bone function:

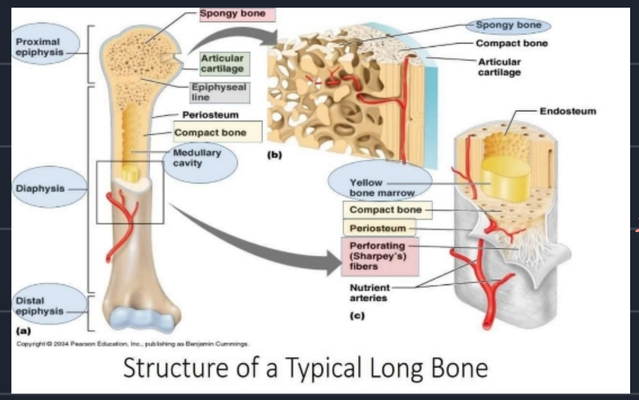
1- mechanical support.

2- forces transmission.

3- protection.

4- mineral homeostasis.

5- hematopoiesis (blood formation).



Structure of a Typical Long Bone

1- epiphysis: 1- where the bone grow.

2- there are two epiphysis: distal and proximal.

2- diaphysis: shaft, between proximal and distal epiphysis.

bone structre:

1- matrix: 35% osteoid, 65% minerals

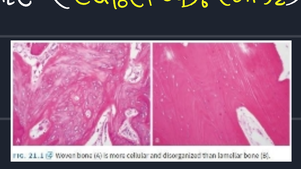
1- organic osteoid: 1- collagen type I.

2- GAGs.

3- other proteins.

2- inorganic hydroxy apetite ($Ca_{10}(PO_4)_6(OH)_2$).

3- woven or lamellar bone.



1- woven 2- lamellar

1- woven: 1- irregular arrangment of collagen type I.

2- found mainly in children bon.

3- sign of disease if it found in adult.

2- lamellar: 1- linear origanized cells.

2- found mainly in adult.

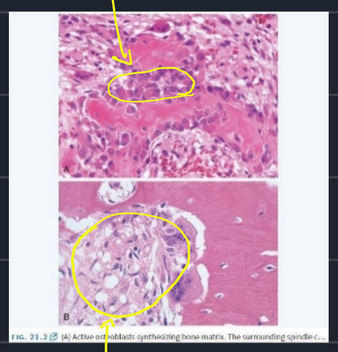
3- more of collagen, stronger.

2- cells:

1- osteoblast: bone formation.

2- osteoclast: bone resorbtion.

3- osteocyte: mature bone cells.



1- osteoblast: 1- smaller in size.

2- mono-nucliated cells.

3- found around osteoid.

2- osteoclast: 1- consider as macrophage.

2- multinucliated cells.

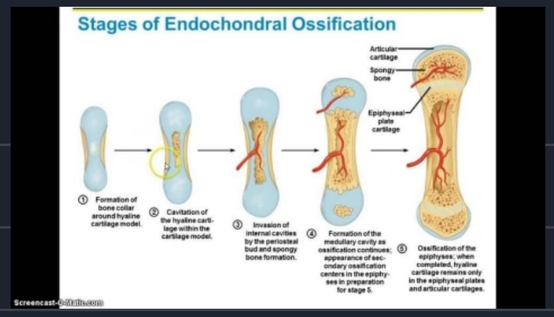
3- left white areas behind it.

development of bones:

→ 1- endochondral ossification: 1- in long bones.

2- formation of bone from young mature cartlige.

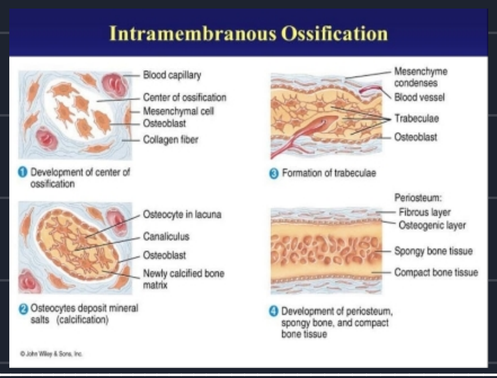
3- cartlige will be replaced by mature bone later except the endings.

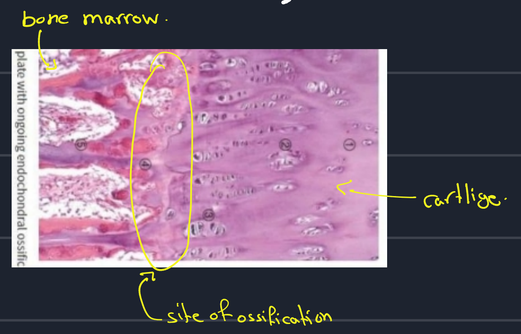


→ 2- intramembranous ossification: 1- in flat bones.

2- formation of bone from mesenchymal cells.

3- no ossification of cartlige.





homeostasis and remodeling: 1- bone formation is continuous and dynamic complex process.

2- highest bone mass is reached in early adulthood.

3- bone resorption will surpass the formation on the 4th decade (40s).

4- the balance between osteoblast and osteoclast is always changing.

osteoclast diffrentiation regulation:

→ 1- stimulation (+): 1- PTH (Parathyroid hormone). 2- IL-1.

3- steroids.

→ inhibition (-): 1- BMPs (bone morphogenic proteins).

2- sex hormons (estrogen, testron).

on the stromal cell (osteoblast): 1- M-CSF

2- RankL (rank Ligand)

the binding of M-CSF and RankL to osteoclast precursor will activate the diffrentiation of osteoclast.

osteoprotegerin will block the rank-rankL interaction.

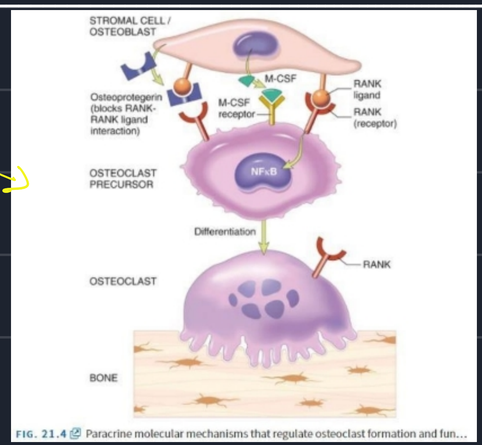
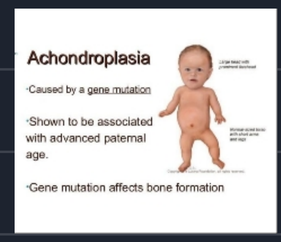


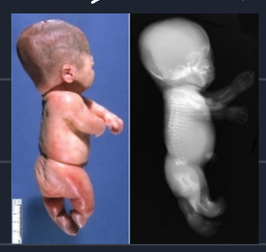
FIG. 21.4 Paracrine molecular mechanisms that regulate osteoclast formation and fun...

congenital disorders:

- 1- dysostosis: 1- abnormal condensation and migration of mesenchyme
  - 1- aplasia.
  - 2- supernumerary digit.
  - 3- syndactyly.
  - 4- craniosynostosis.
  - 2- genatic abnormalities of:
    - 1- homeobox genes.
    - 2- cytokines.
    - 3- cytokines receptors.
- 2- dysplasia: 1- disorganized bone and cartlige.
  - 1- achondroplasia: 1- most common dwarfism.
    - 2- mutation in FGFR3 gene.
    - 3- no effect on longevity, intelligance and reproductive status.



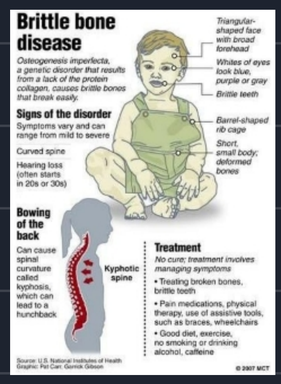
  - 2- thanatophric: 1- most common leathal form of dwarfism.



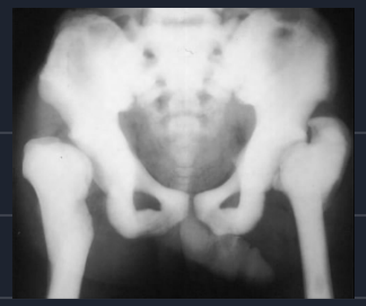
    - 2- mutation in FGFR3 gene but in different site.
    - 3- die at birth or shortly after.
    - 4- small cheast leading to respiratory inssufficiency.
- 3- disorganized bone and cartlige.
- 2- gen mutation that control development and remodeling.
- 3- they are not Premalignant.

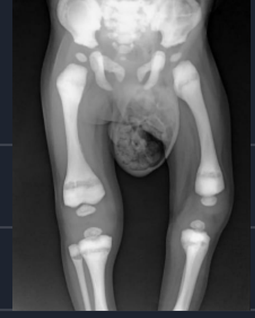
bone diseases:

- 1- osteogenesis imperfecta (brittle bone disease): 1- most common inherited disorders of connective tissue.
  - 2- group of disorders (autosomal dominant).
  - 3- dificency of collagen type I synthesis.
  - 4- fragile bone, boo little bone.
  - 5- diagnosis: blue sclera, hearing loss, teath abnormalities.
  - 1- type one: normal life.
  - 2- type two: Lethal.



2- osteopetrosis (marble bone, stone bone): 1- group of disorders.





2- rare.

3- impaired osteoclast function, reduce bone resorption will lead to sclerosis.

4- DX: X-Ray.

5- will lead to fractures and leukopenia.

* DX: diagnosis.

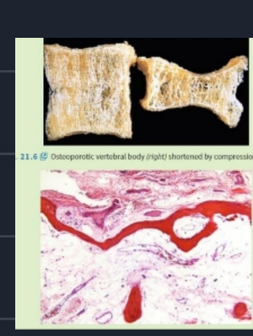
* TX: treatment.

metabolic disorders: → 1- osteopenia and osteoporosis:

→ 1- osteopenia: decreased in bone mass (1-2,5 SD below the mean).

→ 2- osteoporosis: 1- severe osteopenia (more than 2,5 SD below the mean)

2- generalized (more common) or localized.



osteoporosis clinically: 1- Vertebral fractures.

2- Femur and Pelvic fractures.

3- cause immobility, Pulmonary embolism, Pneumonia.

4- DX: BMD scan, DEXA scan.

→ 1- primary osteoporosis: 1- much more common.

2- Caused by: a- senile (aging) b- menopause: 1- ↓estrogen. 2- ↑IL1, IL6, TNF.

3- ↑RANK, RANKL. 4- ↑osteoclast

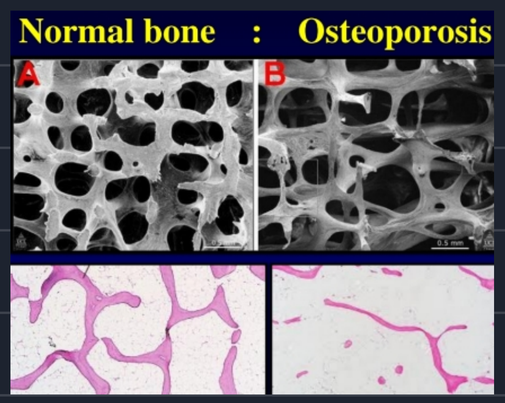
→ 2- secondary osteoporosis: 1- Less common.

2- Caused by: a- hyperthyroidism.

b- malnutrition.

c- steroids.

osteoporosis Prevention and treatment: 1- exercise.

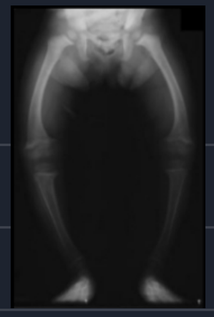


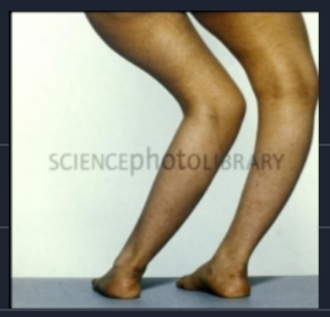
2- Calicium and vitamin D.

3- Bisphosphonates: reduce osteoclast activity.

4- denosumab: anti RankL, blocking osteoclast activation.

5- hormones: etrogen, but it have side effects such as: deep vein thrombosis (DVT), stroke.





2- rickets and osteomalasia: 1- rickets in children.

2- osteomalacia in adult.

3- caused by: a- vitamin D dificiency or abnormal metabolisim of it.

b- decrease mineralization of bone.

4- increase risk of fracture.

3- hyperParathyroidism (HPT):

Hyperparathyroidism classification

Different causes and features of hyperparathyroidism - raised parathormone (PTH).

	primary	secondary	tertiary
pathology	Hyperfunction of parathyroid cells due to hyperplasia, adenoma or carcinoma.	Physiological stimulation of parathyroid in response to hypocalcaemia.	Following long term physiological stimulation leading to hyperplasia.
associations	May be associated with multiple endocrine neoplasia.	Usually due to chronic renal failure or other causes of Vitamin D deficiency.	Seen in chronic renal failure.
serum calcium	high	low / normal	high
serum phosphate	low / normal	high	high
management	Usually surgery if symptomatic. Cincacalcet can be considered in those not fit for surgery.	Treatment of underlying cause.	Usually cinacalcet or surgery in those that don't respond.

1- primary: 1-hyperfunction of Parathyroid cell due to: 1- hyperPlasia.

2- assoiciated with endocrine neoplasia.

2- adenoma.

3- high(↑) ca^{+2}, normal/Low PO_4^{+3}.

3- carcinoma.

secondary: 1- hypocalcaemia stimulate prathyroid glands.

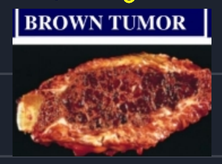
2- associated with chronic renal failure.

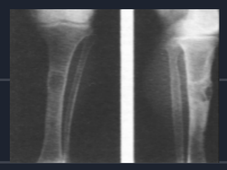
3- normal /Low ca^{+2}, high(↑) PO_4^{+3}.

clinical complications with HPT: 1- osteoporosis (secondary).

2- brown tumor: collection of hematomas, not a real tumor.

3- osteitis fibrosa cystica (OFC).





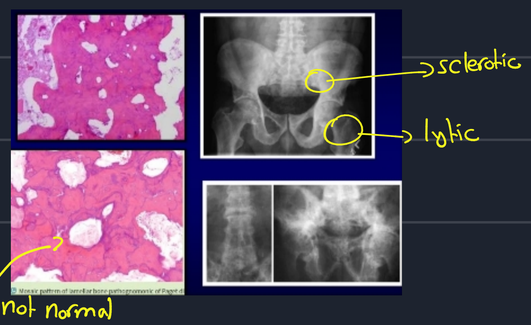
OFC

4- Paget disease (osteites deformans): 1- increased badly formed bone.

2- consist of three Phases: lytic, mixed, sclerotic.

3- geographically variate, genatic and enviromental variation.

4- 50% familial, 10% sporadic, have SQSTM1 gene mutations.



Paget disease clinically: 1- 85% Polystotic (more than one bone), 15% monostotic.

2- axial skeleton more affected.

3- mild and asymptomatic.

4 - Pain because of microfracture or nurve compression.

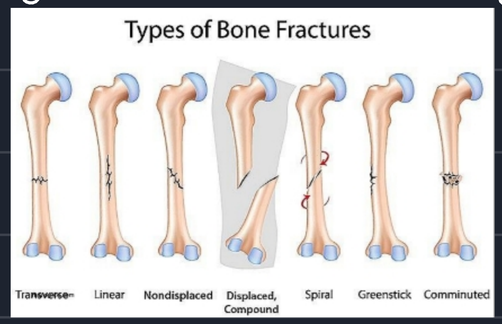
5- in skull cause two diseases: 1- leontiasis ossea (Lion face).

2- Platybasia (invagination of the skull base).

6 - cause: secondary osteoarthritis, fracture, osteosarcoma.

7- DX: high (↑) serum alk P, normal Ca^{+2}, Po_4^{+3}.

Fractures: Loss of bone integrity from mechanical injury and decrease in bone strength.



types of bone fractures: 1- simple : skin is intact.

2- compound: with overlying skin.

3- displaced: end are nd aligned.

4- stress : repetitive slowly progressive. (Paget disease).

5- greenstick: soft bone fracture (seen mostly in children).

6- Pathologic : bone abnormal (tumor).

Factors impacting Propeper bone healing: 1- displaced and comminuted bone.

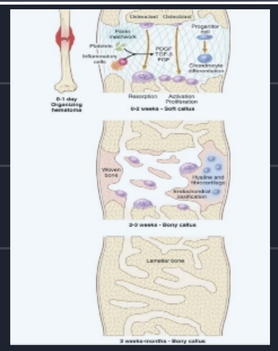
2- inadequate immobilization.

3- Pseudoarthrosis (join formation in site of fracture).

4- infections.

5- malnutrion.

6- steroids.



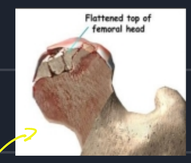
Osteonecrosis (avascular necrosis): infarction (ischemic necrosis) of bone marrow.

Causes: 1- vascular injury : trauma, vasculitis.

2- drugs : steroids.

3- systemic disease : sickle cell anemia.

4- radiations.



most common bone affected by osteonecrosis.

mechanism: 1- mechanical disruption.

2- thrombotic occlusion.

3- extravascular compression.