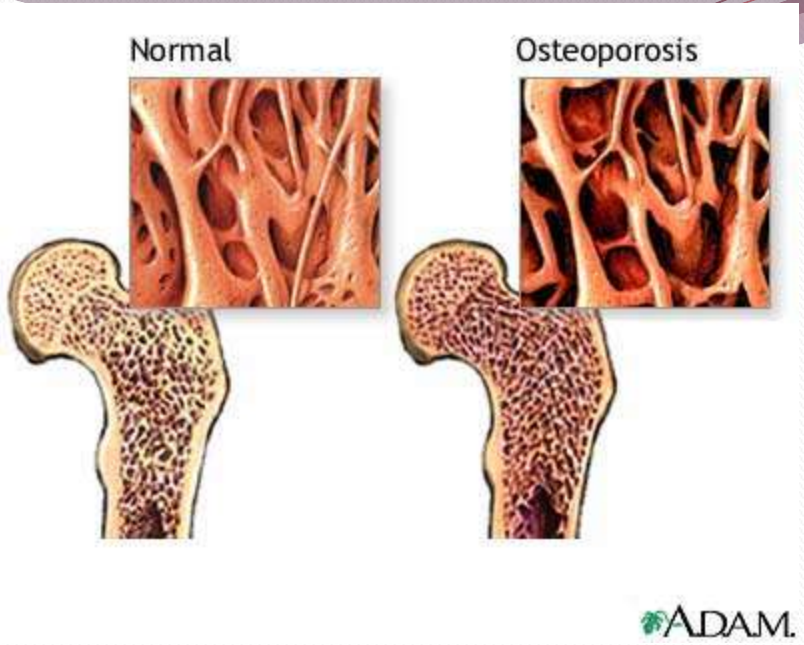
- Failure of osteoclasts to resorb bone leads to increases bone mass.
- Bone has poor mechanical properties.
- Fragility--- fractures

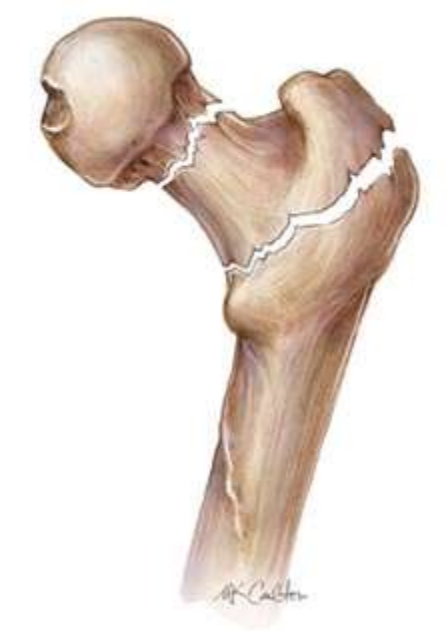


Osteoporosis

- In osteoporosis, the bone mineral density (BMD) is reduced, bone micro architecture is disrupted, and the amount and variety of non-collagenous proteins in bone is altered.

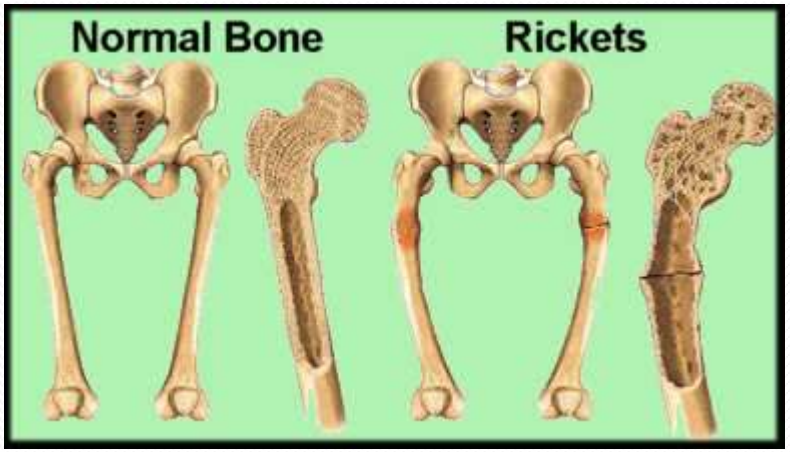
- Osteoporosis is most common in women after the menopause, when it is called postmenopausal osteoporosis





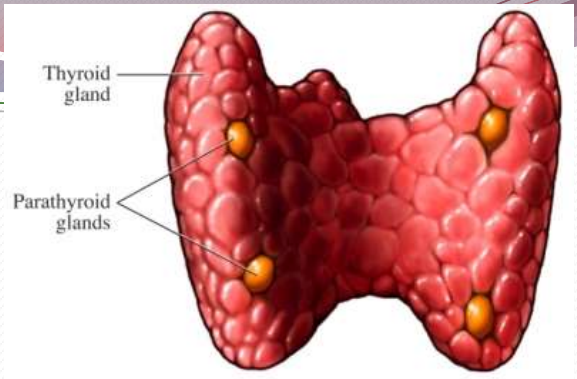
Rickets & Osteomalacia

- "Wricken" = to bend
- Vitamin D deficiency → calcium absorption ↓ weak bones
- RICKETS: Decreased mineralization at the level of growth plate → growth retardation
- Pigeon chest, lumbar lardoisis, rachetic rosary, bowed legs, craniotabes etc.



- OSTEOMALACIA: Adults

Hyperparathyroidism

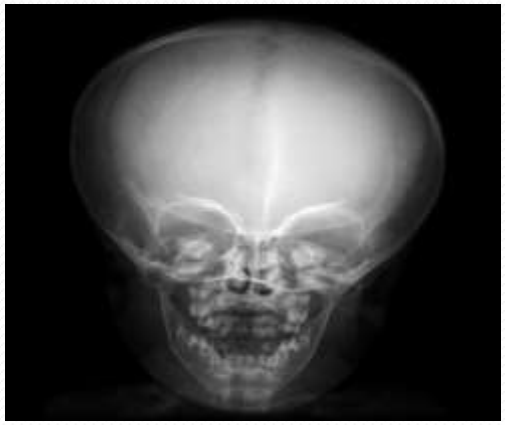


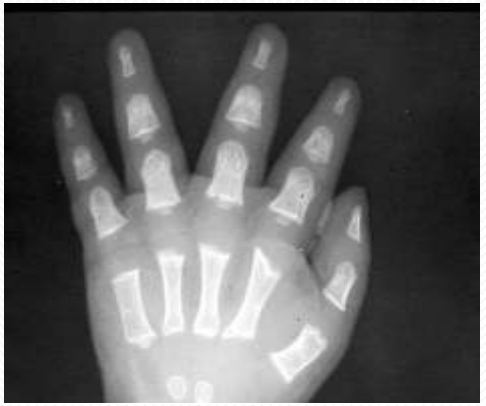
- Primary, secondary, tertiary,
- C/F: bone pain, tenderness, spontaneous fractures, weakness, generalized osteoporosis, abortive attempts at bone repair.

- R/F: generalized radiolucency as compared to normal, later sharply defined radiolucencies in mandible, "ground-glass" appearance, lamina dura lost, osteoclastomas

Achondroplasia

- Mutation in gene for fibroblast growth factor receptor-3 (FGFR-3)
- Short stature, short arms & legs, long trunk
- Midfacial hypoplasia, Frontal bossing
- Mandibular prognathism, malocclusion
- h/p: failure of endochondral ossification





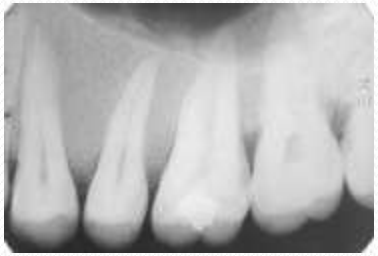
FIBROUS DYSPLASIA

- Developmental condition of replacement of normal bone by an excessive proliferation of cellular fibrous connective tissue intermixed with irregular bone trabeculae.

- Mutation of GNAS 1 gene (guanine nucleotide-binding protein, α-stimulating activity peptide)
- G protein ---- cAMP---- endocrine hyperfunction
  proli of melanocytes
  differentiation of osteoblasts
- 4 patterns:

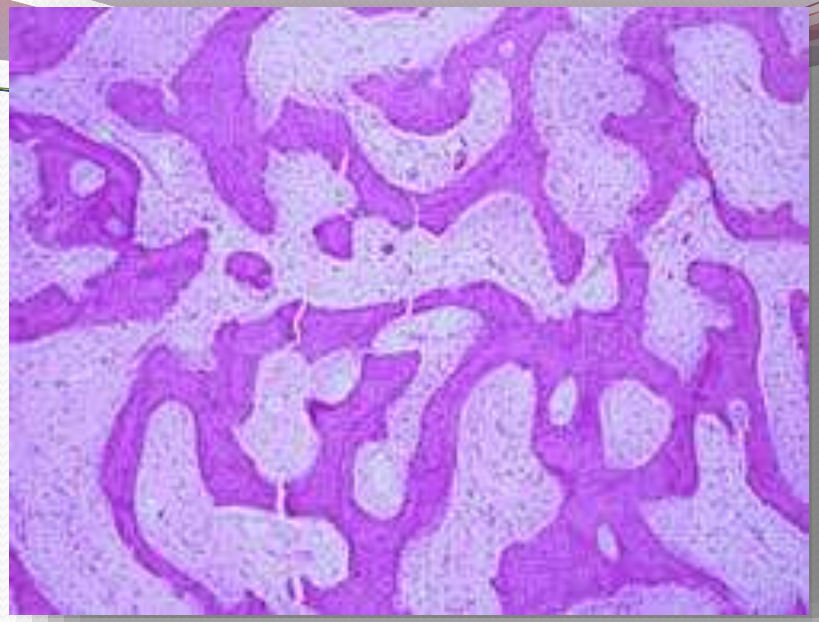
  I) Monostotic II) Polyostotic III) Craniofacial IV) Cherubism

- **Monostotic** accounts for 80-85% of cases; jaws are common location; maxilla > mandible; maxillary lesions sometimes part of wider craniofacial fibrous dysplasia.
- Radiographic poorly demarcated "ground-glass" appearance of affected bone causing expansion; in long bones often radiolucent, multilocular & expansile.
- PDL may be narrow and lamina dura indistinct; inferior alveolar nerve canal displaced superiorly.

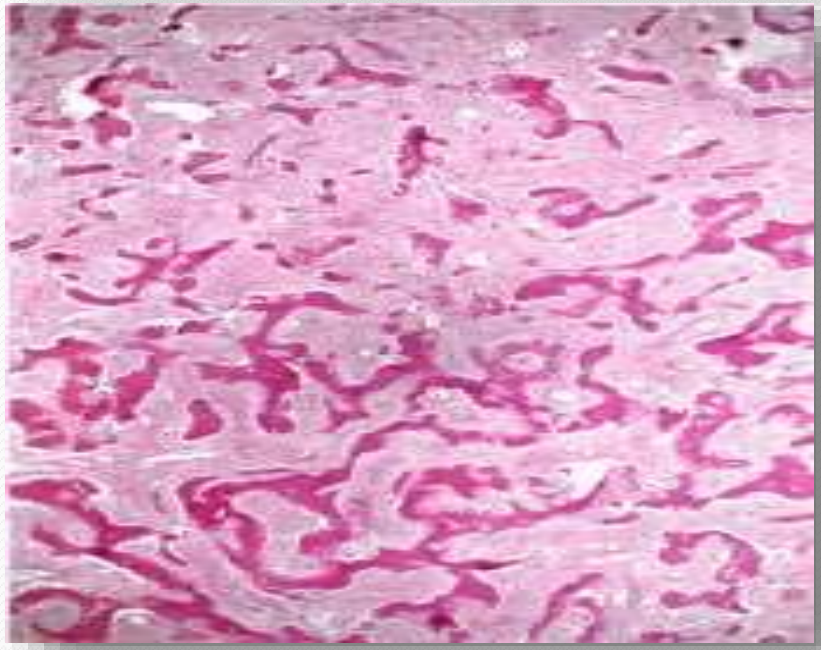


- Polyostotic (PFD) involves two or more bones.
- Jaffe-Lichtenstein syndrome consists of PFD with *café au lait* pigmentation.
- McCune-Albright syndrome consists of PFD, *café au lait* pigmentation and multiple endocrinopathies such precausious puberty , pituitary adenoma or hyperthyroidism.

- Classical histopathologic characteristics of fibrous dysplasia-cellular, active fibrous connective tissue containing irregular, partially calcified bone trabeculae.

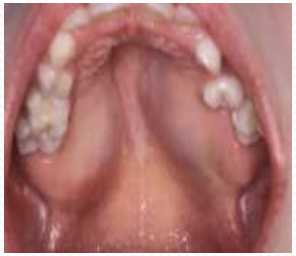


- The **characteristic features** are: · Proliferating stellate fibroblasts in a whorled stroma of interlacing collagen fibres · Metaplastic woven bone trabeculae in different patterns like "C" shape or in the form of "**Chinese letters**.



CHERUBISM

- Given by Jones in 1933
- Autosomal dominant, benign FOL involving more than 1 quadrant
- Stabilizes after growth period
- Facial deformity & malocclusion
- Premature exfoliation of deciduous teeth & delayed eruption of permanent teeth

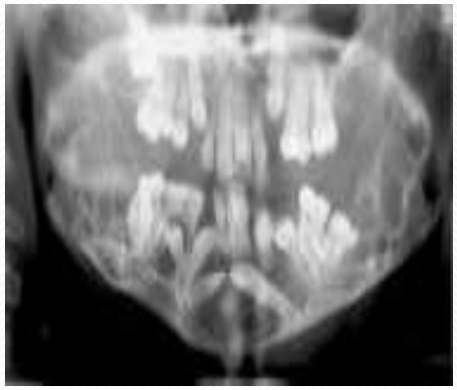


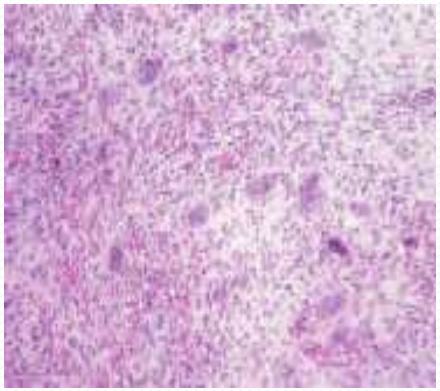
- C/F: Bilateral symmetric painless jaw expansion
- Lymphadenopathy
- "Eyes turned unto heaven" appearance
- a/w Noonan's syndrome & Ramon's syndrome

- ETIOLOGIES:
- Hereditary
- Mutation of non sex linked gene- 4p16.3- responsible for jaw dev.

- R/F: Multilocular- honey comb/ soap bubble app
- Bilat. cystic expansion of jaws
- Floating tooth syndrome
- Ground glass app of bone

- H/P: multinucleated giant cells with strong positivity for TRAP – Characteristic of osteoclasts
- Collagenous stroma – spindle fibroblasts, water-logged granular nature
- Perivascular eosinophilic cuffing



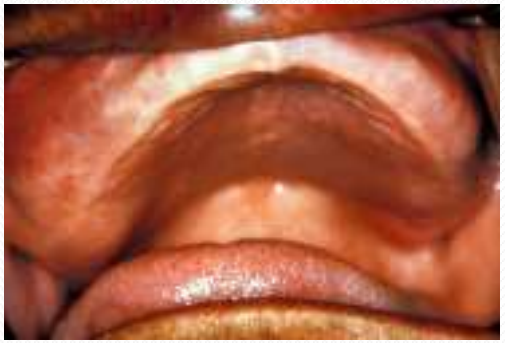


PAGET'S DISEASE

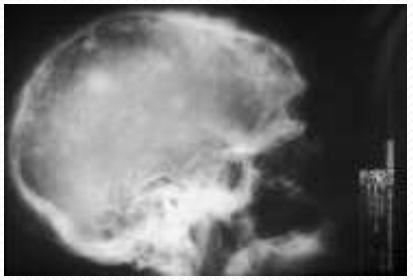
- Excessive & abnormal remodeling of bone
- Seen in middle aged & elderly
- Extensively vascular, weak, enlarged & deformed bones of entire skeleton.

- Suggested etiologies:
- Autosomal dominant inheritence – genetic mutation
- Viral infections
- Chronic inflammation
- Auto-immunity
- Connective tissue & vascular disorders

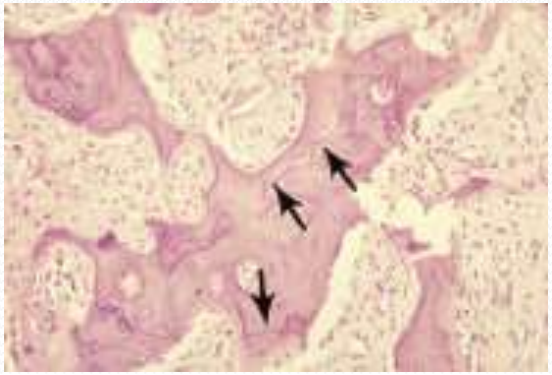
- C/F: leontiasis ossea
- Painful enlargement of maxilla & mandible
- Widened alv. ridges, flat palate
- Exfoliation & spacing in teeth
- Inability to wear dentures



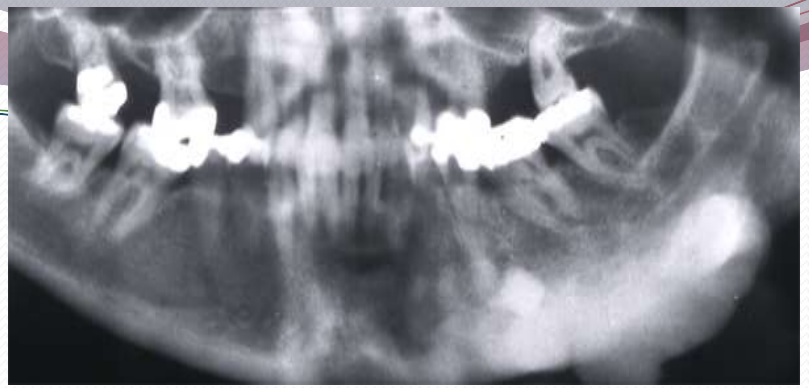
- R/F: Osteoporosis circumscripta
- Gen. radiopacities of jaw=“ cotton wool” app.
- Hypercementosis, loss of lamina dura



H/P: mosaic pattern/ jigsaw

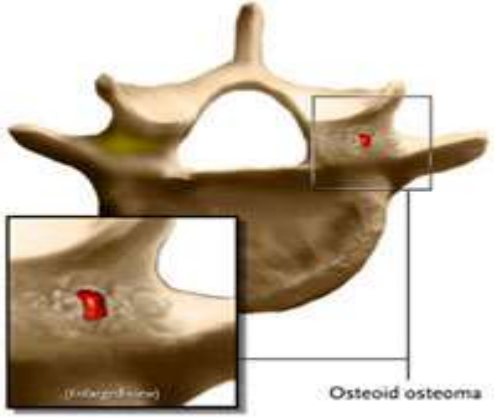


OSTEOMA



- Benign neoplasm characterized by proliferation of either compact or cancellous bone, usually in an endosteal or periosteal location.
- Periosteal: well circumscribed swelling, asymmetry, slow growing
- Endoseal: slower
- Seldom any pain associated with this tumor.
- Multiple osteomas- Gardner's syndrome
- H/P: extremely dense compact bone/ coarse cancellous bone

OSTEOID OSTEOMA



- Benign tumor of bone , True nature unknown.
- C/F: Young children, males
- Frequently- femur or tibia, in jaw- mandible
- Unrelenting, sharp pain. Classically relieved by Aspirin.
- R/F: round radiolucent area surrounded by sclerotic border.
- H/P: Central nidus of compact osteoid tissue, interspersed by vascular C.T, outlined by active osteoblasts.
- Neural staining: many axons throughout---- pain

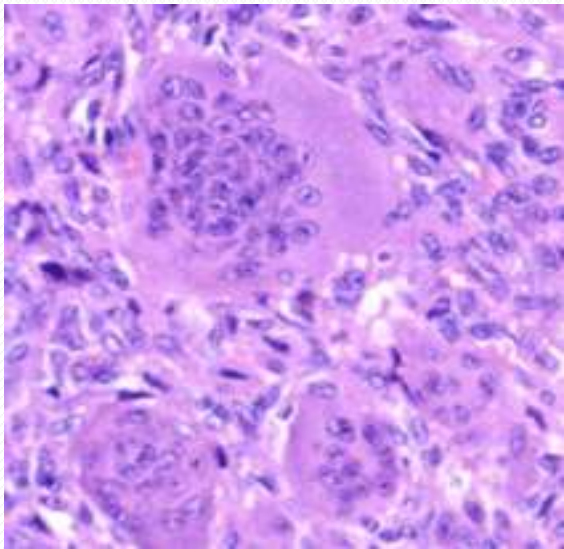
OSTEOBLASTOMA (Giant osteoid osteoma)

- Osteoblastic nature--- histologic resemblance to osteoid osteoma.
- But, has high growth potential, lacks characterisic pain & halo of sclerotic bone

- H/P: Hallmark of osteoblastoma:
- Vascularity of lesion, Moderate no. of multinucleated giant cells, actively proliferating osteoblasts.

OSTEOCLASTOMA (Giant cell tumor of bone)

- Distinctive neoplasm of undifferentiated cells
- Multinucleated giant cells- fusion of mononuclear cells
- H/P: the basic proliferating cell has round to oval or spindle nucleus that is diagnostic of true giant cell tumor.
- Giant cells scattered throughout the lesion
- contain 40-60 nuclei
- Areas of infarct-like necrosis
- Small collection of foam cells common

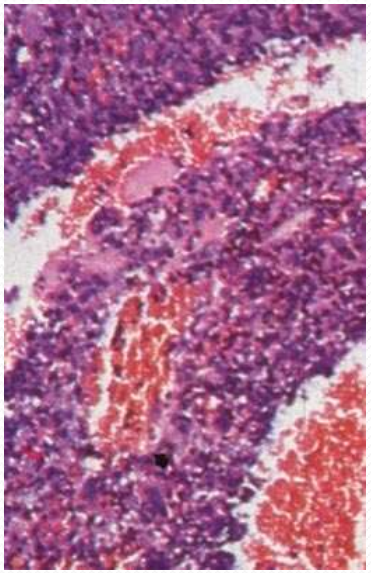


ANEURYSMAL BONE CYST

- ABC is an intraosseous accumulation of variable sized blood filled spaces surrounded by cellular fibrous connective tissue that is admixed with trabeculae of reactive woven bone.

- C/F: young , male=female
  - h/o trauma
  - Lesion is tender or painful, swelling over the region
  - Blood welling up from the tissue
  - Tissue is described as --- blood soaked sponge with large pores that are cavernous spaces

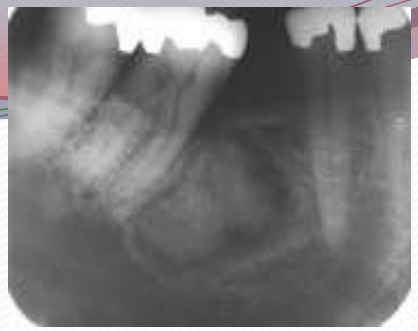
- Pathogenesis:
- Persistent alteration in the hemodynamic ⟶ increased venous pressure ⟶ dev. of dilated/ engorged vascular bed in bone
- Exuberant attempt at repair of hematoma of bone & hematoma maintains circulatory connection with damaged vessel.
- Secondary reactive lesion of bone.



- H/P: fibrous connective tissue with many cavernous/ sinusoidal blood filled spaces.
  - hemosiderin

FLORID OSSEOUS DYSPLASIA

(Gigantiform Cementoma)



- Widespread form of cemental dysplasia.
- Normal cancellous bone is replaced by dense acellular cementoosseous tissue in a background of fibrous C.T

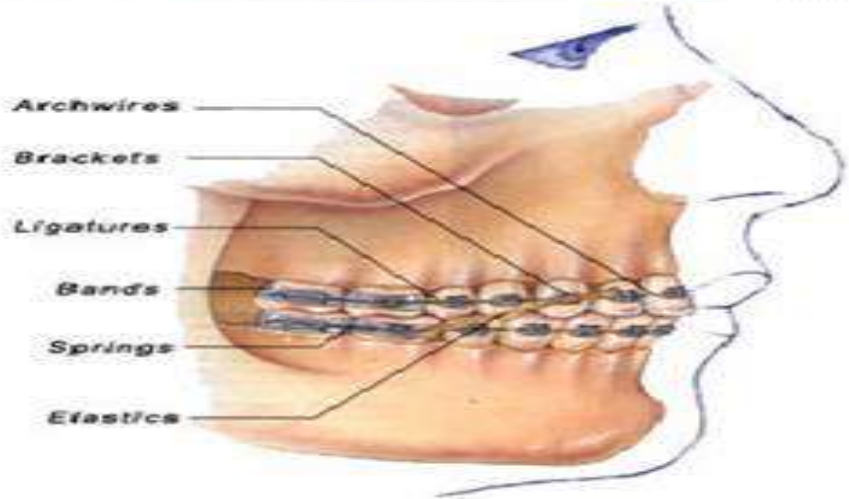
- Asymptomatic painless expansion of Alv. Process of mandible.
- R/F: cotton wool appearance to large areas of calcification
- Periphery is well defined – has sclerotic border

Orthodontic treatment & bone:

- Bone- though one of the hardest tissues, is biologically highly plastic
- Resorption : pressure
- Formation : tension

- On pressure side: cAMP ↑

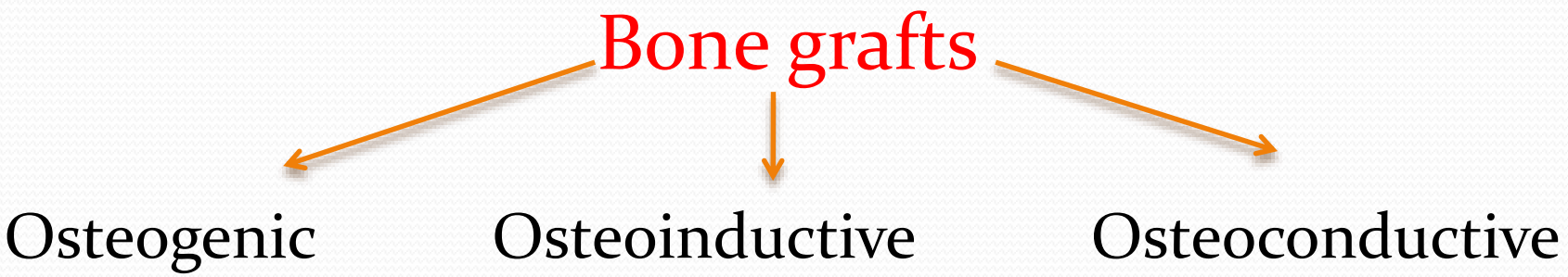
  ⟶ Bone resorption
- On tension side: osteoblasts activated



THERAPEUTIC CONSIDERATIONS:

- Bone Grafts: Autografts, Allografts, Xenografts
- Synthetic bone graft materials:

  hydroxyapatite, calcium carbonate etc.



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- Thank You

Mrinal S part 1 pg