MEDICINE
KING SAUD UNIVERSITY

PATHOLOGY
TEAM 436

Congenital and developmental bone diseases

Objectives:

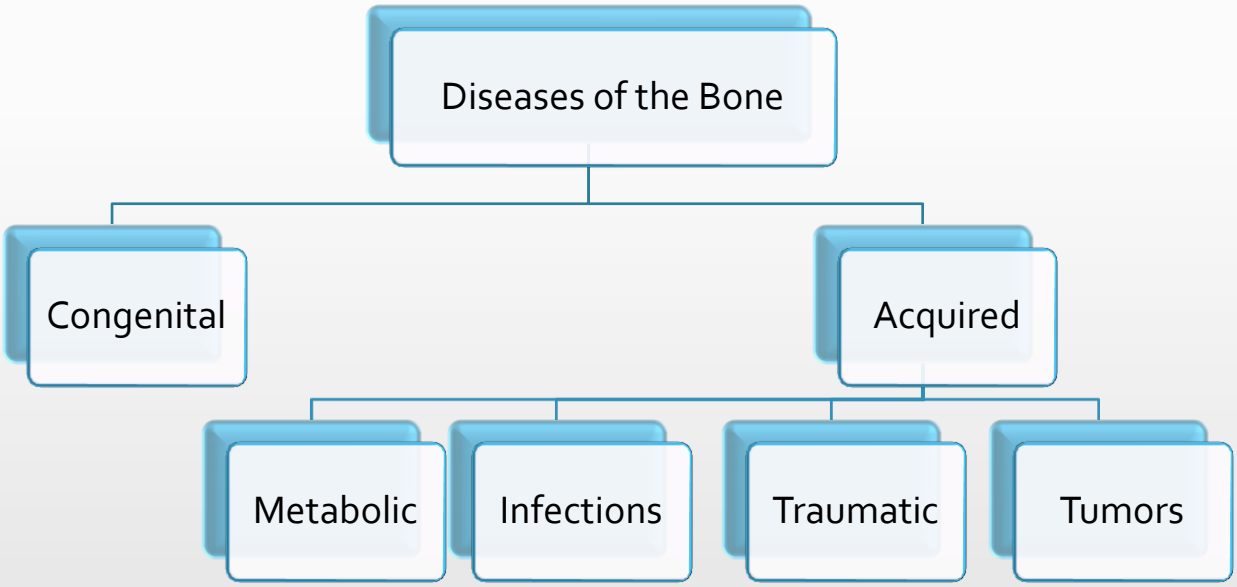
- Be aware of some important congenital and developmental bone diseases and their principal pathological features
- Be familiar with the terminology used in some important developmental and congenital disorders.
- Understand the etiology, pathogenesis and clinical features of osteoporosis.

- Red : Important
- Green: doctors' notes
- Grey: extra

Please check here before viewing the file to know if there any changes or additions.

Bone

- 206 bone.
- Organic matrix 35%.
- Inorganic -calcium hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$]- 65%.
- bone forming cells: osteoblasts and osteocytes.
- bone digesting cells: osteoclasts.
- constant breakdown and renewal called remodeling.



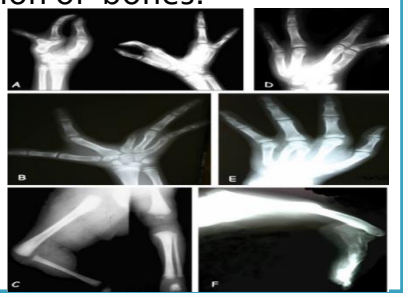
Congenital Diseases of the Bone "localized or entire skeleton"

Dysostoses:

disorder of the development of bone, in particular its ossification.

Example:

- aplasia. (no bone formation)
- extra bones.
- abnormal fusion of bones.



Dysplasia:

Example:

- Osteogenesis imperfecta.
- Achondroplasia.
- Osteopetrosis.

NOTE:
bone dysplasia is different than dysplasia that we studied in neoplasia (bone dysplasia means bad development of bone)

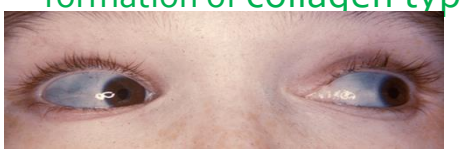
Osteogenesis Imperfecta:

"Brittle Bone Disease"

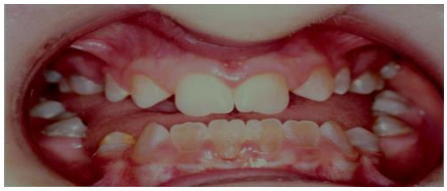
- Group of inherited diseases characterized by brittle bones.
- Defect in collagen type I synthesis .
- Lowers bone mass which makes the skeleton fragile and susceptible to fractures.
- There are 4 main types with different prominent features classified according to the severity of bone fragility , the presence or absence of blue scleras , hearing loss, abnormal dentition and the mode of inheritance (either autosomal dominant or autosomal recessive) , some are fetal.
- Can be related to conduction defects in the middle and inner ear bones. In ear cochlea.

Osteogenesis Imperfecta type 1

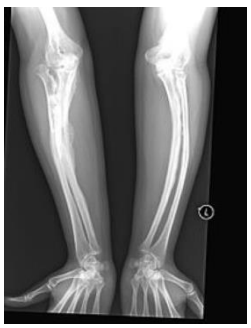
Note: all of them have abnormal formation of collagen type I



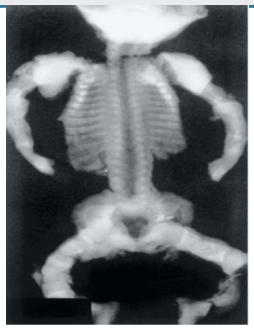
Blue Sclera



Deformed Teeth



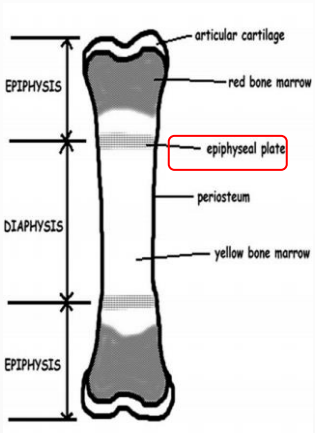
Brittle bones



Fetus with type 2 osteogenesis imperfecta known as osteogenesis imperfecta in utero , (Lethal).

Achondroplasia

- It’s the most common skeletal Dysplasia.
- Major cause of Dwarfism, And known as Dwarfism القزم
- Transmitted as Autosomal Dominant trait, resulting from the defect in the cartilage synthesis at (growth plates) epiphysis plates. due to Gain-of-function mutations in the FGF receptor 3 (FGFR3) (FGF stands for: Fibroblast Growth factor) (on short arm of chromosome 4)



- Approximately 90% of cases stem from new mutations (sporadic mutation), almost all of which occur in the paternal allele (associated with advanced paternal age). (new mutation يعني مو شرط الاب او الام عندهم هذا المرض)
- Characterized by failure of cartilage cell proliferation at the epiphysial plates of the long bones >>Resulting in Failure of longitudinal bone growth and subsequent short limbs.
- Membranous ossification (bone formation)is not affected, So the **Skull**, **Facial bones** and **axial skeleton** develop normally.

individuals have shortened proximal extremities, a trunk of relatively normal length, and an enlarged head with bulging forehead and conspicuous depression of the root of the nose.

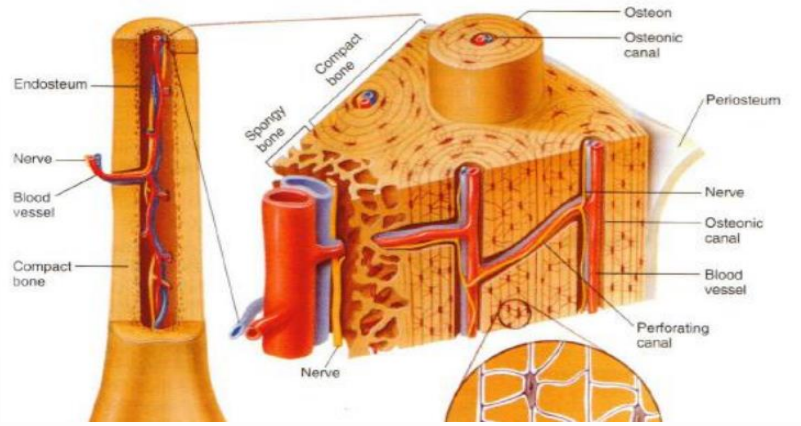
Have Normal: General health, intelligence, reproductive status and life expectancy is normal.

NOTE:(female is shorter than males)

Thanatophoric Dwarfism (lethal variant of dwarfism).

- Features: Thanatophoric means (death-loving) The God of death in ancient greek was called Thanataphor, and because affected patients died prematurely, this disease was called Thanatophoric Dwarfism. It is the same as achondroplasia but is more severe and causes respiratory failure in the infant and death.

- 1. Lethal.
- 2. Extreme shortening of the limbs.
- 3. Extreme frontal bossing of the skull.
- 4. Extreme small thorax, which will be the cause of fatal respiratory failure.



METABOLIC BONE DISESES

- Related to nutrition and mineral deficiency.
- comprises four fairly common conditions in which there is an imbalance between osteoblastic (bone forming) and osteoclastic (bone destroying) activity:

1. Osteoporosis.
2. Osteomalacia in adults, Rickets in children.
3. Paget's disease of Bone.
4. Hyperparathyroidism.

Osteoporosis: (usually it affects pelvic bone, long bones , vertebral column)

It's an acquired condition characterized by reduced bone mass , leading to bone fragility and susceptibility to fractures .

Characteristics of osteoporosis :

The cortical bone is thinned , and the bone trabeculae are thinned and reduced in number

↓

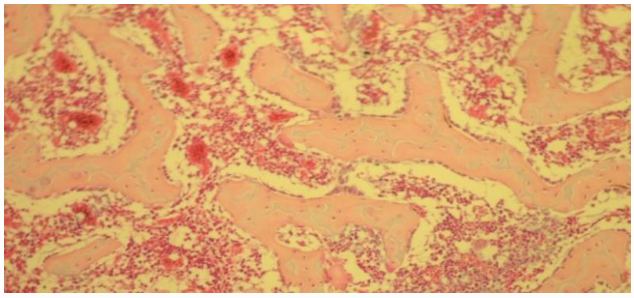
Increased porosity "tiny holes" of the skeleton leading to reduction in bone mass without changing in the form of architecture

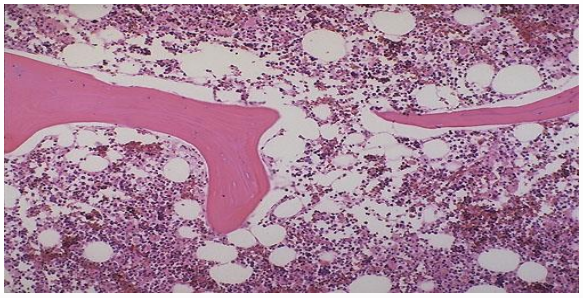
It may be localized Ex :Disuse osteoporosis of a limb "like in case of being paralyzed" . It may not be localized and involve the entire skeleton as a metabolic disease .

NOTE: it doesn't affect mineralization of the bone (ca , Vitamin D , alkaline phosphate are **normal**)

Normal

Osteoporotic bone





Normal

Here the intervertebral disc has protrusion because the bone is weak

Abnormal

Compression fracture

patient suffers from:
back pain , loss of height, kyphoscoliosis (تحدب)
Pathological fracture(neck of femur – colles fracture , vertebral column)

Osteoporosis

Primary

- Idiopathic (Unknown cause)
-Post menopausal probably of declining levels of estrogen .
-Senile "Because of old age "

Post menopausal osteoporosis :

In the decade after menopause , yearly reductions in bone mass may reach up to 2% of cortical bone and 9% of spongy bone . Women may lose 35% of their cortical bone and 50% of their spongy (cancellous) bone by 30 to 40 years after menopause .

Environmental factors may play a role in osteoporosis in the elderly : decreased physical activity and nutritional protein or vitamin deficiency (1-25 dihydroxycholecalciferol)-Vitamin D

Secondary

-Endocrine disorders
-gastrointestinal disorder
-Neoplasia
-drugs
-others (Smoking, immobilization, anemia , pulmonary disease)

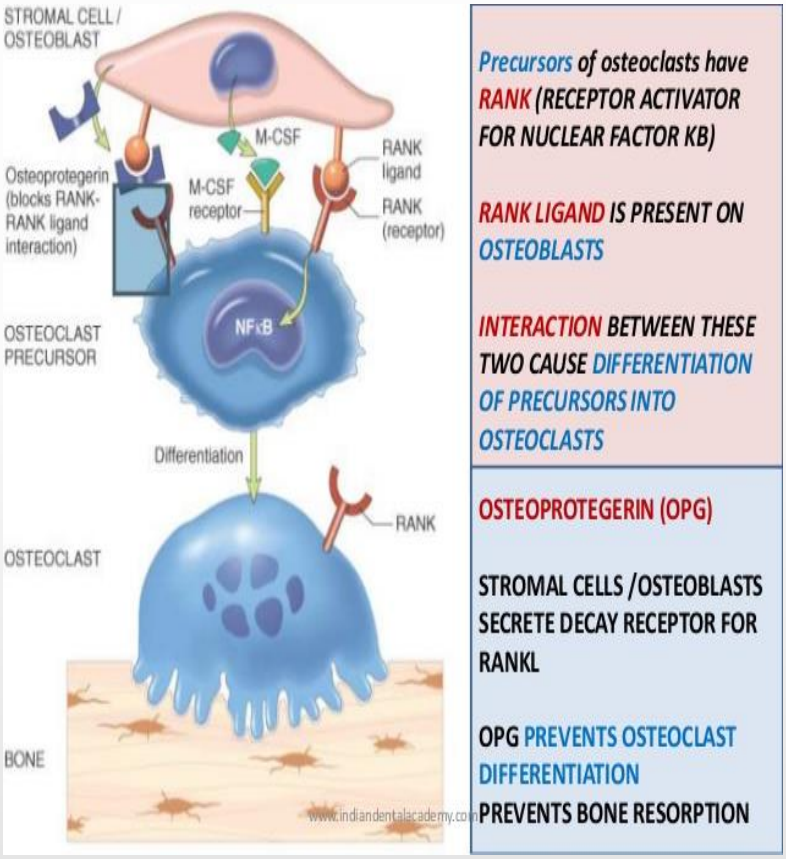
Endocrine → such as Addison disease , DM (diabetes mellitus) type 1 , hypo or hyperthyroidism and acromegaly .
Gastrointestinal disorder → Mal nutrition , malabsorption , hepatic insufficiency , vitamin c and D deficiencies .
Neoplasia → multiple myeloma , Carcinomatosis .

The most common forms of osteoporosis are the senile and postmenopausal types

Estrogen and Osteoporosis

- The post menopausal women are more affected because of low estrogen level which leads to activation of certain lymphokynes (cytokynes) TNF, IL1, IL6.

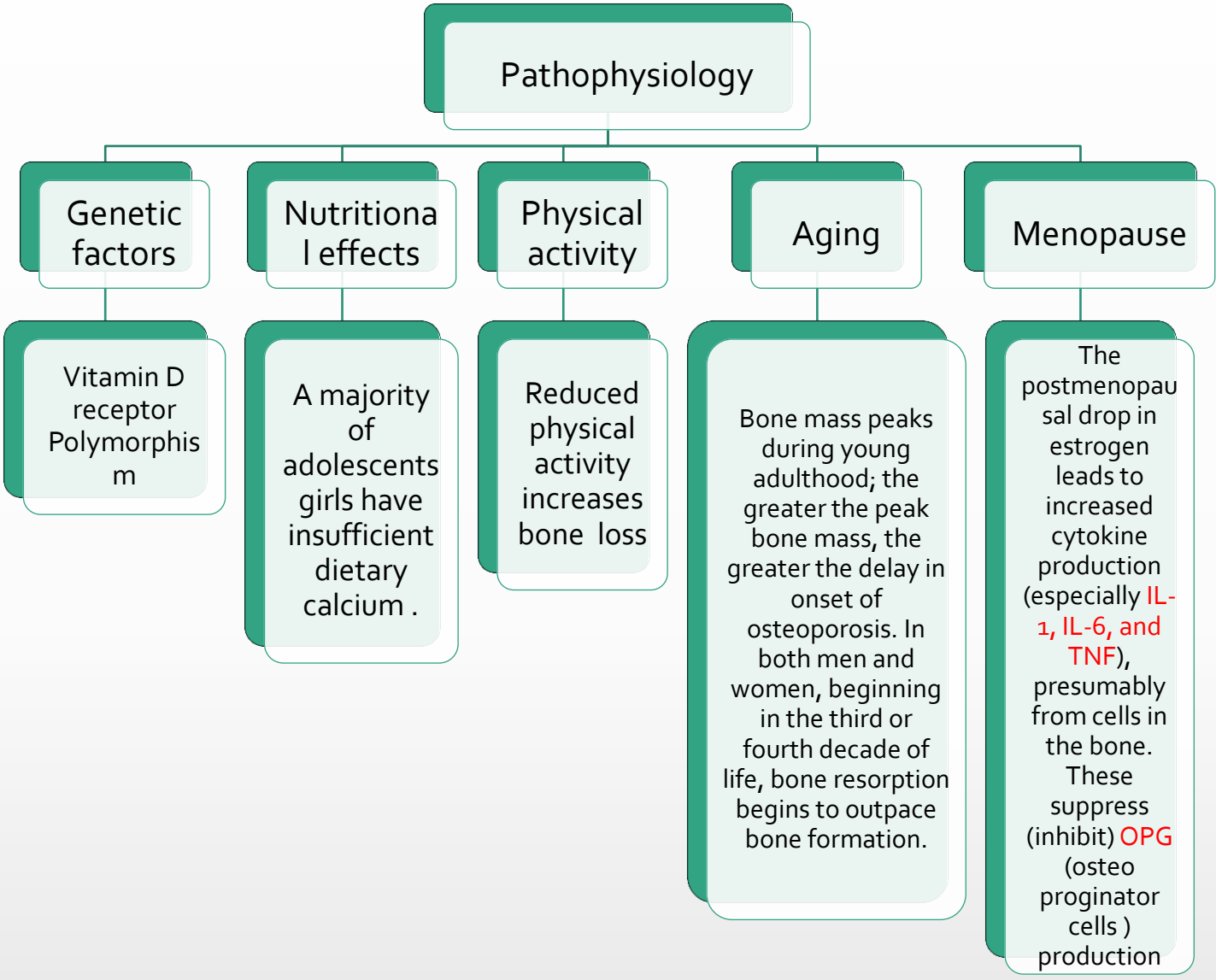
RANK and RANKL and OPG

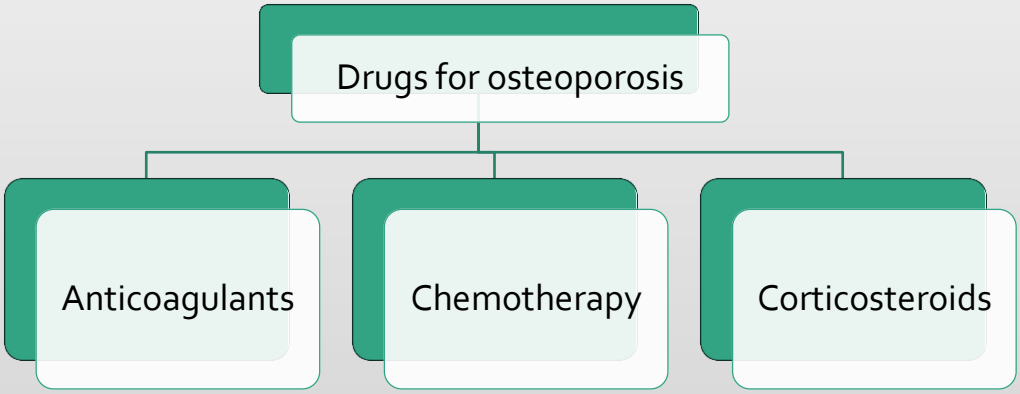


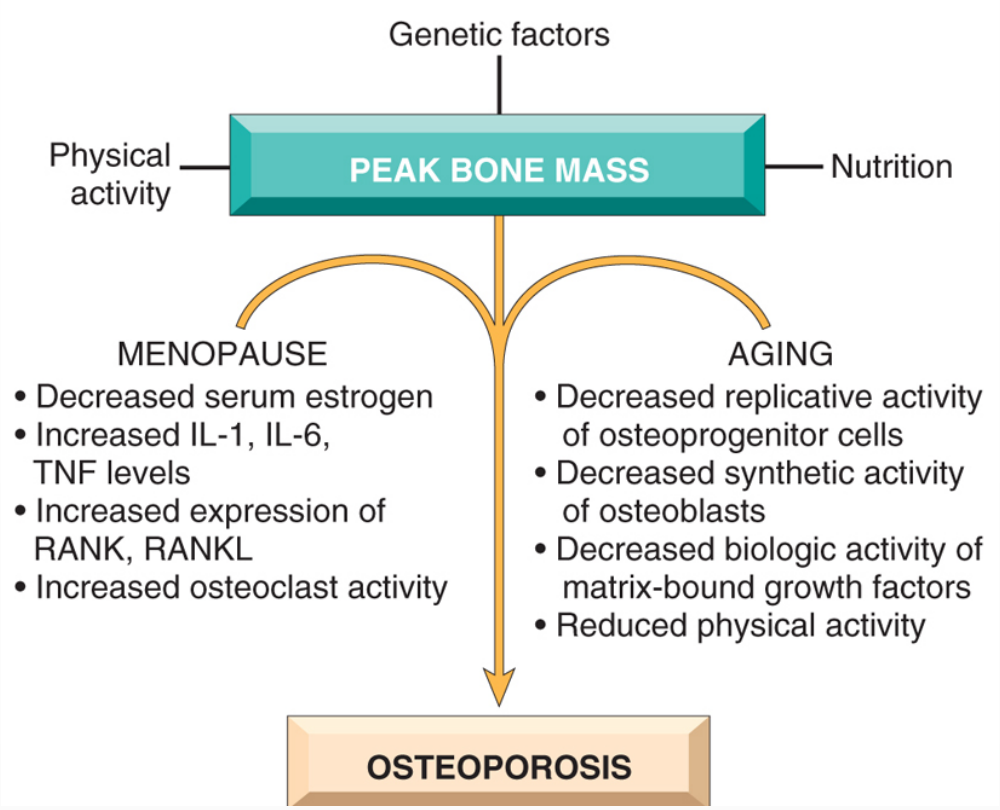
- Please watch this video for better understanding: https://www.youtube.com/watch?v=VwCkyfoIQwo

Pathophysiology of osteoporosis :

It happens when the balance between bone formation and resorption tilts in favor of resorption .







Clinical features of osteoporosis :

- it's Difficult to diagnose .
- Remains Asymptomatic until a fracture occurs .
- Most commonly fractures will happen in Vertebrae and femoral neck .
- Patients with osteoporosis have normal serum levels of calcium , phosphate and alkaline phosphate .

Diagnosis:
Bone density by radiographic measures

- Plain X ray: cannot detect osteoporosis until 30% to 40% of bone mass has already disappeared.

- Dual-emission X-ray absorptiometry (DXA scan): is used primarily to evaluate bone mineral density, to diagnose and follow up pt. with osteoporosis.

DXA scan

Prognosis:

- Osteoporosis is rarely lethal.

- Patients have an increased mortality rate (معدل الوفيات)due to the complications of fracture.

- for example: hip fractures can lead to decreased mobility and an additional risk of numerous complications: deep vein thrombosis, pulmonary embolism and pneumonia.

Prevention Strategies:

- The best long-term approach to osteoporosis is prevention.

- Children and young adults, particularly women, with a good diet (with enough calcium and vitamin D) and get plenty of exercise, will build up and maintain bone mass.

- This will provide a good reserve against bone loss later in life. Exercise places stress on bones that builds up bone mass.

Metabolic bone disease:

In **osteomalacia** (in adults) **and Rickets** (in child), osteoblastic production of bone collagen (organic) is normal but mineralization (inorganic)is inadequate. It is a manifestations of vitamin D deficiency.

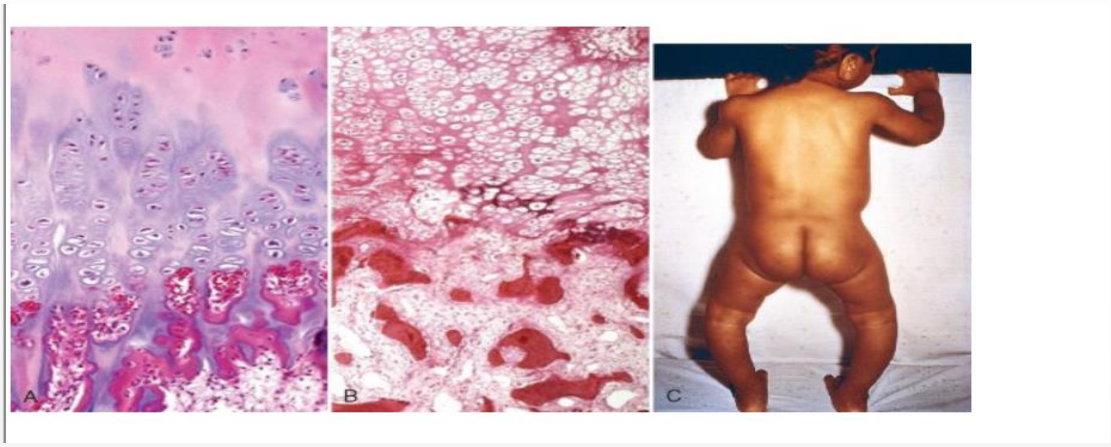
-osteomalacia is sometimes associated with decreased phosphorus and calcium levels.

-Rickets in children is characterized by bowing of bones, bossing of the front of the head.

NOTE:

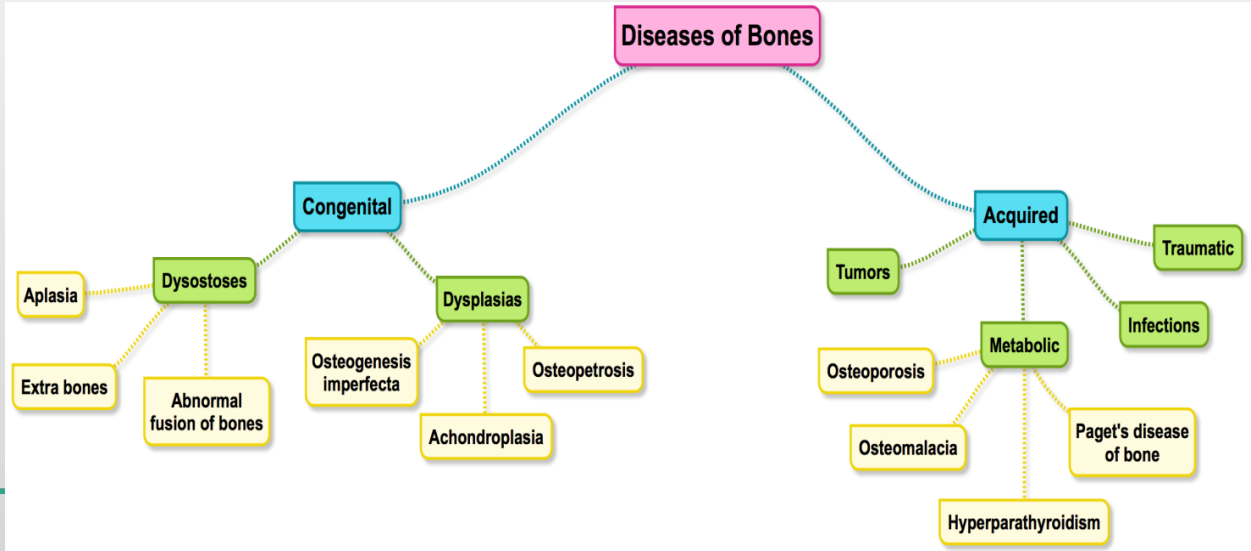
We need Vitamin D for absorption of ca and PO_4 (mineralize) , so deficiency of vitamin D leads to inadequate mineralization.

Increases alkaline phosphatase .



normal **abnormal**

Summary:



Good Luck

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