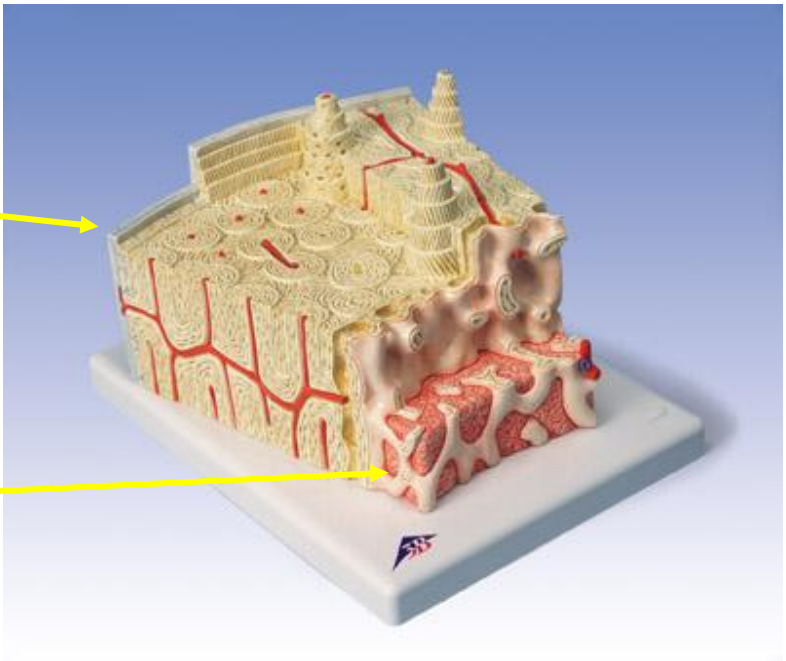
Normal anatomy

- **Parts of a long bones:**
  - diaphysis (shaft)
  - epiphyseal plate (growth plate)
  - epiphysis (ends of bone, partially covered by articular cartilage)
  - metaphysis (junction of diaphysis and epiphysis, most common site of primary bone tumors)
- **Cross section:**
  - Periosteum
  - cortex (composed of cortical bone or compact bone)
  - medullary space (composed of cancellous or spongy bone)

  - Compact or lamellar bone.
  - cancellous or spongy bone .



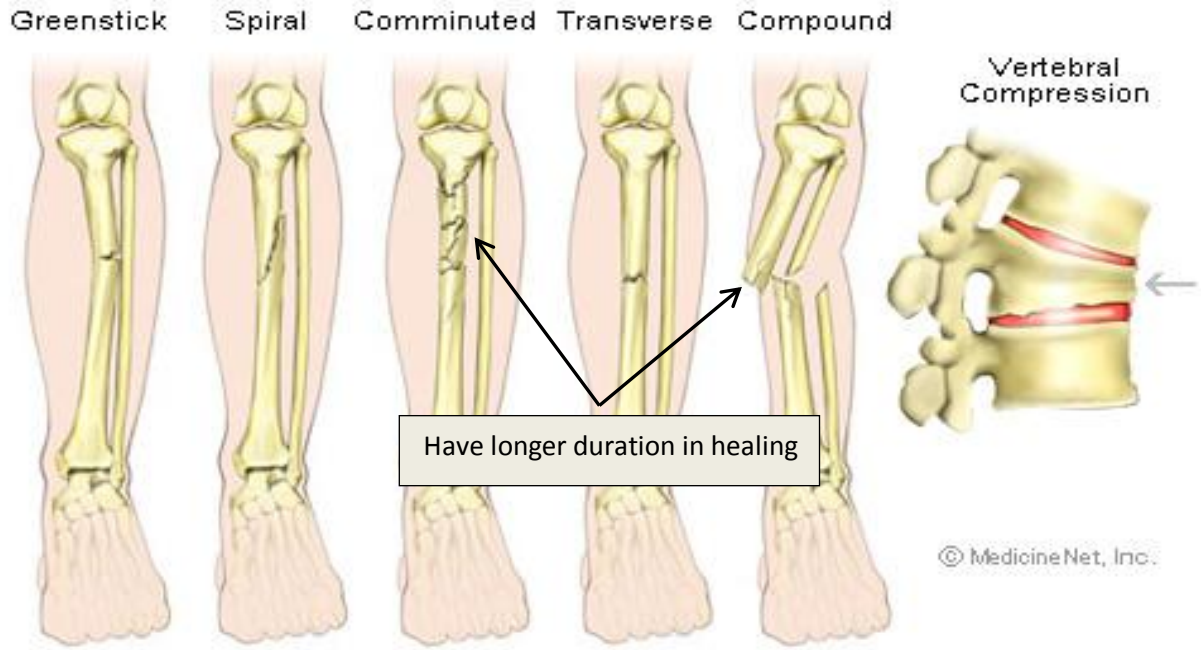
Normal histology

- **Bone:**
  - mineralized osteoid; either lamellar bone or woven bone.
- **Lamellar bone:**
  - layered bone with concentric parallel lamellae
  - gradually replaces woven bone
  - normal type of bone found in adult skeleton
  - stronger than woven bone

Cells of bone

- **Osteoblasts:** arise from marrow mesenchymal cells; when active, are plump and present on bone surface; eventually are encased within the collagen they produce.
- **Osteoclasts**: large multinucleated cells found attached to the bone surface at sites of active bone resorption.

Types of Fractures



Typical Bone Fractures

Classification of Fractures

- **Traumatic fracture**
  Road Traffic Accidents *(most common)*
- **Pathological fracture**
  A fracture that occurs at a site of previous disease *(e.g.: bone cyst , malignant tumor)*
- **Stress fracture**
  Overuse injury , caused by fatigued muscles that cannot absorb repeated impact , result is a small crack or fracture . *(e.g.: military boot camp)*

Healing of Fractures

There are three major phases of fracture healing:

1. **Reactive Phase**

   i. Fracture and inflammatory phase

   ii. Granulation tissue formation

- Fracture → fracture gap → bleeding → inflammatory response and fibrin deposition → inflammatory mediators → granulation tissue formation → formation of soft tissue callus

2. **Reparative Phase**

   iii. Callus formation

   iv. Lamellar bone deposition

- Days after fracture, the cells of the periosteum replicate and transform. The periosteal cells proximal to the fracture gap develop into chondroblasts and form hyaline cartilage. The

fibroblasts within the granulation tissue also develop into chondroblasts and form hyaline cartilage. The periosteal cells distal to the fracture gap develop into osteoblasts and form woven bone.

- Proximal periosteal cells → Chondroblasts → hyaline cartilage
- Fibroblasts within the granulation tissue
- Distal periosteal cells → osteoblasts → woven bone

- These new tissues grow in size until they unite with their counterparts from other pieces of the fracture. This process forms the fracture ***bony callus***. Eventually, the fracture gap is bridged by the hyaline cartilage and woven bone, restoring some of its original strength

- The next phase is the replacement of the hyaline cartilage and woven bone with lamellar bone. The replacement process is known as ***endochondral ossification*** with respect to the hyaline cartilage and ***bony substitution*** with respect to the woven bone. Substitution of the woven bone with lamellar bone precedes the substitution of the hyaline cartilage with lamellar bone.

Ossification : *Transformation of hyaline cartilage to lamellar bone.*
Substitution : *Transformation of woven bone to lamellar bone.*

- Woven bone characterized by random organization of collagen fibers and is mechanically weak.
- Lamellar bone has a regular parallel alignment of collagen fibers into sheets (lamellae) and is mechanically strong.

3. **Remodeling Phase** *" final touch "*

v. Remodeling to original bone contour

- The remodeling process substitutes the trabecular bone with compact bone. The trabecular bone is first resorbed by ***osteoclasts*** creating a shallow resorption pit known as a "Howship's lacuna". Then ***osteoblasts*** deposit compact bone within the resorption pit. Eventually, the fracture callus is remodeled into a new shape which closely duplicates the bone's original shape and strength.

Two cells responsible for remodeling:

- ***1- osteoblast***
- ***2- osteoclast***

- **Factors disrupting healing process:**

- Displaced and comminuted fractures
- Inadequate immobilization
  - *Delayed union*
  - *Nonunion*
  - *Pseudoarthrosis*

- ***Infection*** *(Usually with compound fracture)*
- Vascular insufficiency
- Inadequate minerals and vitamins

Diseases of Bones

• Congenital Diseases of Bones

- **Localized or entire skeleton** *(e.g.: increase in number of fingers ,absence of a rib)*

- **Dysostosis**:

Developmental anomalies resulting from localized problems in the migration of mesenchymal cells and the formation of condensations

- **Dysplasias :**

Mutations that interfere with bone or cartilage growth and/or maintenance of normal matrix components .

  - ***Osteogenesis imperfect***

- Also known as "*brittle bone* disease", is actually a group of *hereditary disorders* caused by *defective synthesis of type I collagen*.

- *Extreme fragility of skeleton#*with susceptibility to fractures.

  # يكون طول حياته معرض للكسر بأدنى ضربة

- Four main types with different clinical manifestations.

– ***Achondroplasia*** *(Dwarfism)*

- Defect in the cartilage synthesis at growth plates
- *Mutation in (FGFR3)* lead to inhibition of chondrocytes proliferation
- Epiphyseal growth plate expansion is suppressed

– ***Osteopetrosis***

- Rare genetic disorders characterized by reduced osteoclast-mediated bone resorption and therefore defective bone remodelling.
- Osteopetrosis results in a dense bone

- **Acquired Diseases of Bones**

  - Metabolic
  - Infections
  - Traumatic
  - Tumors

○ METABOLIC BONE DISESE *‘‘most common acquired diseases ’’*

i. Osteoporosis *" هشاشة العظام "*

- A slowly progressive increase in bone erosion, which is not adequately counteracted by new bone formation. The cortical bone is thinned, and the bone trabeculae are thinned and reduced in number. *General reduction in bone mass, but without distortion of architecture.*

نوعية العظم طبيعية لكن كتلة العظم تقل

- May be localized → disuse osteoporosis of a limb. Or may involve the entire skeleton, as a metabolic bone disease.

▪ **Classification :**

❖ Primary : *“ most common “*
– postmenopausal , senile *(aging)*

❖ Secondary :
- Endocrine Disorders → growth of skeleton
- Gastrointestinal disorders → loss of Calcium , vitamin.D
- Neoplasia → tumor
- Drugs → steroid

▪ Pathophysiology :

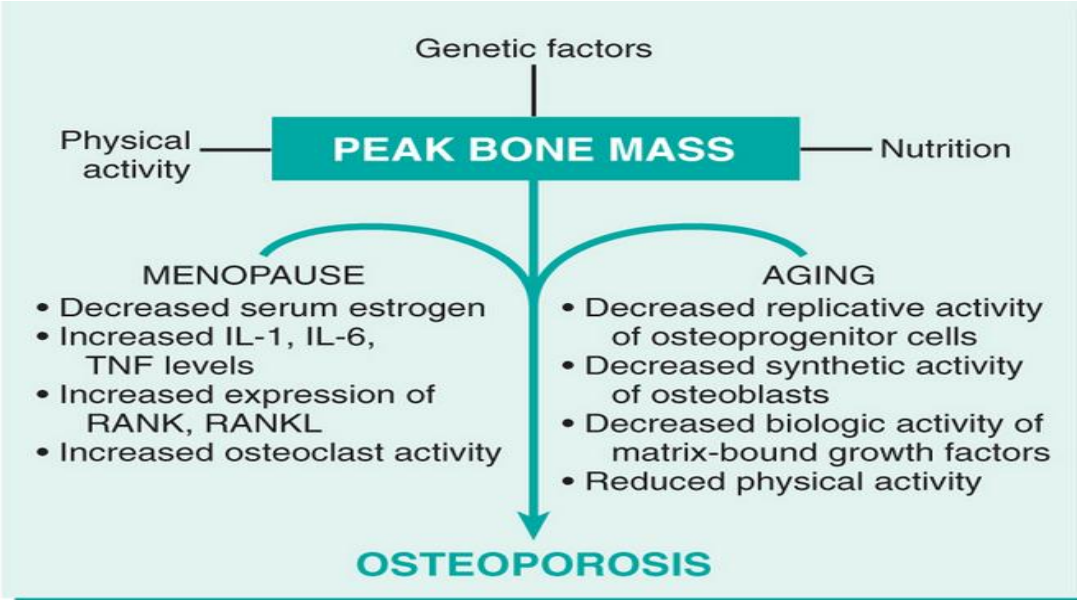
- Genetic factors
- Nutritional effects
- Physical activity
- **AGING**
  - ↓ replicative activity of the osteoprogenitor cells
  - ↓ synthetic activity of the osteoblasts.
  - ↓ activity of the matrix bound growth factors.

osteoprogenitor cells = osteogenic cells (which develop to osteoblasts).

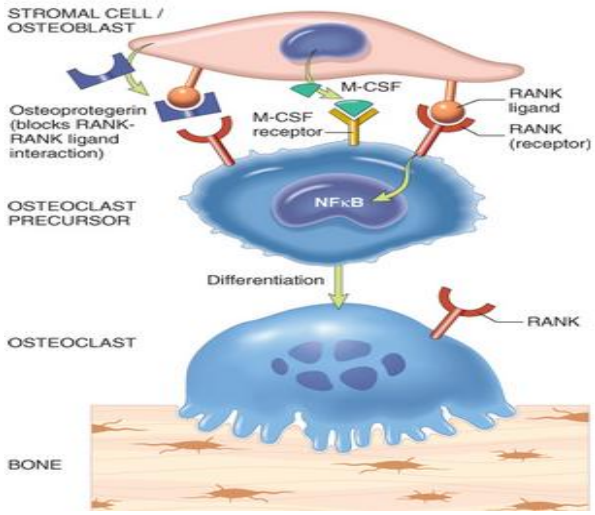
Thus a decrease in the number and function of osteoblasts, which leads to less mass of bone.

- **Menopause**
  - ↓ serum ,, ↑ estrogen
  - ↑ IL-1, IL-6 levels
  - ↑ osteoclast activity*

** Osteoclast activity=bone resorption (breaking down of the bone)*



- **Paracrine mechanisms regulating osteoclast** :



- *RANK (receptor activator for nuclear factor-κB) receptors on osteoclast precursors bind RANK ligand (RANKL) expressed by osteoblasts and marrow stromal cells.*

- *Along with macrophage colony-stimulating factor (M-CSF), the RANK-RANKL interaction drives the differentiation of functional osteoclasts.*

- *Stromal cells also secrete osteoprotegerin (OPG) that acts as a decoy receptor for RANKL, preventing it from binding the RANK receptor on osteoclast precursors.*

Osteoblast have something called RANK, which has receptor on the osteocalst.

Osteocalst responsible for increase osteocalstic activity .

There is somthenig called osteoprotegerin (OPG) blocking the RANKL to block the activity of RANK

- **Clinical Features** :

  - Thoracic and lumbar vertebral fractures are extremely common, and produce loss of height and various deformities, including kyphoscoliosis* that can compromise respiratory function.

    **kyphoscoliosis=kyphosis+scoliosis=abnormal curvature in the back.*
    Kyphosis=hunch back=curvature of upper back.

Scoliosis=crooked=person's spine is curved from side to side.

- *Pulmonary embolism# and pneumonia## are common complications of fractures* of the femoral neck, pelvis, or spine

#أشهر مكان يروح له الرئة أي شيء يتحرك في الدائرة الدموية ويروح لأي مكان ويسكره يسمى بالـ(إمبلوميزم)

هو الذي يقتل كبار السن عادة لما يناموا على السرير مدة طويلة ##

- **Diagnosis** :
  - Osteoporosis is difficult to diagnose because it remains asymptomatic until skeletal fragility is announced with a fracture.
  - Osteoporosis cannot be reliably detected in plain radiographs until 30%-40% of bone mass has already disappeared
  - serum levels of calcium, phosphorus, and alkaline phosphatase are insensitive.
  - The current state of the art for bone loss estimation involves *specialized radiographic techniques to assess density*
  - The two main biochemical markers for bone formation are :
    *serum **alkaline phosphatase** and serum **osteocalcin**.*
  - Markers for bone resorbtion include urinary calcium and urinary hydroxyproline.
- **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

ii. ***Osteomalacia*** *"لين العظام ، الكساح"*

Osteoblastic production of bone collagen is normal but *mineralization is inadequate.*
This leads to trabecular bone that is only partially mineralized and therefore *soft and weak*.

المشكلة هنا الكثافة تقل لأن التمعدن قليل أما هشاشة العظام المشكلة في الكتلة وليس الكثافة

iii. Paget's disease of bone

Very rare disease , appear only in the meddle age , Cause by viral infection , Bone formation is abnormal (mosaic) , and have a higher risk to have tumor.

iv. Hyperparathyroidism

Excessive secretion of *PTH produces increased osteoclastic activity*. There is excessive destruction of cortical and trabecular bone, with inadequate compensatory osteoblastic activity.

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