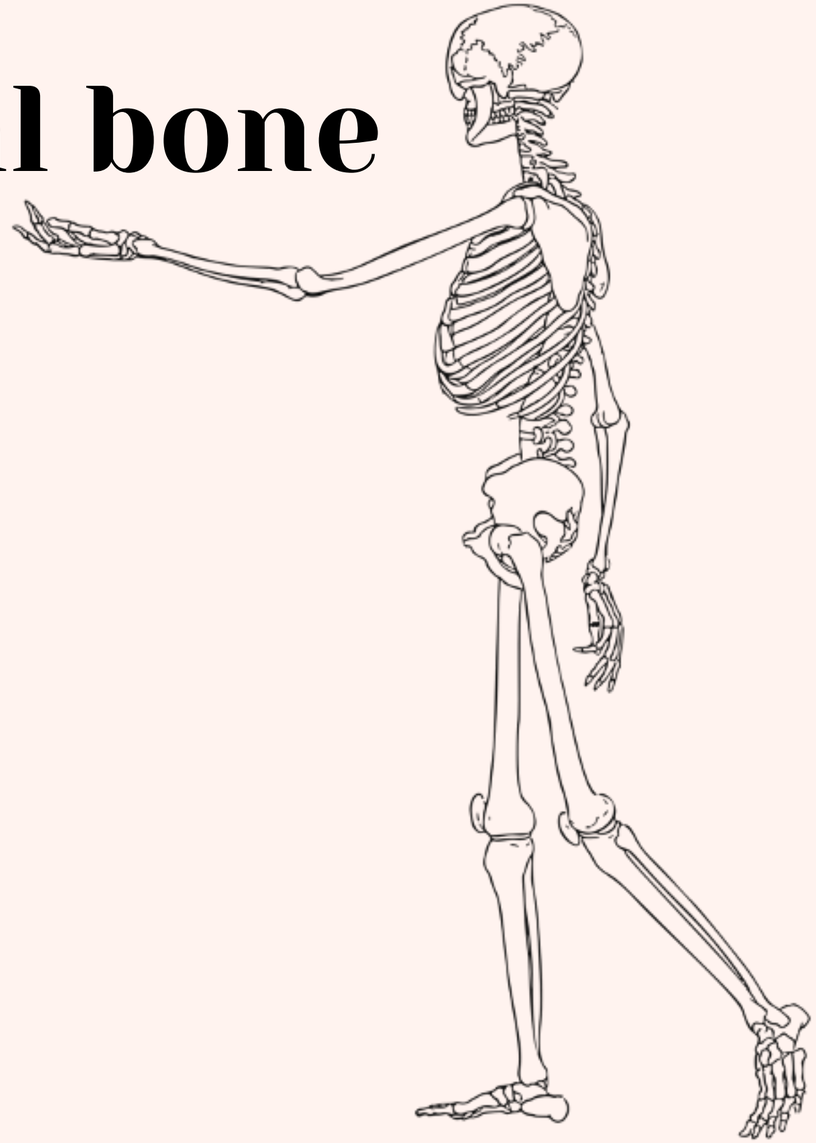
# Congenital and developmental bone diseases



PATHOLOGY TEAM
MED 444

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**Editing File**

Color index:

Main text ( black)

Important (Red)

Dr.Notes (green)

Male slides only (blue)

Female slides only (pink)

Extra info(gray)

# Objectives

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

# Resources to understand better

Click For BOOK

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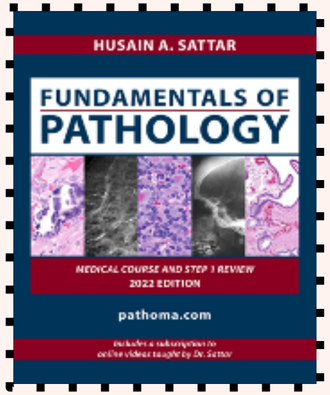
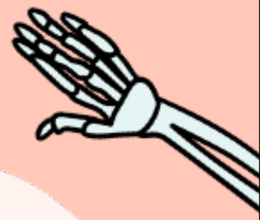


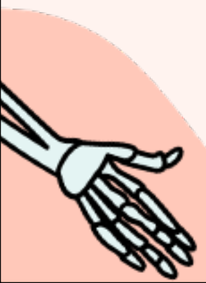

For videos → **CLICK HERE** 🦦

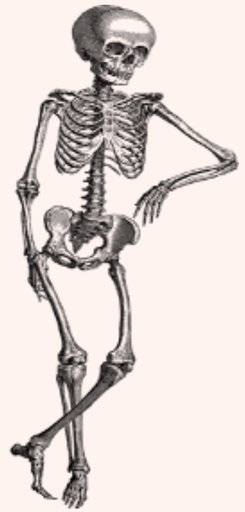
Built different 🧠

# Diseases of bones



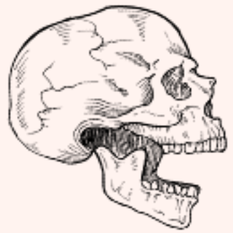
- Diseases of Bones
  - Congenital
    - Dystoses
    - Dysplasia
  - Acquired
    - Tumors
    - Traumatic
    - Infections
    - Metabolic





# Congenital & Development bone diseases/Developmental Disorders of Bones and Cartilage

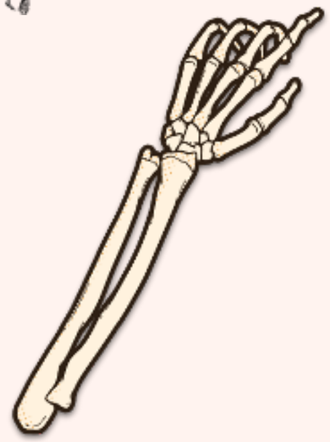
1. Frequently from the result of inherited mutations and first become manifest during the earliest stages of the bone formation (childhood).
2. The spectrum of disorders of bone development is broad and the classification system is not standardized .
3. More than 350 skeletal dysostoses (the problem in a specific bone like the finger of the hand) and dysplasias (the problem in the whole skeleton) , most extremely rare, have been recognized.
4. The classification has evolved from purely clinical and radiographic descriptions to include recently identified genetic defects.



| Congenital diseases of bones | Dysotosis | Dysplasia |
|---|---|---|
| **Definition** | -Defect in a localized(single bone) group of bones arise from defects in the migration and condensation of mesenchyme<br>-Localized problems (in embryo life) in the migration and condensation of mesenchyme | Global disorganization of bone and/or cartilage |
| **Causes** | Result from defects in transcription factors(factors transcript RNA from DNA) Especially those encoded by the homeobox genes(responsible for formation of organs in embryo), cytokines and cytokine receptors. | -Mutations that interfere with bone or cartilage formation, growth,and/or maintenance of normal matrix components.<br>- abnormal bone growth<br>-Result from defects in Hormones and Signal Transduction Proteins<br>-Affect entire skeleton |
| **Types** | 1. **Aplasia**: complete absence of a bone or a digits(example absence of fibula)<br>2. **Supernumerary digit/Extra bones:** extra bones or digits<br>3. **Syndactyly/Craniosynostosis:** abnormal fusions of bones | 1. **Osteogenesis Imperfecta (OI , Brittle bone disease)**<br>2. **Achondroplasia**<br>3. **Osteopetrosis "Marble bone disease"**<br>4. **Thanatophoric dysplasia (more severe form of Achondroplasia)** |

These Types that we will be talking about mainly

# 1. Osteogenesis Imperfecta



called (brittle bone disease)The most common inherited disorder of connective tissue.

1

Result from autosomal dominant mutation in gene that encode α1 and α2 chain of type I collagen.
-More than 800 mutations have been identified.

2

Defect in the synthesis of type I collagen affects (impacts other tissues rich in type I collagen) : Bone, Joints, Eyes, Ears, Skin and Teeth. It leads to too little bone resulting in extreme skeletal fragility with susceptibility to fractures

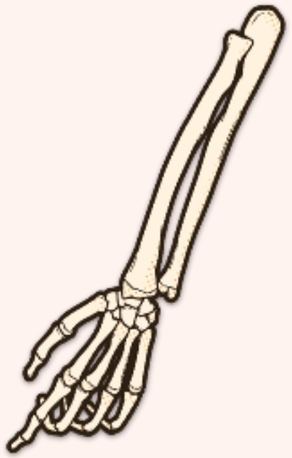
3

Many of these mutations lead to replacement of a glycine residue with another amino acid resulting in defective assembly of higher order collagen polypeptides

4

-These defects (replacement of glycine with another amino acid) cause misfolding of the mutated collagen polypeptides, and they interfere with the proper assembly of collagen chains.
-Divided into multiple types with different clinical manifestations classified according to the severity of bone fragility,based on the location of the mutation in the protein.

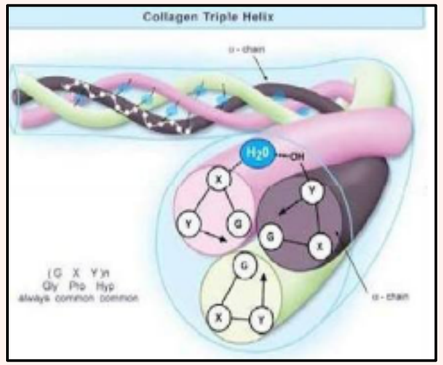
5



# cont. Osteogenesis Imperfecta

**The severity of the disease is based on :**

- location of the mutation within the protein
- Mutations resulting in decreased synthesis of **qualitatively** normal collagen are associated with mild skeletal abnormalities
- More severe or lethal phenotypes have abnormal polypeptide chains that cannot be arranged in a triple helix




**Division:**
Divided clinically into four main types
( only two are mentioned here)

**Type 1**

- Have a normal life span despite a susceptibility to fractures, particularly during childhood.
-Mildest and most common form
-Most have a normal life span but experience childhood fractures that decrease in frequency following puberty

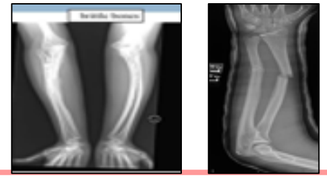
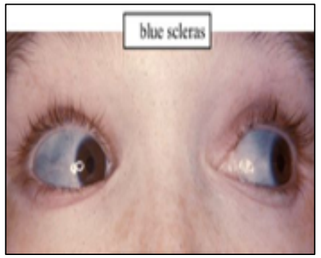
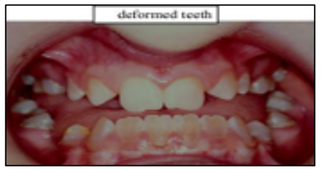
فقط نقص في عدد الكولاجين -> التركيب سليم

**Type 2**

-Variant is at one end of the spectrum and is uniformly fatal in utero or during the perinatal period
-It is characterized by extraordinary bone fragility with multiple intrauterine fractures.

الخلل في تركيب الكولاجين

# Clinical Manifestation

| Site/organ<br>Type 1 | Signs | Notes | Picture |
|---|---|---|---|
| **Bone**<br>brittle bones | **Fragile bones particularly during childhood (repeated easy fractures).** | **DDX child abuse**<br>DDX= Differential diagnosis<br>**( some doctor suspect a child abuse )** |  |
| **Eye** | **Blue sclerae (translucent sclera)** | **Caused by decreased collagen content making the sclerae translucent and allowing partial visualization of the underlying choroid (why sclerae because is contain lots of collagen type 1 , if its little you will be able to see the blue color of veins below)** |  |
| **Teeth**<br>Deformed | **-Small<br>-Misshapen(مشوهة)<br>-blue-yellow teeth<br>[Deficiency in dentin]** | **dentin : the yellowish tissue that makes up the bulk of all teeth.** |  |
| **Ear** | **Hearing loss: Due to it affecting bones in middle ear. related to a sensorineural deficit and impeded conduction due to abnormalities in the bones of the middle ear** | **because ossicles(3 small bones in ear) is not formed , so it will cause conductive hearing loss and neurons defect (neurons of sensory )** | ——— |


Defective bone formation and skeletal fragility

# 2. Achondroplasia

helpful video

## Overview :

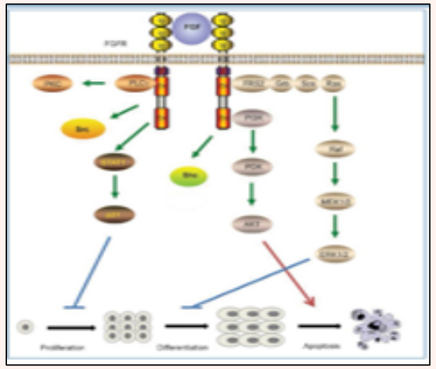
- The most common skeletal dysplasia and a major cause of dwarfism.
- known as Dwarfism .
- transmitted as an autosomal dominant trait resulting from: Defect in the cartilage synthesis (retarded cartilage growth) at growth plates due to gain-of-function mutations in the fibroblast growth factor receptor 3 (FGFR3)
- Approximately 90% of cases stem from new mutations (sporadic mutation), almost all of which occur in the paternal allele (associated with advanced paternal age).

There are two types of dwarfism(According to causes):
1-Achondroplasia
2-Hypothyroidism (thyroid hormone in baby is very important in development of bone and mental thinking)


## Causes

1. Gain-of -function mutation of FGFR3(becomes active all the time) FGF-mediated activation of FGFR3 inhibits endochondral growth Therefore gain-of-function mutation lead to inhibition of chondrocytes proliferation.
(mechanism in point number 3)

2. A receptor with tyrosine kinase activity that transmits intracellular signals.



3. Signals transmitted by FGFR3 inhibit the proliferation and function of growth plate Chondrocytes; consequently, the growth of normal epiphyseal plates is suppressed (like causing apoptosis in cartilage)

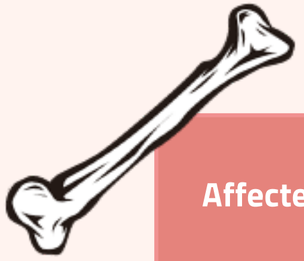
# Clinical Manifestation

-It is characterized by failure of cartilage cell proliferation at the epiphyseal plates of the long bones, resulting in failure of longitudinal bone growth and subsequent short limbs

-Membranous ossification is not affected (no stem of cartilage), so that the skull, facial bones, and axial skeleton develop normally.(Only affects the long bone , hand, lower limbs)

There are two way for ossification :
1- from fibrous tissue to bone directly (this is membranous ossification)
2- fibrous tissue—->cartilage—->bone(this is Endochondral ossification)

**Thanatophoric dysplasia:** is the most common **lethal form** of dwarfism,results from diminished proliferation of chondrocytes and disorganization in the zone of proliferation, affecting about 1 in every 20,000 live births.
-Affected individuals have shortening of the limbs, frontal bossing, relative macrocephaly, a small chest cavity.
-Affected individuals have underdeveloped thoracic cavity leads to respiratory insufficiency, and these individuals frequently die at birth or soon after.



| Affected parts of the patient | Normal part of the patient |
|---|---|
| Shortened proximal extremities | A trunk of relatively normal length |
| Enlarged head with bulging forehead | general health, Longevity, intelligence, or reproductive status are not affected |
| Conspicuous depression of the root of the nose | Normal life expectancy (Able to reproduce). |

**Deep Focus Question**

What condition is caused by a mutation of the FGFR3 protein, which results in early failure of endochondral ossification due to premature closure of the epiphyseal plates?

A. Achondroplasia.
B. Osteomyelitis
C. Rackets
D. Hyperparathyroidism

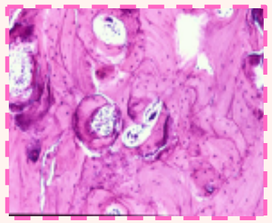
Answer: A

special thanks to 443!

# 3.Osteopetrosis

(Marble bone disease) In female slides only

(means when bone become more harden and denser)



## Characteristics:

1. Rare autosomal recessive diseases.
2. Due to abnormal function of osteoclasts(deficiency of carbonic anhydrase(An enzyme that produce acidic environment to let Osteoclasts to work correctly) leads to an abnormal environment around the osteoclast,resulting in defective bone resorption).
3. Failure of normal bone resorption by osteoclasts results in uniformly thickened, dense bones.
4. Increased tendency to fractures (لان ما عندها مرونة), osteomyelitis , anemia and extramedullary hematopoiesis (because of narrow space of bone marrow).

# METABOLIC BONE DISEASES

Comprises four fairly Common conditions in which there is an imbalance between osteoblastic (bone forming) and osteoclastic (bone destroying) activity.

*Acquired*

1. Osteoporosis/Osteopenia
2. Osteomalacia and Rickets
3. Hyperparathyroidism
4. Paget's disease of bone

# Osteoporosis

( there is different between
Osteopetrosis and osteoporosis )

## DEFINITION

**Osteoporosis is an acquired condition characterized with sever reduced bone mass, leading to bone fragility and susceptibility to fractures.**
**Occur when the balance between bone formation and resorption tilts in favor of resorption.**

Osteopenia : refers to decreased bone mass.

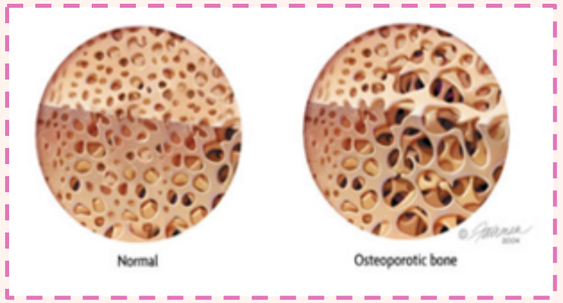
Osteoporosis : is defined as osteopenia that is severe enough to significantly increase the risk of fracture.

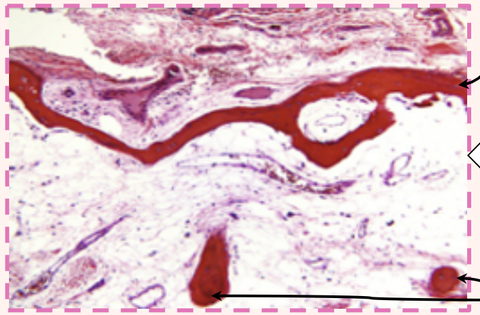
- There is a slowly progressive increase in bone erosion.
- The cortical bone are thinned, with dilated haversian canals.
- Trabeculae are thinned (reduced in thickness) and reduced in number and lose their interconnections.
- The Mineral content is normal.
- Increased porosity of the skeleton leading to reduction in the bone mass but without distortion of architecture.
- Susceptibility to fractures increases

**Can be**

- **Localized**: Disuse Osteoporosis of limps as a metabolic bone disease
- **Involve**: Entire skeleton as a metabolic disease

Vertebral bone with osteoporosis and a compression fracture (fracture in one of the vertebrae)

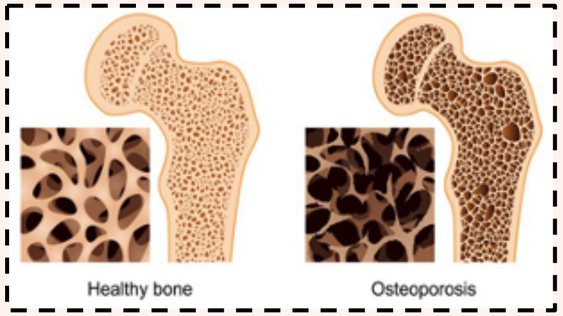


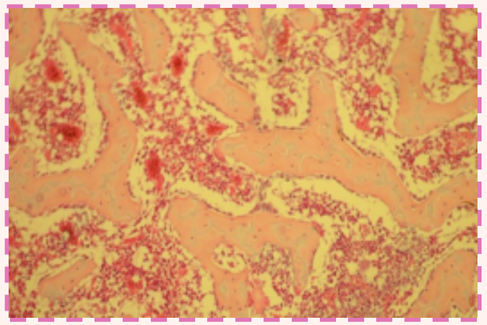



cortical bone

Osteoporosis represent histologically normal bone that is decreased in quantity (less bone mass)

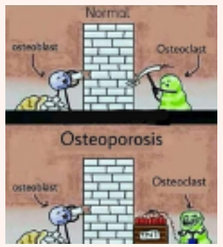
trabecular bone

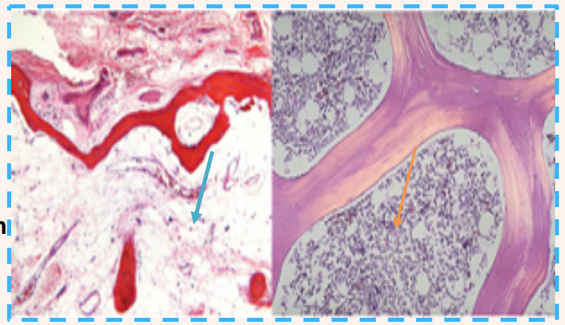


normal bone mass

remember me in exam



normal

osteoprotic bone

# Classification of Osteoporosis:

<table>
<tr><th>Primary<br>Idiopathic (unknown cause)</th><th>secondary<br>Has specific cause or etiology</th></tr>
<tr><td>The most common forms of osteoporosis are the senile and postmenopausal types.<br>Occur when there is imbalance between bone formation and resorption .</td><td rowspan="2">Endocrine disorders<br>• Addison disease<br>• DM type 1 (diabetes mellitus)<br>• hypo or hyperthyroidism<br>• acromrgaly (ضخامة في الاطراف )<br>• Miscellaneous</td></tr>
<tr><td>Post menopausal (most common) ( بعد سن انقطاع الطمث)<br>• decreased estrogen levels after menopause increase both bone resorption and formation but the latter does not keep up with the former, leading to high-turnover osteoporosis.<br>• In the decade after menopause, yearly reductions in bone mass may reach up to 2% of cortical bone and 9% of cancellous bone.<br>• Women may lose as much as 35% of their cortical bone and 50% of their cancellous bone by 30 to 40 years after menopause.<br>• Estrogen deficiency plays the major role (40% of postmenopausal women are affected by osteoporosis).</td></tr>
<tr><td></td><td>Gastrointestinal disorders<br>• Malnutrition<br>• Malabsorption<br>• Hepatic insufficiency<br>• Vitamin C & D deficiencies</td></tr>
</table>

| Primary<br>Idiopathic (unknown cause) | secondary<br>Has specific cause or etiology |
| --- | --- |
| **Senile** (Age-related change)(most common)<br>• categorized as a low-turnover variant<br>• Osteoblasts from older individuals have reduce proliferation and biosynthetic potential and reduced response to growth factors compared to osteoblasts in younger individuals.<br>• Cellular response to growth factors bound to the extracellular matrix becomes attenuated.<br>• The net result is a diminished capacity to make bone.<br>• Reduced physical activity increases the rate of bone loss is associated with normal aging contributes to senile osteoporosis | **Neoplasia**<br>• Multiple myeloma<br>• carcinomatosis<br><br>**Drugs**<br>• Anticoagulants<br>• Chemotherapy<br>• Corticosteroids<br>• Anticonvulsants<br>• Alcohol |
| **Environmental factors**<br>**may play role in elderly :**<br>• decrease physical activity<br>• decrease nutritional protein<br>• vitamin deficiency (Vitamin D) (1,25-dihydroxycholecalciferol)<br>**Others:**<br>• Resistance exercises such as weight training are effective stimuli for increasing bone mass.<br>• Single gene defects (eg LRP5 mutations) account for only a small fraction of osteoporosis cases.<br>• Adolescents (particularly girls) tend to have low dietary calcium intake, a factor that restricts peak bone mass.<br>• Calcium deficiency, increased PTH concentrations, and reduced levels of vitamin D. | **Others:**<br>• Smoking<br>• Immobilization<br>• Anemia<br>• Pulmonary disease |

# Pathophysiology

*FEMALE SLIDES ONLY

DR. maha said it is extra

**Imbalance between bone formation and resorption ( in favour of resorption).**

| | |
|---|---|
| **Genetic Factors** | Vitamin D receptor polymorphisms. |
| **Nutritional effects** | A majority of adolescent girls have insufficient dietary calcium. |
| **Physical activity** | reduced physical activity increases bone loss. |
| **Aging** | Bone mass peaks during young adulthood; the greater the peak bone mass, the greater the delay in onset of osteoporosis. In both men and women, beginning in the third or fourth decade of life. The bone loss, averaging 0.5% per year. |
| **Menopause** | The postmenopausal drop in estrogen leads to increased cytokine production (especially IL-1, IL-6, and TNF), presumably from cells in the bone.<br>These stimulate RANK-RANK ligand activity and suppress OPG production. |

# Pathophysiology

1. Peak bone mass is achieved during young adulthood

2. Its magnitude is determined largely (influenced) by hereditary factors, physical activity, muscle strength, diet, and hormonal state

3. Once maximal skeletal mass is attained, a small deficit in bone formation occurs with every resorption and formation cycle of each bone metabolic unit.

   After maximal skeletal mass is attained, bone turnover continues with a net deficit in bone formation resulting in an average loss of 0.7% of bone mass per year.

4. Age-related bone loss (average 0.7% /year) is a normal

5. Both sexes are affected equally and whites more so than blacks

6. Gender and racial differences in peak bone mass may partially explain why certain populations are prone to develop this disorder.

# Estrogen

**Decrease in Estrogen will cause:**

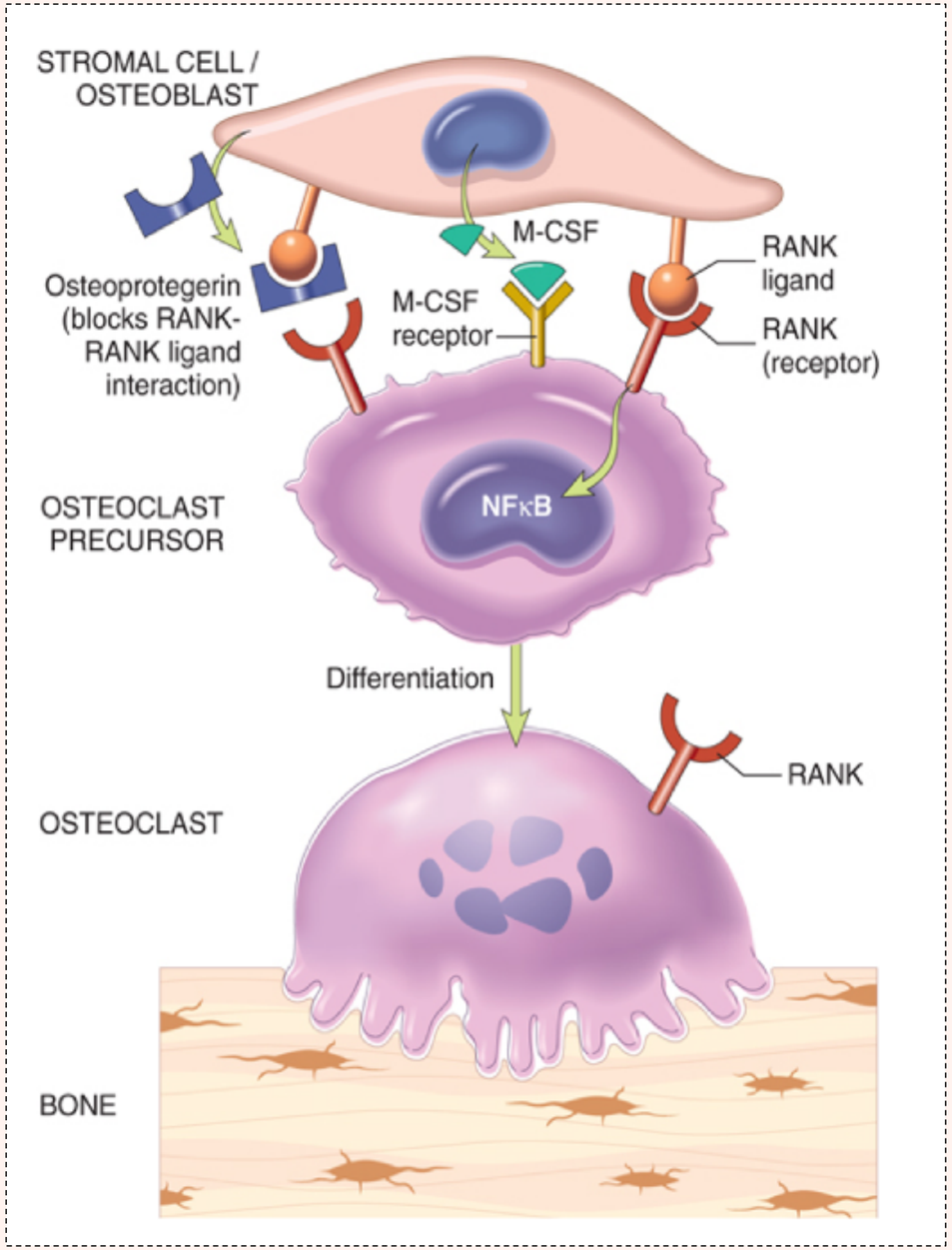
**increase** secretion of inflammatory cytokines by monocytes (IL-1, IL-6,TNF-α)

will stimulate

+Osteoclast recruitment and activity by increase RANKL and decrease expression of osteoprotegerin **(OPG )**, decreasing osteoclast proliferation, and prevent osteoclast apoptosis.

**DR. notes**:
OPG(osteoprotegerin) blocks RANKL(RANK ligand)Activity.

When estrogen is decreased OPG will also decrease (See the picture).



# Clinical Features of Osteoporosis

## Clinical course

1. **Difficult to diagnose**

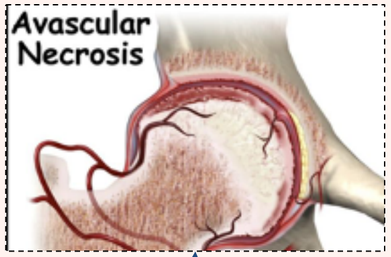
2. Remain asymptomatic witch lead to fracture

3. Depend on which bones are involved , **Fractures of:**
   - **Vertebrae (frequently occur in thoracic and lumbar regions)**
   - **Femoral neck**

4. **Can cause significant loss of height and various deformities, including lumbar lordosis and kyphoscoliosis**

5. **Patients with osteoporosis have normal serum levels of calcium, phosphate, and alkaline phosphatase**

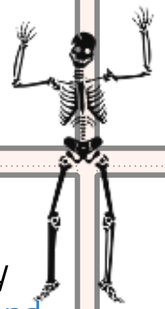
6. complication of fracture.
(a fracture to the femoral neck could lead to Avascular Necrosis by stopping blood supply to the femoral head).



# Diagnosis

Difficult condition to screen for in asymptomatic people

Plain X-ray (radiograph): cannot detect osteoporosis until 30% to 40% of bone mass has already disappeared (lost)



Dual-emission(energy) X-ray absorptiometry (DXA scan) and quantitative computed tomography:
-used primarily to evaluate bone mineral density, to diagnose and follow up pt. with osteoporosis
-the best estimates of Bone loss

Bone biopsy (rarely performed)

# Prognosis

- **Osteoporosis is rarely lethal**
- **Patients have an increased mortality rate due to the complications of fracture.**

e.g:
hip fractures can lead to decreased mobility and an additional risk of numerous complications: deep vein thrombosis(DVA), pulmonary embolism (PE) and pneumonia.

## Prevention strategies:

1. The best long-term approach to osteoporosis is prevention
2. 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
3. This will provide a good reserve against bone loss later in life.
4. Exercise places stress on bones that builds up bone mass

# Osteomalacia and Rickets

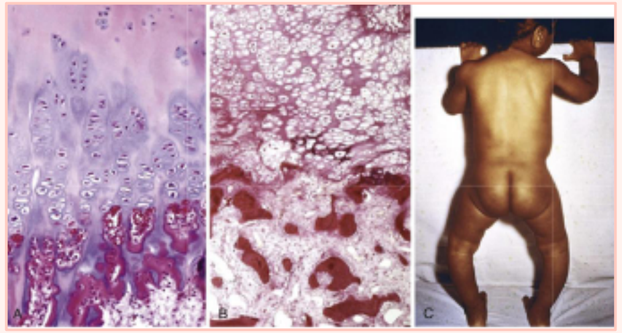
| Comparison | Osteomalacia | Rickets |
|---|---|---|
| Clinical manifestation | Both are manifestations of vitamin D deficiency. | |
| Explanation | Osteoblastic production of bone collagen is normal but mineralization is inadequate. | |
| Result | Impairment of mineralization and a resultant accumulation of unmineralized matrix , with loss of structural rigidity of the bone. | |
| Age group | Adults | Children |
| Pathogenesis (Process of disease) | - bone formed during remodeling is undermineralized resulting on predisposition to fracture,<br>- which are most likely to affect vertebral bodies and femoral neck) | - interferes with deposition of bone at growth plates<br>- Lead to deformity of growing bone due to loss of structural rigidity of the developing bone |

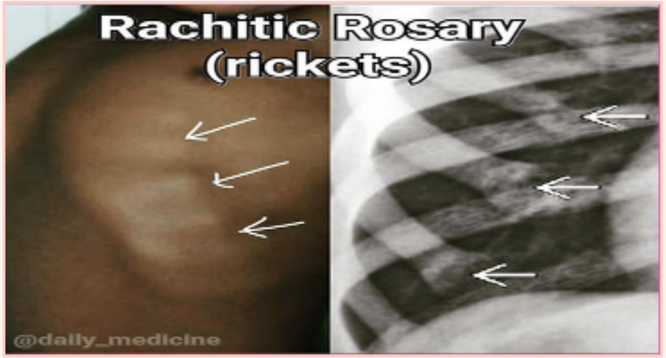
# Morphology

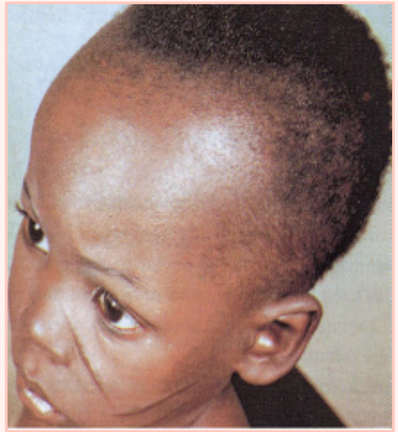
*MALE SLIDES ONLY

- Overgrowth of epiphyseal cartilage due to inadequate provisional calcification and failure of the cartilage cells to mature and disintegrate
- Persistence of distorted, irregular masses of cartilage, which project into the marrow cavity
- Deposition of osteoid matrix on inadequately mineralized cartilaginous remnants
- Disruption of the orderly replacement of cartilage by osteoid matrix, with enlargement and lateral expansion of the osteochondral junction
- Abnormal overgrowth of capillaries and fibroblasts in the disorganized zone resulting from microfractures and stresses on the inadequately mineralized, weak, poorly formed bone
- Deformation of the skeleton due to the loss of structural rigidity of the developing bones

# Pictures





Frontal bones are prominent and bossed

# Hyperparathyroidism (PTH)

**1**

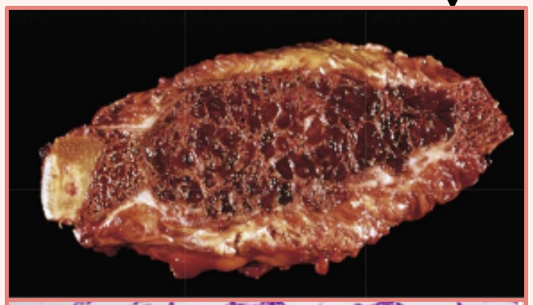
Excessive secretion of PTH (a hormone your parathyroid glands release to control calcium levels in your blood) produces increased osteoclastic activity, and bone resorption.

**2**

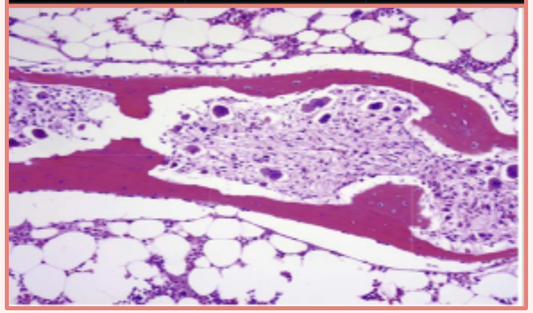
There is excessive destruction of cortical and trabecular bone, with inadequate compensatory osteoblastic activity, amd osteopenia (Primary, secondary or tertiary), osteoporosis ( severe in phalanges, vertebrae and proximal femur), fibrosis. As component to multiple endocrine necrosis (MEN, type I and II).

**3**

lead to brown tumor, Osteitis fibrosa cystica



**Brown Tumor**



**Dissecting osteitis**

## Brown Tumor

-Bone loss predisposes to microfractures and secondary hemorrhages that elicit an influx of macrophages and an ingrowth of reparative fibrous tissue, creating a mass of reactive tissue

- The brown color is the result of the vascularity, hemorrhage, and hemosiderin deposition, and it is not uncommon for the lesions to undergo cystic degeneration

## Generalized osteitis fibrosa cystica (von Recklinghausen disease of bone)

The combination of increased bone cell activity, peritrabecular fibrosis, and cystic brown tumors is the hallmark of severe hyperparathyroidism

## Dissecting osteitis

Osteoclasts may tunnel into and dissect centrally along the length of the trabeculae, creating the appearance of railroad tracks

# Paget's disease of bone

1. There is excessive uncontrolled destruction of bone by abnormally large and active osteoclasts, with concurrent inadequate attempts at haphazard new bone formation by osteoblasts, producing physically weak woven bone (A condition of increased, but disordered and structurally unsound bone)
2. It may result from a paramyxovirus infection in genetically susceptible persons.
3. it's common in whites
4. Risk of fracture and malignancy

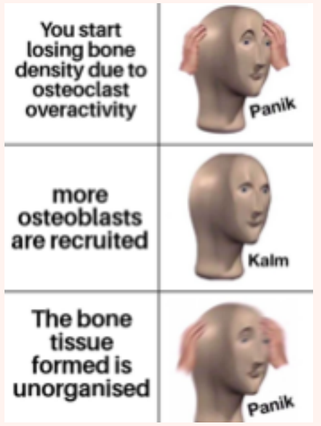
# Stages of Paget's disease

**First Stage** — Initial osteolytic stage

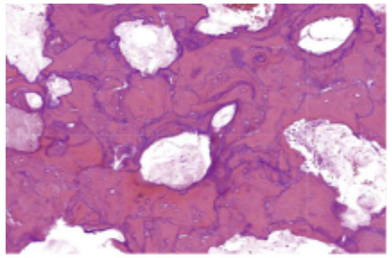
**Second Stage** — Mixed osteoclastic-osteoblastic stage, which ends with a predominance of osteoblastic activity

**Third Stage** — Final burned-out quiescent osteosclerotic stage

Picture in the last slide



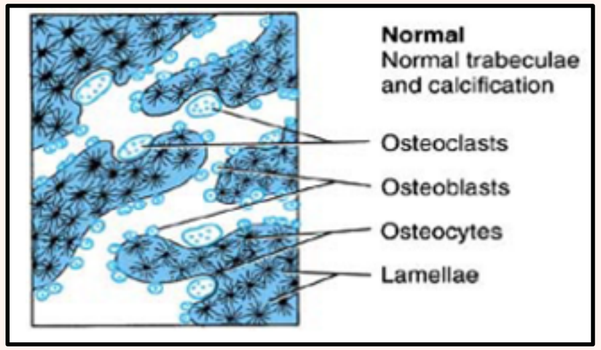
# Diagnosis Paget's disease

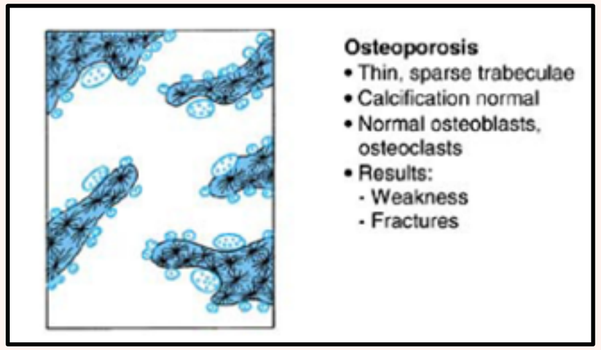
| Way of Diagnosis | Signs/Symptoms | Pictures |
|---|---|---|
| **Histopathology** | - The hallmark is a mosaic pattern (فسيفساء) of lamellar bone, seen in the sclerotic phase.<br>- This jigsaw puzzle-like appearance is produced by unusually prominent cement lines, which join haphazardly oriented units of lamellar bone.<br><br>-In the end, the bone is composed of coarsely thickened trabeculae and cortices that are soft and porous and lack structural stability, these aspects make the bone vulnerable to deformation under stress; consequently, it fractures easily. |  <br>Jigsaw puzzle<br>  |

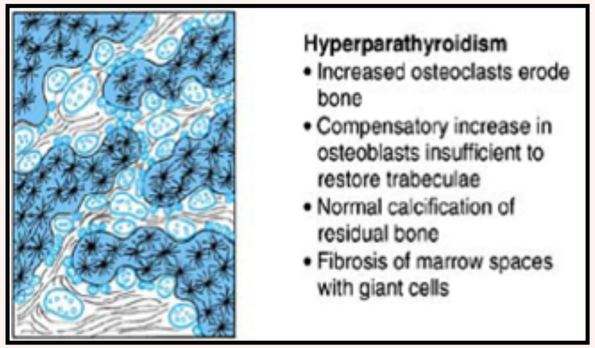
# Pictures

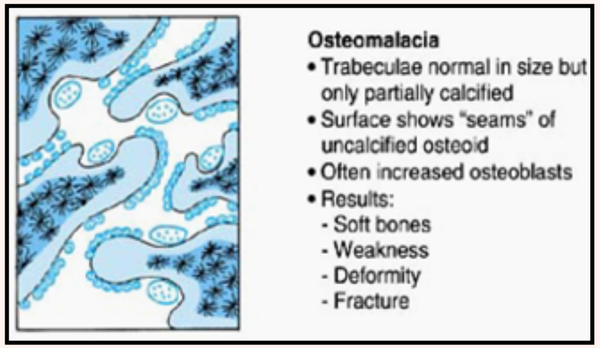
## Summary of metabolic disease of bone

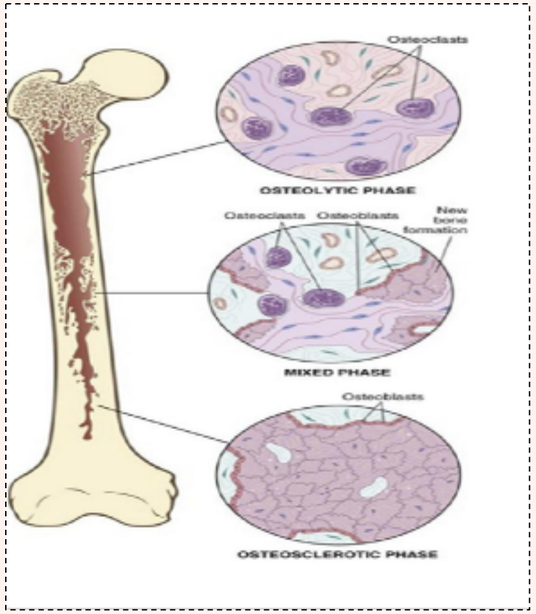
*FEMALE SLIDES ONLY




## Stages of Paget's Disease

## Lab findings in metabolic bone disease

| dr maha said it is not important | Serum Calcium | Serum Phosphorus | Alkaline Phosphatase | Parathyroid Hormone (PTH) |
|---|---|---|---|---|
| Osteoporosis | N | N | N | N |
| Osteomalacia (rickets) | ↓ | ↓(↑)[1] | ↑ | N(↑) |
| Primary hyperparathyroid bone disease | ↑ | ↓ | N↑ | ↑ |
| Bone disease in renal failure—with secondary hyperparathyroidism | N↓ | ↑ | ↑ | ↑ |
| Lytic bone neoplasms | N↑ | N↑ | N↑ | N |
| Paget's disease of bone | N | N | ↑ | N |

443 Female doctor note:
-Important to know Paget's disease findings
-There is 2 types of hyperparathyroidism: Primary (due to diseases of parathyroid gland) and Secondary (due to kidney diseases)

Summary

# Bone Diseases

Thanks to 443 for this amazing summary

## Acquired

- Metabolic
- Infections
- Traumatic
- Tumors

## Congenital

- Achondroplasia
- Osteogenesis imperfecta
- Osteopetrosis (Marble bone disease)
- Thanatophoric dysplasia

### Osteoporosis/Osteopenia

Osteopenia: decreased bone mass.

Osteoporosis: Osteopenia that is severe enough to increase the risk of fracture.

### Osteomalacia & Rickets

Both are manifestations of vitamin D deficiency.

Osteomalacia Occur in adults.

Rickets Occur in adults.

### Hyperparathyroidism

Excessive secretion of PTH produces increased osteoclastic activity, and bone resorption.

### Paget's disease of bone

excessive uncontrolled destruction of bone by abnormally large and active osteoclasts.

# Keywords

| Word (disease) | The word that leads to the disease ( symptoms, features or a word ) |
|---|---|
| Congenital | A disease or physical abnormality present from birth. |
| Acquired | An acquired disease is one that began at some point during one's lifetime. |
| Dysostosis | Developmental anomalies resulting from Localized problems of bone. |
| Dysplasia | Global disorganization of bone and/or cartilage (Not Tumor) |
| Osteogenesis Imperfecta | Defect in the synthesis of type I collagen affect Bone, Joints and other tissues rich in type I collagen. It leads to fragility with susceptibility to fractures |
| Achondroplasia | Known as Dwarfism, transmitted as an autosomal dominant trait. |
| Metabolic bone disease | Comprises four fairly Common conditions in which there is an imbalance between osteoblastic (bone forming) and osteoclastic (bone destroying) activity. |
| Osteoporosis | Acquired condition characterized with severly reduced bone mass, |

| Word (disease) | The word that leads to the disease ( symptoms, features or a word ) |
|---|---|
| Osteomalacia and Rickets | Osteoblastic production of bone collagen is normal but mineralization is inadequate. Bone formed during remodeling is undermineralized (Osteoid) resulting on predisposition to fracture |
| Hyperparathyroidism | Excessive secretion of PTH produces increased osteoclastic activity, and bone resorption. |
| Paget's disease | A condition of increased, but disordered and structurally unsound bone. It may result from a paramyxovirus infection in genetically susceptible persons. |
| Osteoporosis | Acquired condition characterized with severly reduced bone mass, leading to bone fragility and susceptibility to fractures. |
| | |
| | |
| | |

# MCQs

| Q1) which of following is affected in Achondroplasia: | | | | | | |
|---|---|---|---|---|---|---|
| A) Skull | | B) Axial skeleton | | C) Metacarpals bone | | D) Facial bones |
| **Q2) Which of following is a result of abnormal function in Osteoclasts:** | | | | | | |
| A) Osteopetrosis | | B) Osteoporosis | | C) Osteomalacia | | D) Achondroplasia |
| **Q3) When estrogen decrease,The expression of OPG will decrease then the OPG won't block RANKL and that will lead to:** | | | | | | |
| A) Decrease osteoblastic activity | | B) Increase osteoblastic activity | | C) Increase osteoclastic activity | | D) Decrease osteoclastic activity |

1-C 2-A 3-C

# MCQs

| | | | | | | |
|---|---|---|---|---|---|---|
| Q4) Post menopause it will lead to increase both bone resorption and bone formation BUT bone resorption will be faster than formation this will lead to : | | | | | | |
| A) Rickets | | B) High-turnover | | C) Hyper-parathyroidism | | D) Low-turnover |
| Q5) Patient with osteoporosis have normal serum levels of: | | | | | | |
| A) Calcium | | B) Phosphate | | C) Alkaline phosphate | | D) All are correct |
| Q6)The findings of a patient' serum level test shows increased alkaline phosphate level and normal calcium, serum phosphate and PTH levels, the diagnosis is: | | | | | | |
| A) Hyper-<br>B) parathyroidism | | B) Paget's disease | | C) osteomalacia | | D) osteoporosis |

4-B 5-D 6-B

# Cases

Special thanks for 443!

| 1. A 23 year old female experiences a stillbirth. This is her first pregnancy, and she has received no prenatal care. The baby is noted to have multiple fractures, blue sclera, and short/bent extremities. Her past medical history is remarkable for a seizure disorder, for which she was taking phenytoin regularly during the course of her pregnancy. She explains at she had been eating poorly, and occasionally was drinking alcohol during the course of her first trimester.Also, she explains that she underwent various episodes of abuse during the pregnancy. What was most likely responsible for the death of her fetus? | | | |
|---|---|---|---|
| A. Osteogenesis imperfecta | B. Acondroplasia | C. Osteopetrosis | D. Osteoporosis |
| 2. A 25 year old woman comes to the clinic for a routine visit. She is 3ft 10 in tall, and has short extremities. Her torso length is within normal limits. Her physical exam is notable for depression of the nasal bridge, and a bulging forehead. The patient's husband has none of these physical findings and is 5ft 10 in in height. The patient is counseled that she has a 50% chance of passing on her condition to her children. What condition does she have? | | | |
| A. Osteogenesis imperfecta | B. Acondroplasia | C. Osteopetrosis | D. Osteoporosis |

1-A 2-B

Special thanks for 443!

# Cases

| 3. T.S. is a 52-year-old female experiencing diffuse bone pain over the past several years after menopause. She has a history of fractures to her left hip and wrist. She states, “The pain is becoming worse and it is keeping me from doing my daily activities.” She currently complains that any weight-bearing activity causes her severe discomfort. What is the most likely diagnosis? | | | |
|---|---|---|---|
| A. Osteogenesis imperfecta | B. Acondroplasia | C. Osteopetrosis | D. Osteoporosis |

| 4.A 10 month old boy is brought to the pediatrician for a routine visit. His birth history is unremarkable, and he is primarily breastfed by his mother. He has begun eating baby food. He has been growing well and consistently gaining weight. While he has not begun walking, he has started cruising. He is able to say both “mama” and “dada”. He has no remarkable past medical history, allergies, and is not taking any medications. A physical exam reveals an anterior fontanel that is wide open. Skull palpation demonstrates pliable skull bones that have no step-offs. There are bony prominences at the costochondral junctions bilaterally. The patient’s legs are bowed. The rest of his exam is non-contributory. What is a possible diagnosis? | | | |
|---|---|---|---|
| A. Osteogenesis imperfecta | B. Acondroplasia | C. Osteopetrosis | D. Osteoporosis |

3-D 4-D

# Pathology Team

## leaders:

Layal alkhalifah

Abdulaziz Nasser

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- Sahar Alfallaj
- Norah Alnoshan
- Raseel Aldajany
- Abdulaziz Alanazi
- Waleed Alanazi
- Faisal alghamdi
- Faisal Alamoud
- Mouath al abdussalam