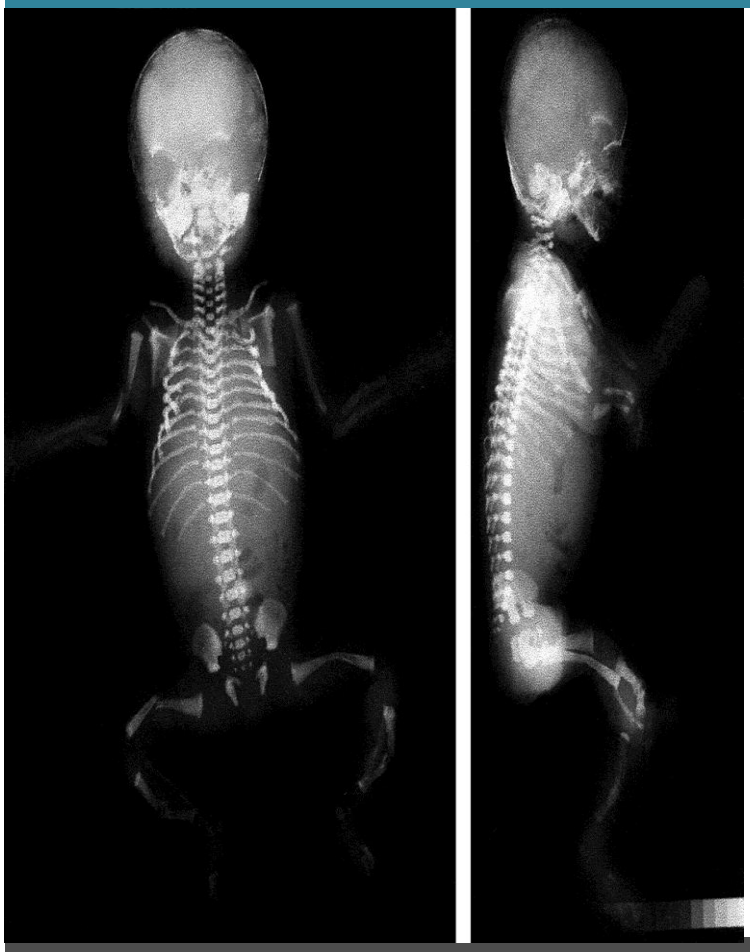
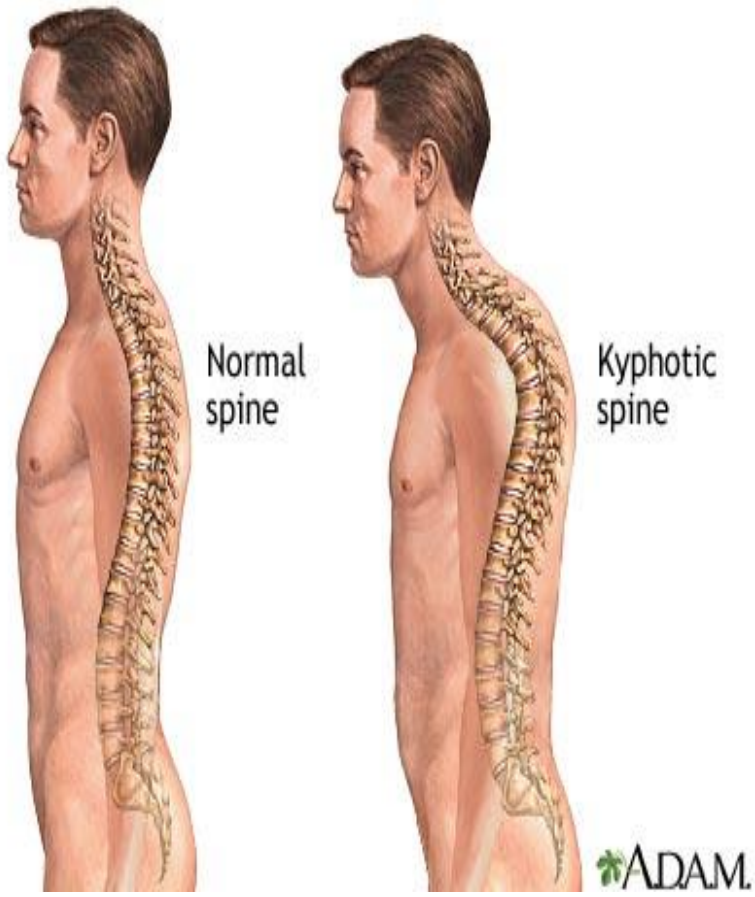




CONGENITAL, DEVELOPMENTAL AND METABOLIC BONE DISEASES

Lecture Two

432 Pathology Team

1-CONGENITAL DISEASES:

A.Achondroplasia (dwarfism):

(Autosomal – dominant)

Mutation in fibroblast growth rcecptor gene type III (FGPR-III)

This gene promotes endochondral ossification.

The patient suffer from pre-mature closure of the epiphyseal line يلتحم مبكرا قبل اكتمال النمو . Therfore, the stature القامة of the child does not continue to grow until he/she reaches 15,16 or 17 years old , instead it stops at 2 or 3 years old .

The patient continues his growth except for the limbs and therefore he/she remains short (dwarf).

The patient usually has normal IQ.معدل ذكاء المريض يكون عادة طبيعيا

Characteristics:

1- Big skull – compared to the rest of the body .
2- Normal trunk
3- Short stature قامته قصيرة caused by short limbs.
4- Compression in mid facial area

B.OSTEOGENIC IMPERFECTA (Brittle bone disease) :

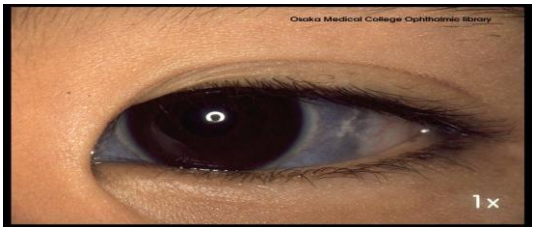
(Autosomal – dominant)

Abnormality and deficiency in **collagen 1** affecting all the sites that collagen 1 takes part in .

Collagen 1 is a major part of the matrix of any connective tissue (mesenchyma) , thus, it's deficiency affects bones, dentins, tendons, ears, sclera of the eye...etc.

Characteristics:

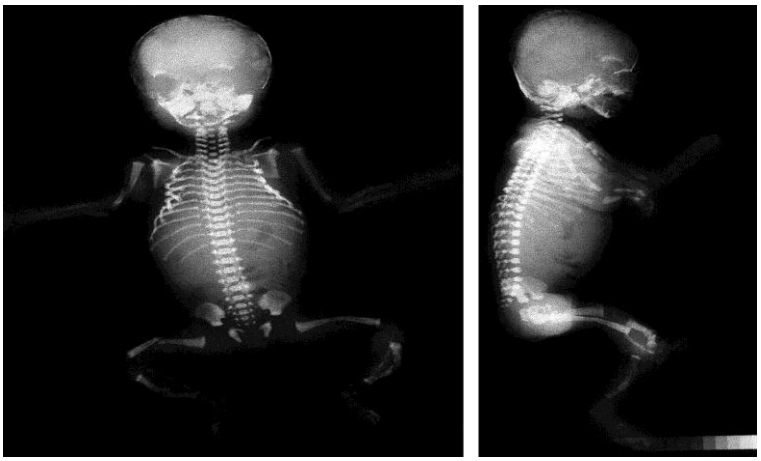
1- Sclera of the eye is very thin and weak. It appears bluish in the examination. This bluish color is because the vessels of the choroid plexus (part of the eye under the sclera) can be seen due to the thinness of the sclera.



2- Problems in listening
3- Small and irregular teeth.

There are several types of brittle disease, some are very severe causing death in fetal life, and some are not (the patient can live a normal life with fractures that decrease with growth and strengthening of the bone.)

This is a child affected with osteogenic imperfect. The X-Ray shows multiple fractures and deformed femur.



2-ACQUIRED DISEASES:

A. OSTEOPROSIS:

Osteoprosis is the loss of bone mass or volume, increasing in the without affecting the amount of minerals in the trabeculae.

1- **Characteristics**:
- Bones are generally weak and exposed to pathological fractures following minor trauma.
- Trabeculae are narrow, and marrow spaces are wider than normal.
- The Haversian canal in compact bone is wide.
- The amount of minerals within the trabeculae is **NORMAL** → very important character of osteoprosos.
- General reduction of the bone.
- It affects mainly long bone of the skeleton and vertebrae.

2- **Clinical presentation**:

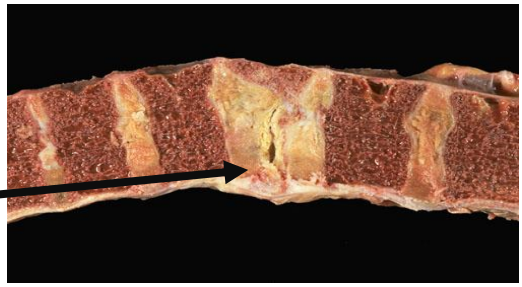
The patient can be:

a. Asymptomatic
b. present with pain in the lower back and limbs
c. present with a pathological fracture following minor trauma.

N.B : The mass of the bone is measured by bone densitometry test.

3- **Main sites of fractures**:

a. Vertebrae:



Beacause of the weakening of the vertebrae, the patient may suffer COMPRESSION fractures.

In addition, osteoprosis of the vertebrae may cause deformities (Kyphosis حدبة) in the back thus, skin creases تسفط is seen.

b. Head of the femur
c. Collis fracture in the wrist.

So, if an old women or sometimes an old man is present with a fracture in one of these sites, the physician should suspect OSTEOPROSIS.

4- **Causes of osteoporosis**:

a. Genetic deposition
b. Women are generally 3-4 times more exposed to osteoporosis than men after menopause.
c. Lack of Exercise in young age : The more you exercise you do while you are young the lesser you are exposed to osteoporosis in old age .
d. Nutrition : bad nutrition can play a role in developing osteoporosis.

5- **Types of osteoporosis**:

a. Primary Osteoporosis
   1. (Postmenopausal women):
      Reduced estrogen → activation of certain cytokines especially IL-1, IL-6 and Tumor necrosis factor(TNF) → stimulation of rank and rank L molecules → Stimulation of Osteoclasts activity.

2. Old men:
   It is thought that osteoporosis in old men is caused by the decreasing of fibro- osteogenic- progenator cells that develop into Osteoblasts.

b. Secondary Osteoporosis :Sometimes the patient is present with osteoporosis without the primary factors, his osteoporosis maybe caused by malnutrition, prolonged bed rest, corticosteroids… etc. (see the table below)

Table 21-1. Categories of Generalized Osteoporosis

Primary Osteoporosis
Postmenopausal
Senile
Secondary Osteoporosis
ENDOCRINE DISORDERS
Hyperparathyroidism
Hypo or hyperthyroidism
Hypogonadism
Pituitary tumors
Diabetes, type 1
Addison disease
NEOPLASIA
Multiple myeloma
Carcinomatosis
GASTROINTESTINAL DISORDERS
Malnutrition
Malabsorption
Hepatic insufficiency
Vitamin C, D deficiencies
Idiopathic
DISEASE DRUGS
Anticoagulants
Chemotherapy
Corticosteroids
Anticonvulsants
Alcohol
MISCELLANEOUS
Osteogenesis imperfecta
Immobilization
Pulmonary disease
Homocystinuria
Anemia
Prolonged bed rest

B. Osteomalacia & Rickets:

Osteomalacia is characterized by defective mineralization of the osteoid matrix and is associated with lack of vitamin D. (The bone mass does NOT change)

When the condition occurs in the growing skeleton (children) it is called rickets.

- The main cause of osteomalacia and rickets is nutritional defficencies ex:(Malabsorbtion caused by diarrhea leading to less absorption of calcium and vitamin D)

The patient is usually exposed to fractures due to minr trauma.

VITAMIN D:

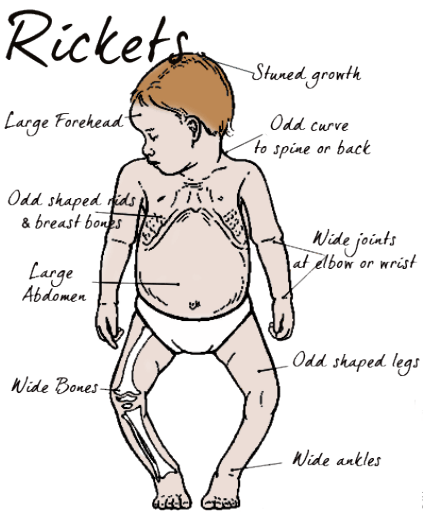
Vitamin D is important in the maintenance of adequate serum calcium and phosphorous levels .

Deficiency of vitamin D impairs يؤثر على normal mineralization of osteoid laid down in the remodeling of bone. The result is osteomalacia.

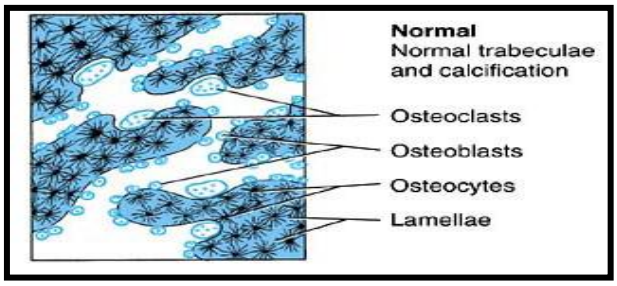
In children, lack of vitamin D leads to inadequate mineralization of the epiphyseal cartilage as well as the osteoid, resulting in **rickets**.

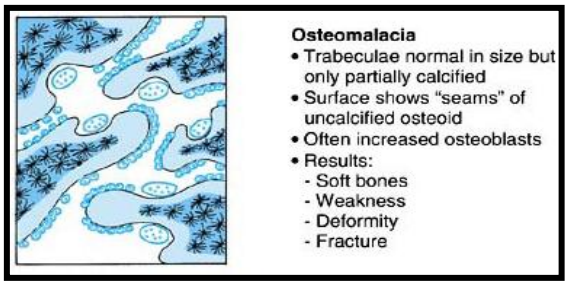
Signs of rickets:

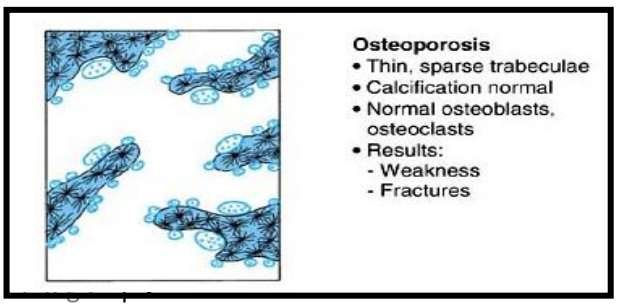
- The head is big related to the trunk.
- The forehead is protruding بارز out.

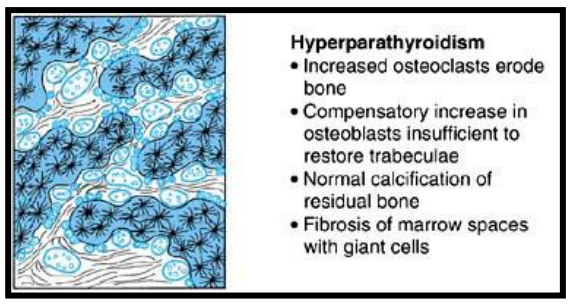


Osteoporosis	Osteomalacia
Mineralization is normal	↓Mineralization
↓Bone mass	Normal bone mass









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*Good Luck ^_^*