BONE FUNCTIONS

- Mechanical support
- Forces transmission
- Protection
- Mineral homeostasis
- Hematopoiesis

Mineral homeostasis

Bones store minerals like calcium (Ca^{2+}) and phosphate (PO_4^{3-}).

When blood calcium drops, bones release calcium (via osteoclasts).

When blood calcium rises, bones store excess calcium (via osteoblasts).

Hematopoiesis

is the process of blood cell formation, occurring primarily in the bone marrow, where stem cells produce red blood cells, white blood cells, and platelets.

BONE STRUCTURE

- **Matrix (osteoid 35% and minerals 65%):**
  - **Osteoid: organic type I collagen and glycosaminoglycans & other proteins**
  - **Inorganic hydroxyapetite [$Ca_{10}(PO_4)_6(OH)_2$]**
  - **Woven vs lamellar bone**
- **Cells:**
  - **Osteoblasts: forms bone**
  - **Osteoclasts: resorbs bone**
  - **Osteocytes: mature bone cells**

Bone Structure

The structure of bone is composed of two main components: the matrix and the cells.

The matrix is made up of 35% organic material, known as osteoid, and 65% inorganic minerals. The osteoid is primarily composed of Type I collagen, glycosaminoglycans, and various other proteins. These organic elements provide flexibility to the bone. The remaining 65% is made up of inorganic minerals, mainly hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$), a compound that gives bone its strength and hardness.

The bone cells

1-**Osteoblasts** : responsible for the formation of bone. They produce osteoid

2-**Osteoclasts**: resorb bone by breaking down the bone matrix

When osteoblasts mature, they transform into osteocytes.

Comparison between Osteocytes and Osteoblasts:

Osteocytes:

Less active.

Smaller in size.

Have fewer cytoplasmic organelles for metabolic activity.

Osteoblasts:

More active.

Larger in size.

Contain more cytoplasmic organelles to support metabolic activity and bone formation.

In **osteoporosis**, bone resorption (by osteoclasts) happens faster than bone formation (by osteoblasts), making the bones weak and brittle. This leads to a higher risk of fractures.

Note: This will be explained in more detail later.

#>bone cells like **osteocytes** are embedded in small spaces within the **bone matrix**

#>**Osteoblasts**, on the other hand, are located on the **bone surface**, secreting bone matrix before transforming into osteocytes.

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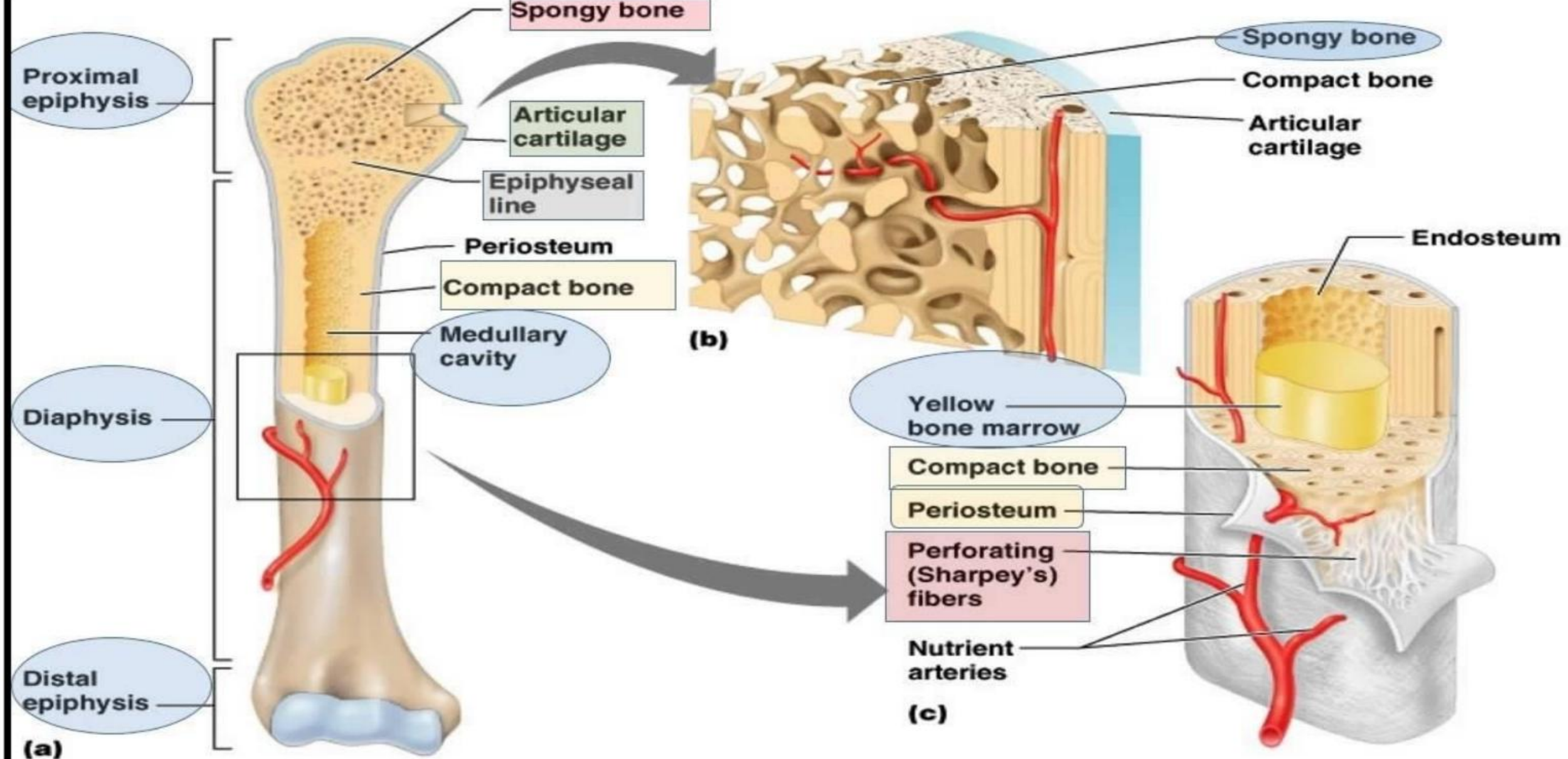


Structure of a Typical Long Bone

Remember from histology

Key Parts of a Long Bone:

1. Epiphysis (Proximal & Distal)

The ends of the long bone.

Contains spongy bone, which has a porous structure and houses red bone marrow.

Covered with articular cartilage to reduce friction in joints.

The epiphyseal line is a remnant of the growth plate (epiphyseal plate), which allows bone growth in children.

2. Diaphysis

The shaft of the bone.

Composed of compact bone, which provides strength.

Houses the medullary cavity, which contains yellow bone marrow (stores fat).

3. Periosteum

A dense connective tissue layer covering the outer surface of the bone.

Contains blood vessels and nerves that help in bone nourishment and repair.

4. Compact Bone

Dense and strong, providing structural support.

Contains nutrient arteries that supply blood to bone tissues.

5. Spongy Bone

Found in the epiphyses.

Contains trabeculae, which form a lightweight but strong structure.

Stores red bone marrow, which produces blood cells.

6. Endosteum

A thin membrane lining the inner surface of the medullary cavity.

Involved in bone growth and remodeling.

WOVEN VS LAMELLAR BONE

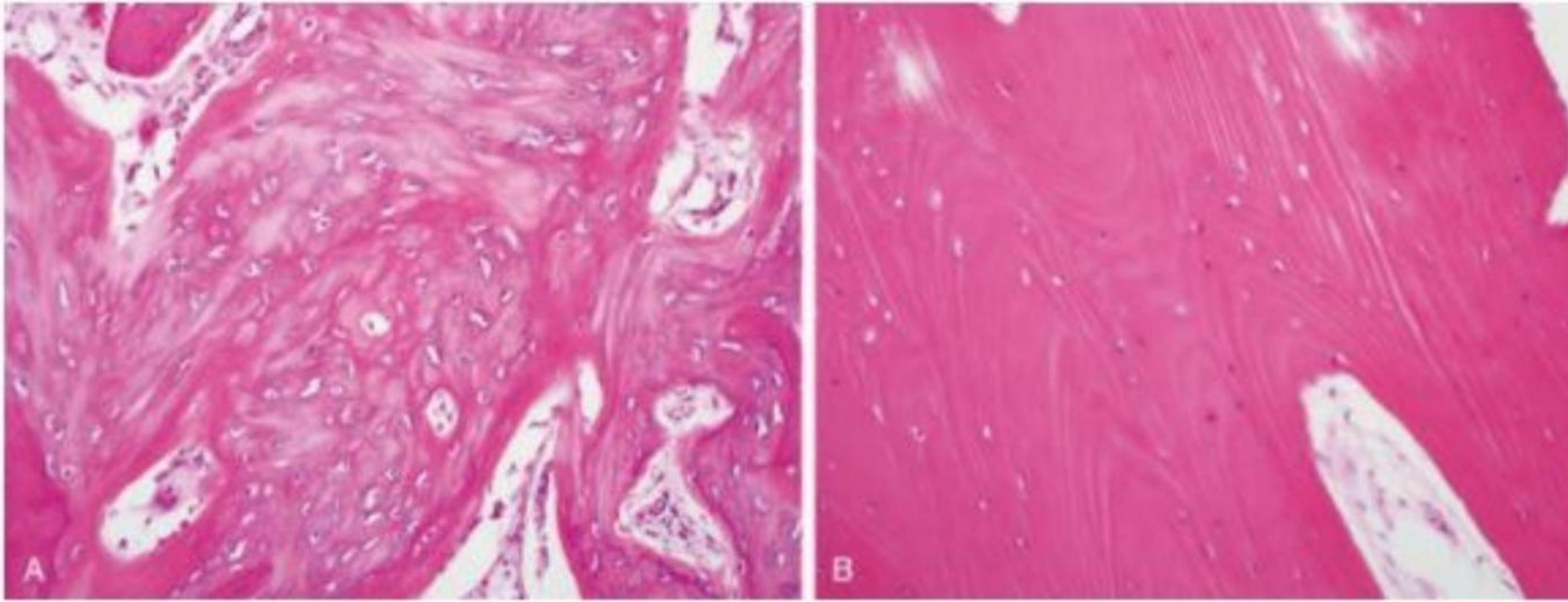


FIG. 21.1 Woven bone (A) is more cellular and disorganized than lamellar bone (B).

1-Woven Bone

More cellular: Contains a higher number of osteocytes per 1 cm^2 compared to lamellar bone.

Disorganized collagen fibers: Irregular and randomly arranged.

Immature and early bone: Found in **young individuals** and during early bone formation.

Rapidly formed: Appears at fracture sites and in conditions like **malignancies** (bone tumors).

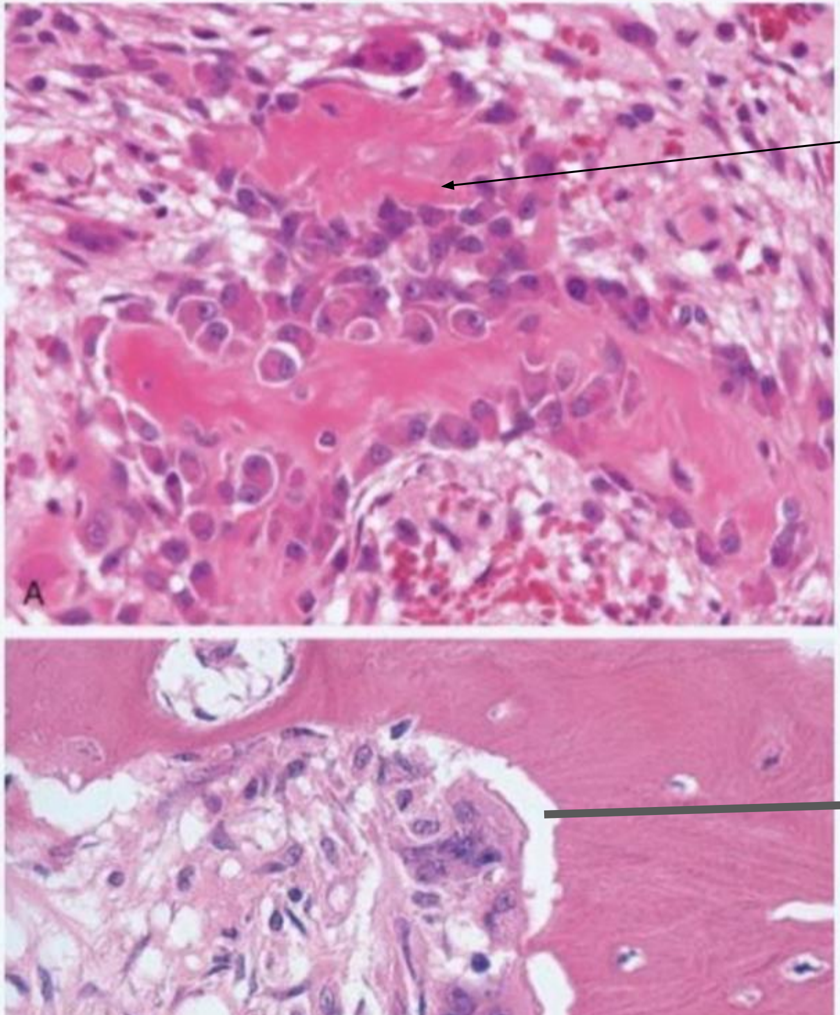
Weaker structure: Less organized, making it mechanically weaker but temporarily useful for rapid bone repair.

2-Lamellar Bone

Organized collagen fibers: Arranged in parallel or concentric layers (lamellae).

Mature bone: Found in normal **adult** bones.

Stronger structure: More resistant to mechanical stress.



Osteoid

OSTEOBLASTS

represent bone resorption by osteoclast

OSTEOCLASTS

Comparison Between Osteoblasts and Osteoclasts

Osteoblasts (Bone-Forming Cells)

1-Small cells with a single nucleus.

2-Higher nuclear-to-cytoplasmic ratio

3-Found around areas where osteoid is being formed.

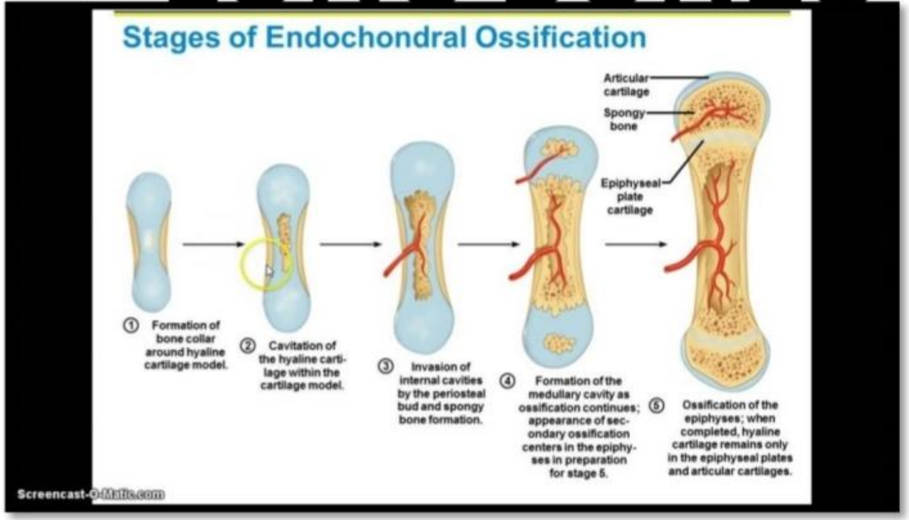
Osteoclasts (Bone-Resorbing Cells)

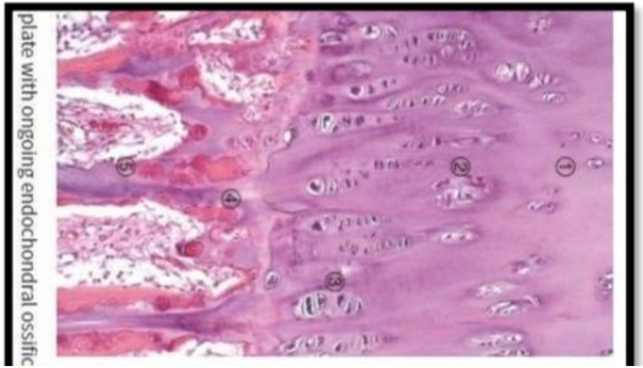
1 -Large, multinucleated cells (typically 100–150 nuclei)

2-Derived from the monocyte-macrophage system.

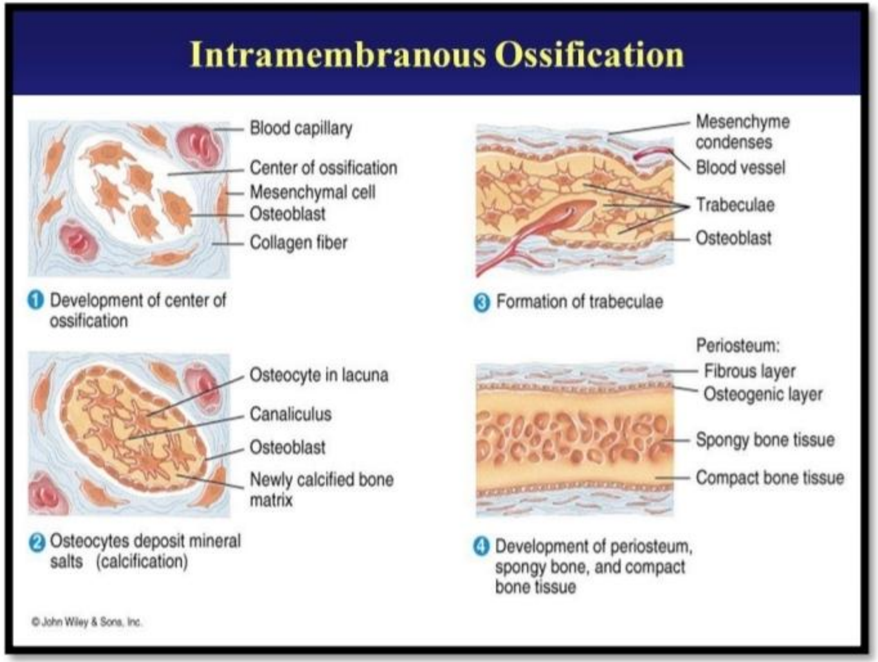
3-Classified as multinucleated giant cells, unlike osteoblasts, which have a single nucleus.

LONG BONES





FLAT BONES



Endochondral Ossification (Cartilage → Bone) for long bones

1️⃣ Mesenchymal cells → Differentiate into chondroblasts → Form hyaline cartilage model

2️⃣ Cartilage grows → Chondrocytes in the center enlarge (hypertrophy) → Matrix calcifies → Chondrocytes die

3️⃣ Primary ossification center (diaphysis) → Blood vessels invade → Osteoblasts replace cartilage with bone

4️⃣ Secondary ossification centers (epiphyses) → Form later at the ends of the bone

5️⃣ Epiphyseal plate (growth plate) → Allows bone elongation until adulthood

6️⃣ Epiphyseal plate closure → Growth stops → Only articular cartilage remains at joint surfaces

Intramembranous Ossification (Mesenchyme → Bone)

1️⃣ Mesenchymal cells → Differentiate into osteoblasts → Begin forming osteoid

2️⃣ Osteoid mineralizes → Forms small bone spicules (early bone tissue)

3️⃣ Spicules fuse → Form a network of trabeculae (woven bone)

4️⃣ Compact bone formation → Periosteum develops → Outer layers become lamellar bone

5️⃣ Mature bone → Forms flat bones (e.g., skull, clavicle)

HOMEOSTASIS & REMODELING

- Continuous and dynamic complex process even in adult mature skeleton (microscopic level)
- Peak bone mass is reached in early adulthood after completion of skeletal growth
- Resorption > bone formation on 4th decade

+ Osteoclast differentiation	- Osteoclast differentiation
PTH IL-1 Steroids	BMPs (bone morphogenic proteins) Sex hormones (estrogen & test.)

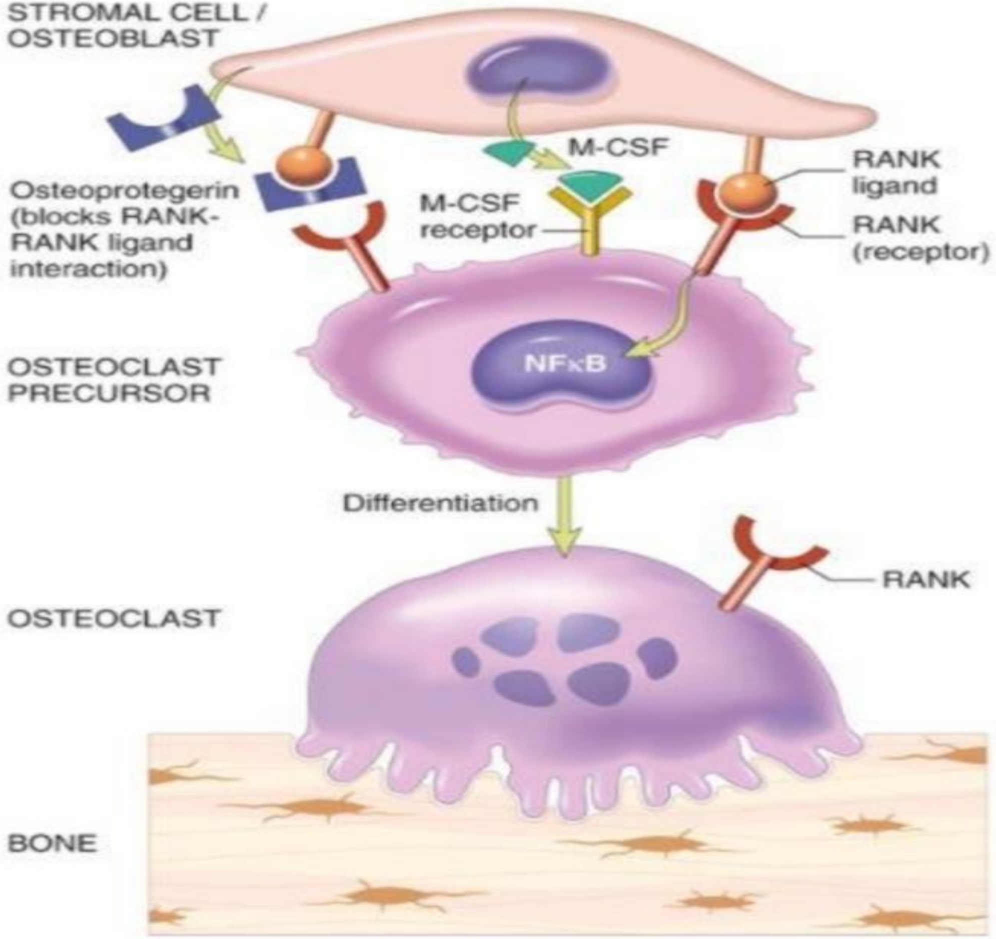


FIG. 21.4 Paracrine molecular mechanisms that regulate osteoclast formation and fun...

1-Osteoblasts/Stromal cells release M-CSF (Macrophage Colony-Stimulating Factor) → Binds to M-CSF receptor on osteoclast precursors → Promotes survival and differentiation

2 -RANK ligand (RANKL), expressed by osteoblasts, binds to RANK receptor on osteoclast precursors → Activates NF-κB, leading to osteoclast differentiation and activation

3- Osteoprotegerin (OPG), secreted by osteoblasts, acts as a decoy receptor that blocks RANK-RANKL interaction → Inhibits osteoclastogenesis and bone resorption

4- Mature osteoclasts attach to bone and resorb it, playing a crucial role in bone remodeling.