Bone

Bone

Function:

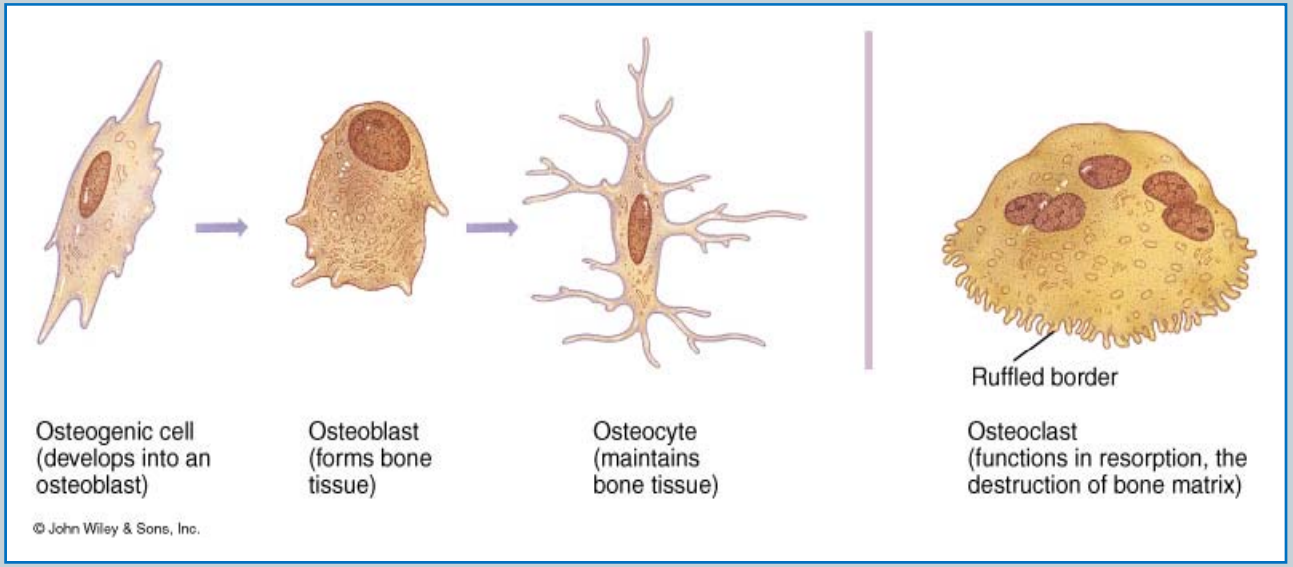
- Protection
- Ion storage
- Movement

- Bon matrix
- Cells

Cells:

- Osteocytes
- Osteoblast
- Osteoclast

- Endosteum
- periosteum



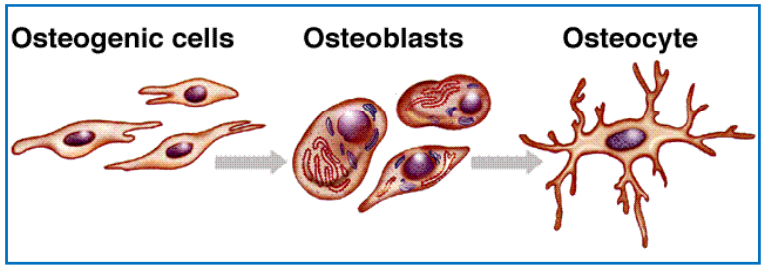
Osteogenic cells

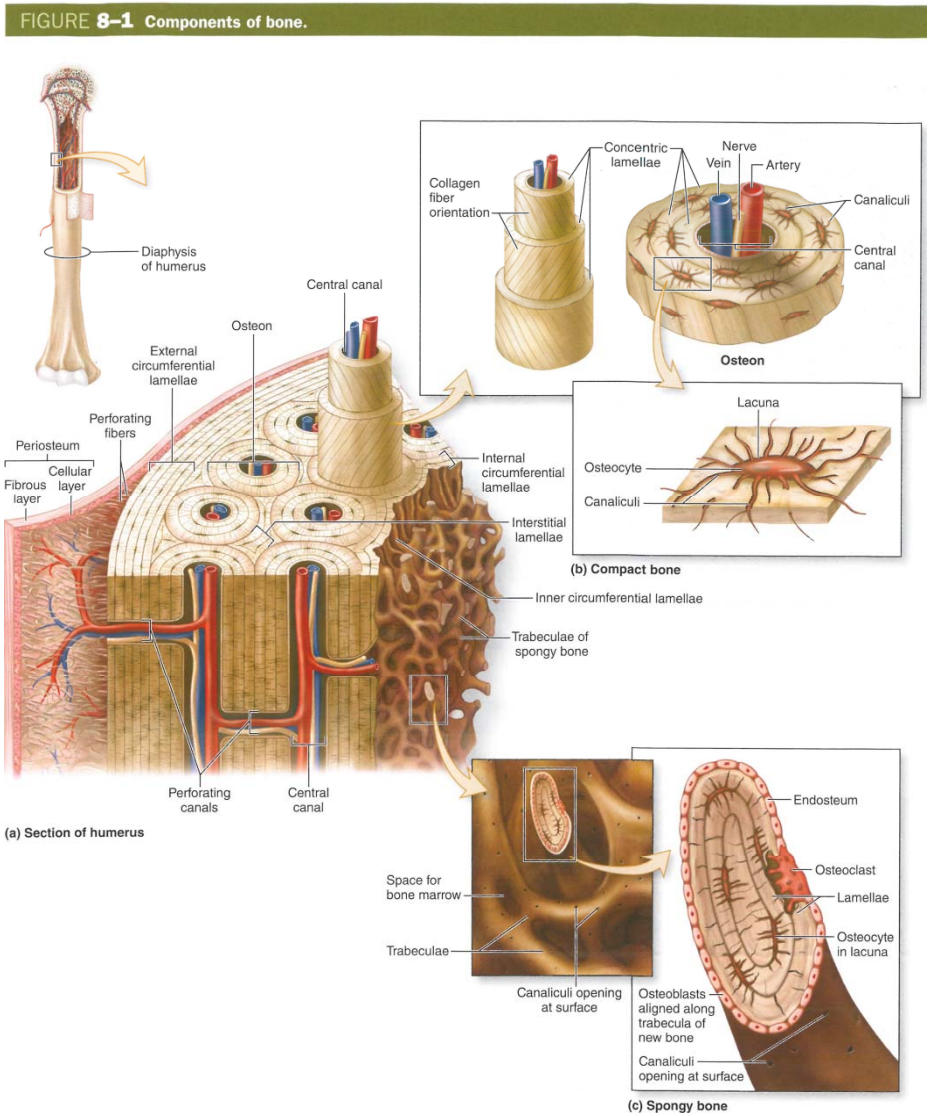
Location:

- endosteum,
- inner layer of periosteum,
- central canals

Function:

- source of new bone cells
- divide to form osteoblasts





A schematic overview of the basic features of bone, including the three key cell types: **osteocytes**, **osteoblasts**, and **osteoclasts**; their usual locations; and the typical **lamellar organization** of bone. Osteoblasts secrete the matrix that then hardens by calcification, trapping the differentiating cells now called **osteocytes** in individual **lacunae**. Osteocytes maintain the calcified matrix and receive nutrients from microvasculature in the central canals of the osteons via very small channels called **canaliculi** that interconnect the lacunae. Osteoclasts are monocyte-derived cells in bone required for bone remodeling.

The **periosteum** consists of dense connective tissue, with a primarily fibrous layer covering a more cellular layer. Bone is vascularized by small vessels that penetrate the matrix from the periosteum. **Endosteum** covers all **trabeculae** around the marrow cavities.

Osteoblasts

Organic matrix synthesis:
- Collagen I
- Proteoglycans
- Glycoproteins

Osteonectin

Inorganic substance

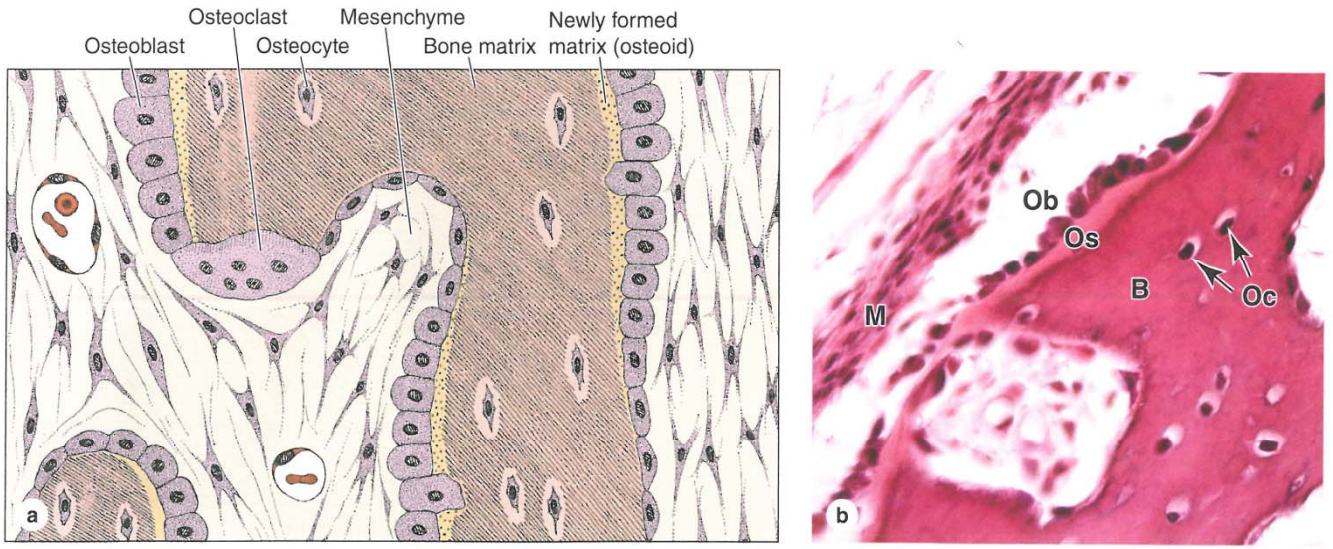
Location:
On matrix surface
(like simple epithelium)

Active osteoblast
Cuboid to columnar
Basophilic

Declined activity
Flattened
Less basophilic ap.

Inactive osteoblast
Bone lining cells in endosteum & periosteum

FIGURE 8–3 Osteoblasts and osteocytes.



(a) Diagram showing the relationship of osteoblasts to osteoid, bone matrix, and osteocytes. Osteoblasts and most of the larger osteoclasts are part of the endosteum covering the bony trabeculae.

(b) The photomicrograph of developing bone shows the location and morphologic differences between active osteoblasts (**Ob**) and osteocytes (**Oc**). Rounded osteoblasts, derived from cells in the adjacent mesenchyme (**M**), appear as a layer of cells adjacent to a very thin layer of lightly stained osteoid (**Os**) that covers the more heavily stained bony matrix (**B**). Inactive osteoblasts are more flattened and cover the bony surface shown near the top here. Osteocytes are located within lacunae surrounded by matrix. X300. H&E.

Osteoblasts

- Protein secretion
- Polar cells
- Osteoid (Uncalcified substance)
- Calcium salts deposition

Calcification:

- **Osteocalcin** (K vitamin dependent pp)

Osteocalcin & other glycoproteins bind to Ca2+

- **vesicle matrix**

Rich alkaline phosphatase & other enzymes

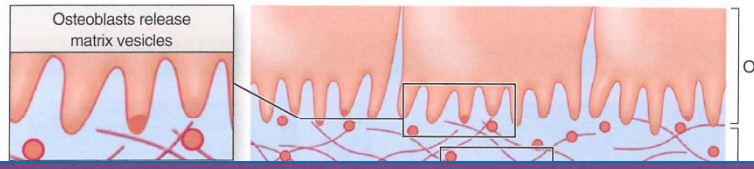
Enhance PO4- concentration

PO4- & Ca2+

Hydroxyapatite crystals [Ca10 (PO4)6 (OH)2]

Collagen & proteoglycans

FIGURE **8–4** **Mineralization in bone matrix.**



» MEDICAL APPLICATION

Cancer originating directly from bone cells (a primary bone tumor) is fairly uncommon (0.5% of all cancer deaths), although a cancer called **osteosarcoma** can arise in osteoprogenitor cells. The skeleton is often the site of secondary, **metastatic tumors**, however, arising when cancer cells move into bones via small blood or lymphatic vessels from malignancies in other organs, most commonly the breast, lung, prostate gland, kidney, or thyroid gland.

From their ends adjacent to the matrix, osteoblasts secrete type I collagen, several glycoproteins, and proteoglycans. Some of these factors, notably osteocalcin and certain glycoproteins, bind Ca^{2+} with high affinity, thus raising the local concentration of these ions. Osteoblasts also release very small membrane-enclosed **matrix vesicles** with which alkaline phosphatase and other enzymes are associated. These enzymes hydrolyze PO_4^- ions from various macromolecules, creating a high concentration of these ions locally. The high ion concentrations cause calcified nanocrystals to form in and around the matrix vesicles. The crystals grow and mineralize further with formation of small growing masses of calcium hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$], which surround the collagen fibers and all other macromolecules. Eventually the masses of hydroxyapatite merge as a confluent solid bony matrix as calcification of the matrix is completed.

Osteocytes

- surrounded by their secreted matrix
- Differentiated to osteocytes
- Singly in lacunae
- Long dendritic process in canalicules
- Gap j.
- Less RER, Golgi ap., more condensed chromatin

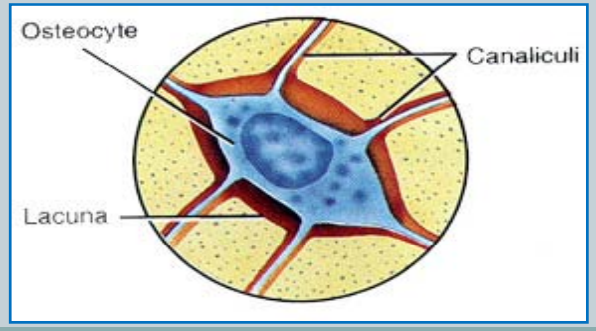
Function:

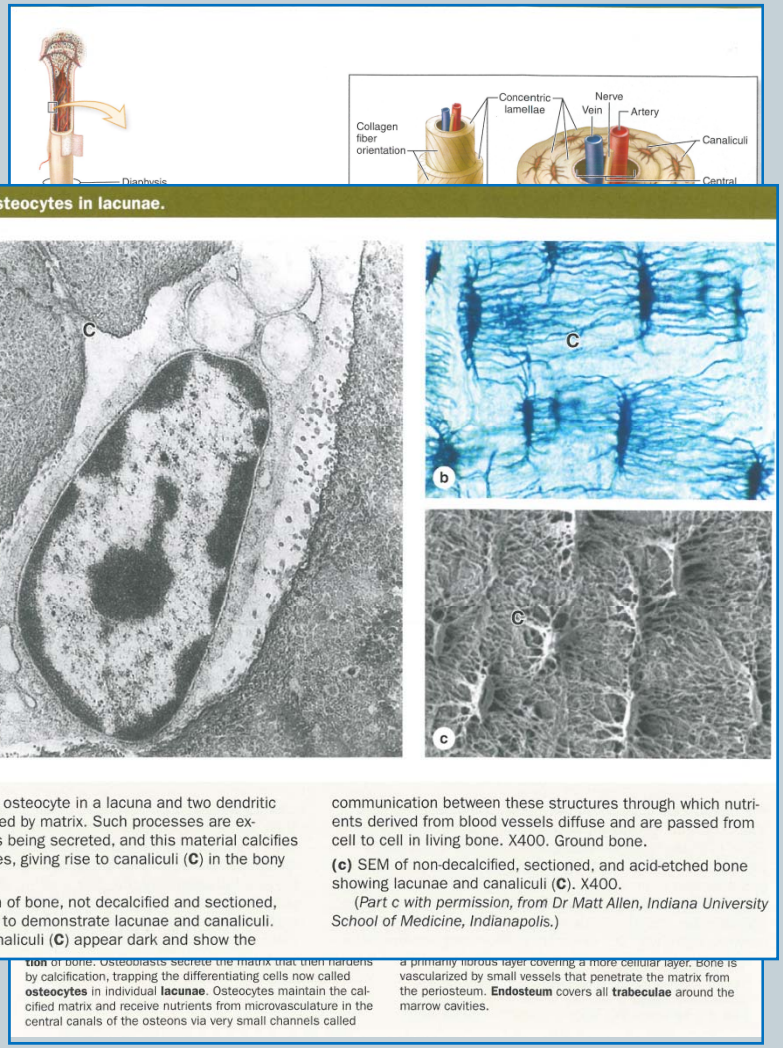
- Matrix protection
- Different gene expression

Sclerostin

Cytokines

Bone modeling regulation





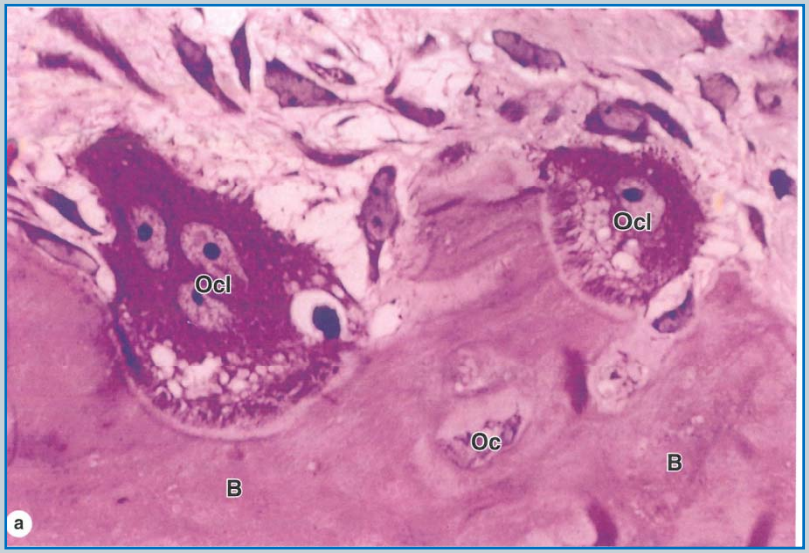
- Dendritic processes
- Have sensor for mechanical stress
- Lack of exercise & weightlessness
- Decreased bone density

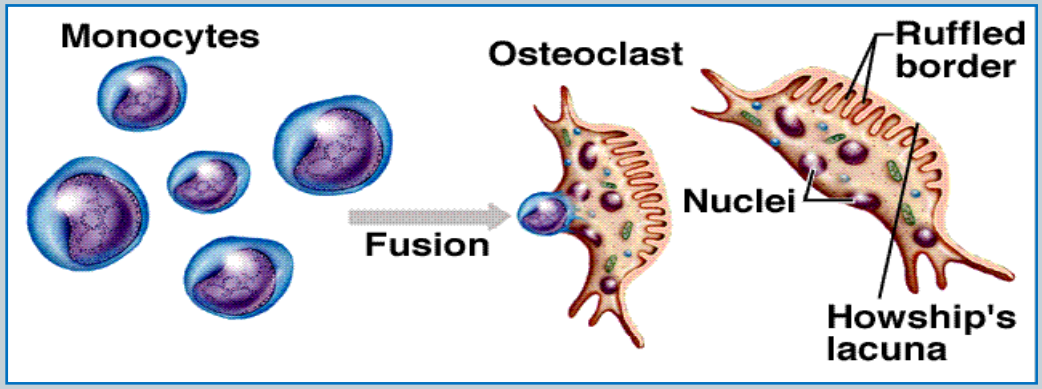
>> MEDICAL APPLICATION

The network of dendritic processes extending from osteocytes acts as a sensor detecting **mechanical stresses** on bone, monitoring areas within bones where loading has been increased or decreased, and maintaining the adjacent bone matrix accordingly. **Lack of exercise** or the weightlessness experienced by astronauts leads to **decreased bone density**.

Osteoclasts

- Big cell
- Multiple nuclei
- Matrix resorption
- Fusion of bone marrow derived cell

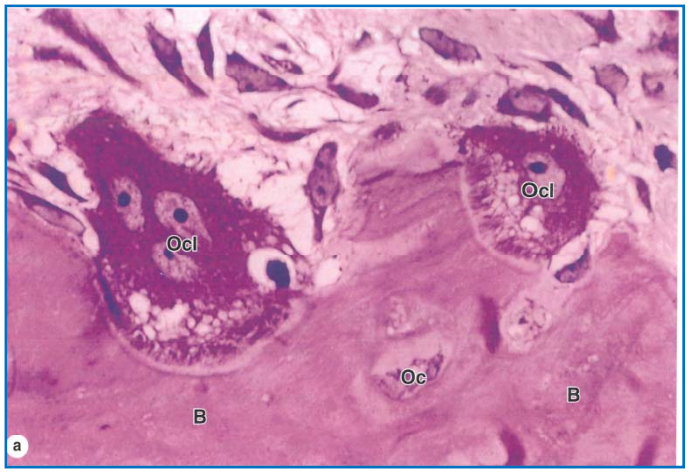


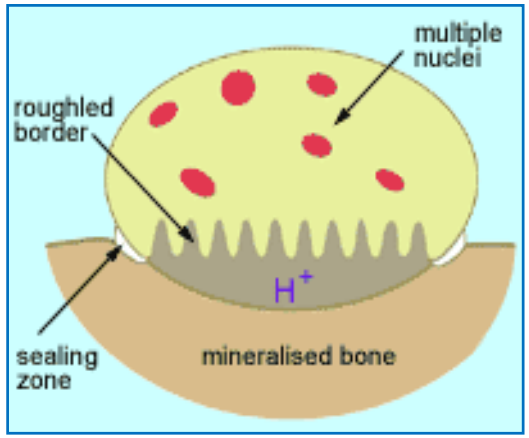


Osteoclasts

Osteoclast development by:

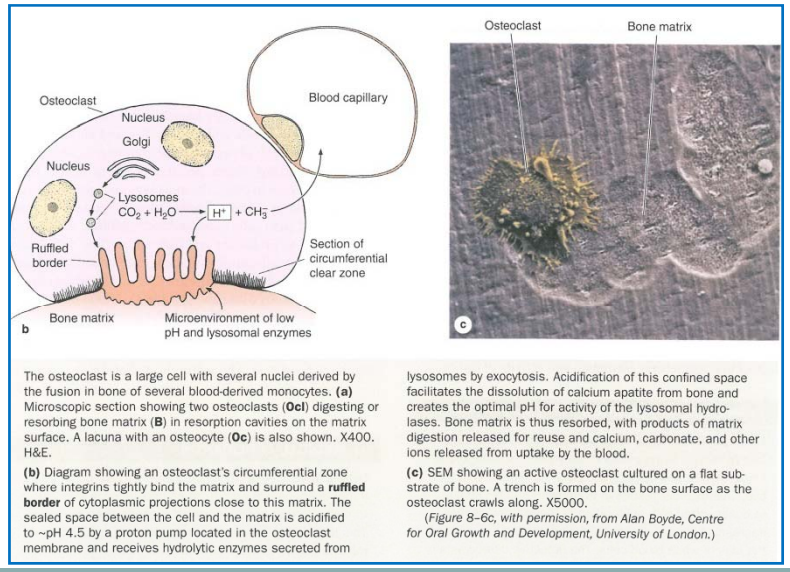
- Macrophage colony stimulating factor (M-CSF)
- Receptor activator of nuclear factor-KB ligand (RANKL)
- Resorption cavities (howship lacunae)
- Ruffled border (Actin rich area for bone absorption)





Osteoclast secret:

- Collagenase
- Cathepsin K
- Pump protein for hydroxyapatite & protons digestion



The osteoclast is a large cell with several nuclei derived by the fusion in bone of several blood-derived monocytes. **(a)** Microscopic section showing two osteoclasts (**Ocl**) digesting or resorbing bone matrix (**B**) in resorption cavities on the matrix surface. A lacuna with an osteocyte (**Oc**) is also shown. X400. H&E.

(b) Diagram showing an osteoclast's circumferential zone where integrins tightly bind the matrix and surround a **ruffled border** of cytoplasmic projections close to this matrix. The sealed space between the cell and the matrix is acidified to ~pH 4.5 by a proton pump located in the osteoclast membrane and receives hydrolytic enzymes secreted from lysosomes by exocytosis. Acidification of this confined space facilitates the dissolution of calcium apatite from bone and creates the optimal pH for activity of the lysosomal hydrolases. Bone matrix is thus resorbed, with products of matrix digestion released for reuse and calcium, carbonate, and other ions released from uptake by the blood.

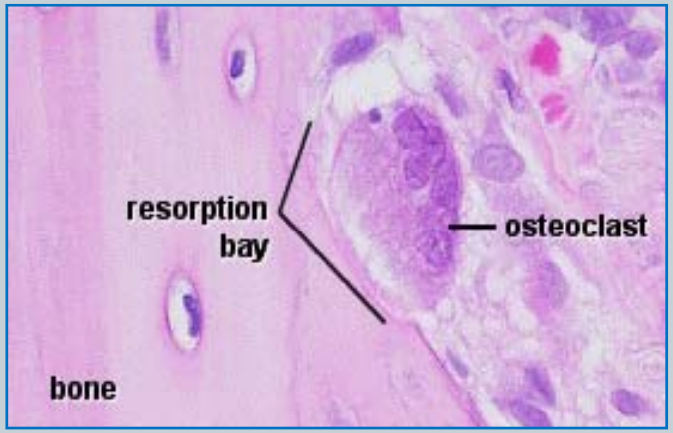
(c) SEM showing an active osteoclast cultured on a flat substrate of bone. A trench is formed on the bone surface as the osteoclast crawls along. X5000.

(Figure 8–6c, with permission, from Alan Boyde, Centre for Oral Growth and Development, University of London.)

Osteoclast function

Regulated by:

- Receptor for **calcitonin**
- No receptor for PTH
- Inderectly by **M-CSF** & **RANKL** of osteoblast
- Osteoblasts have receptor for PTH



Osteopetrosis:

- No Ruffled border
- No H+ pump
- Bone thikenning

>> MEDICAL APPLICATION

In the genetic disease **osteopetrosis**, which is characterized by dense, heavy bones ("marble bones"), the osteoclasts lack ruffled borders and bone resorption is defective. This disorder results in overgrowth and thickening of bones, often with obliteration of the marrow cavities, depressing blood cell formation and causing anemia and the loss of white blood cells. The defective osteoclasts in most patients with osteopetrosis have mutations in genes for the cells' proton-ATPase pumps or chloride channels.

Bone matrix

Inorganic part (50%)

- Calcium hydroxyapatite(hydrated)
- Bicarbonate
- Citrate
- Mg2+
- K+
- Na+
- Amorph calcium phosphate

Organic part:

- Collagen 1
- Proteoglycans
- Glycoproteins

Osteonectin

Ca2+ binding glycoprotein

Osteocalcin, phosphatase

Endosteum & periosteum

- Priosteum like perichondrium

- **External layer**

Dense connective tissue
Small vessel
Collagen bundle
Fibroblasts

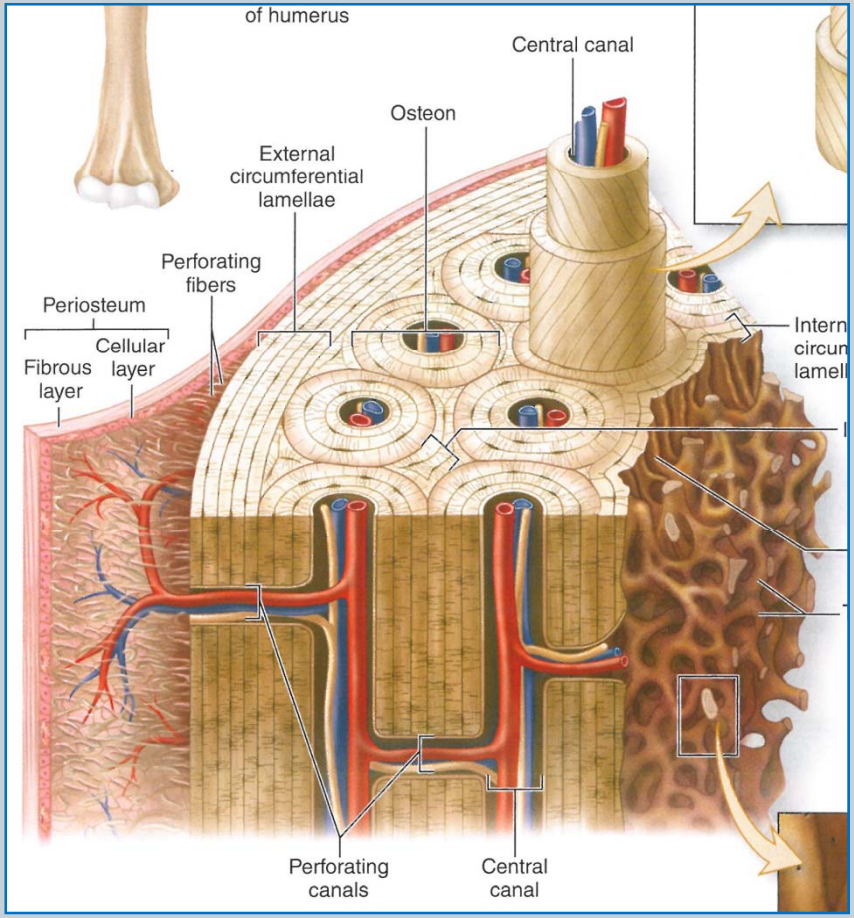
Periosteum bind to bone matrix by:
Perforating or sharpey fibers (periosteal collagen bubdles)

- **Internal layer**

More cells
Bone covering cells
Osteoblast
Osteoprogenitor cell

Periosteum function:
Bone nourishment
New osteoblast supply

Appositional bone growth
repair



Endosteum

- Thin layer
- Cover trabeculae
- Contain:

Osteoprogenitor cells

Osteoblasts

Bone lining cells

Osteoporosis:

- Immobilized & postmenopausal
- Bone turnover
- Calcium loss
- ↓ bone mineral density
- Dual-energy X-ray absorbtiometry

>> MEDICAL APPLICATION

Osteoporosis, frequently found in immobilized patients and in postmenopausal women, is an imbalance in skeletal turnover so that bone resorption exceeds bone formation. This leads to calcium loss from bones and reduced **bone mineral density** (BMD). Individuals at risk for osteoporosis are routinely tested for BMD by **dual-energy x-ray absorptiometry** (DXA scans).

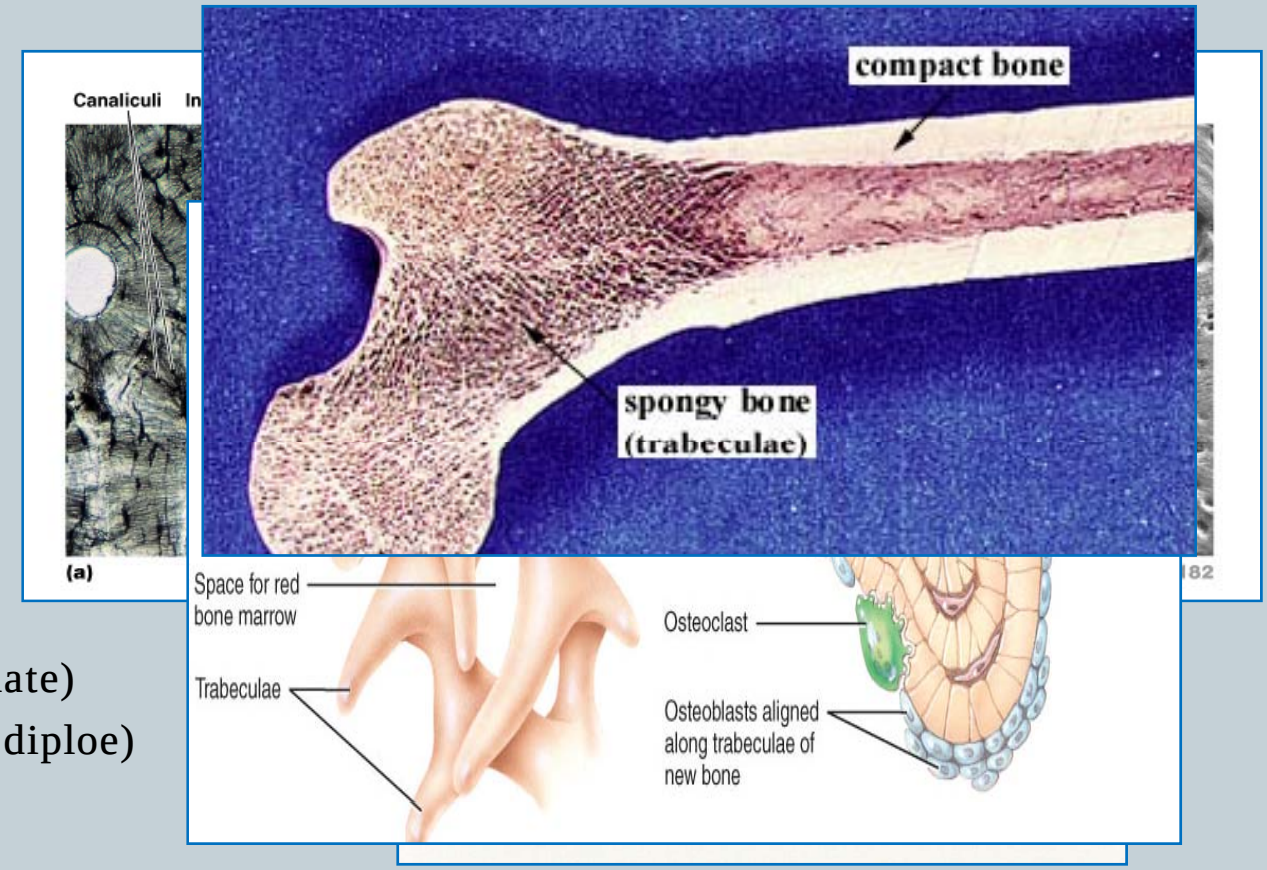
Bone types

1. **Compact or cortical bone (80%)**
2. **Cancellus, trabecular or spongy bone (20%)**

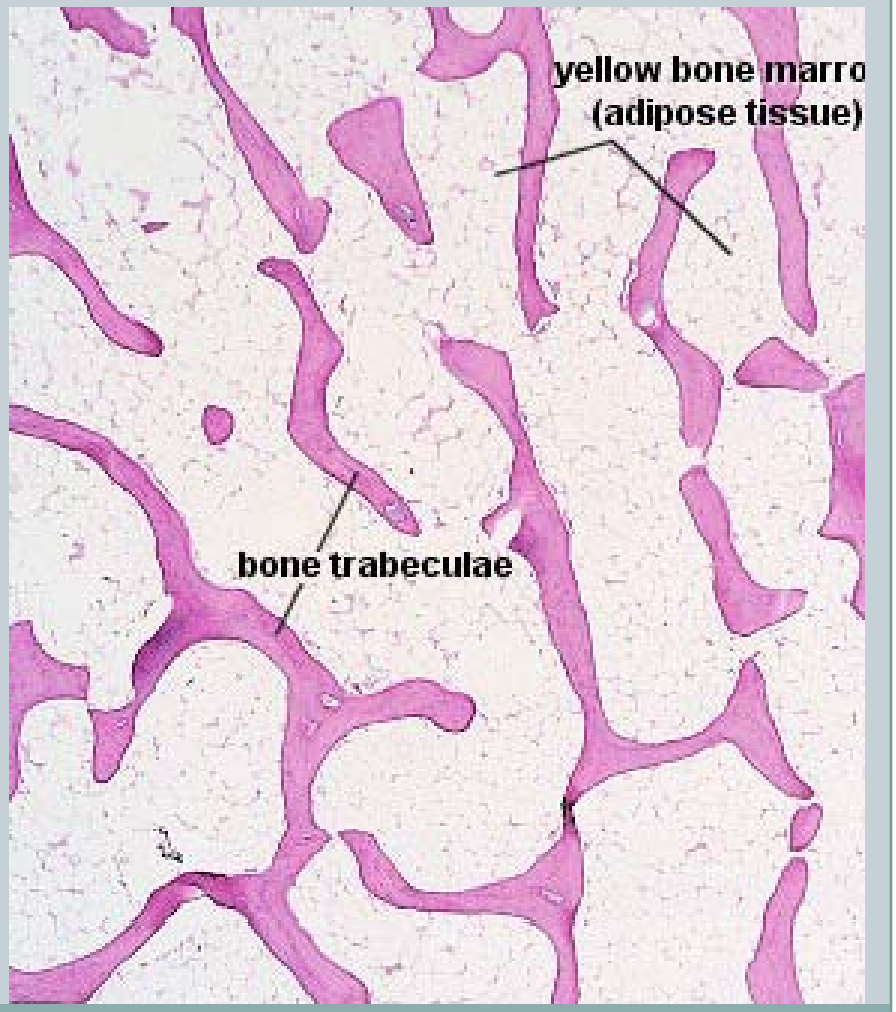
In long bone:
Epiphysis
Diaphysis

In Short bone:
spongy bone in center
Covered by compact bone

In flat bone:
2 layers of compact bone (plate)
thick layer of spongy bone (diploe)



Compare compact and spongy bone (light microscope)



Bone tissue organization

- Lamellar bone
- Woven bone

Lamellar bone

- In adult
- Multiple (4-10) layers or lamellae (each 3-7 µm)
- Parallel or Around central canal
- Parallel layer of collagen fibers

Osteon or Haversian system

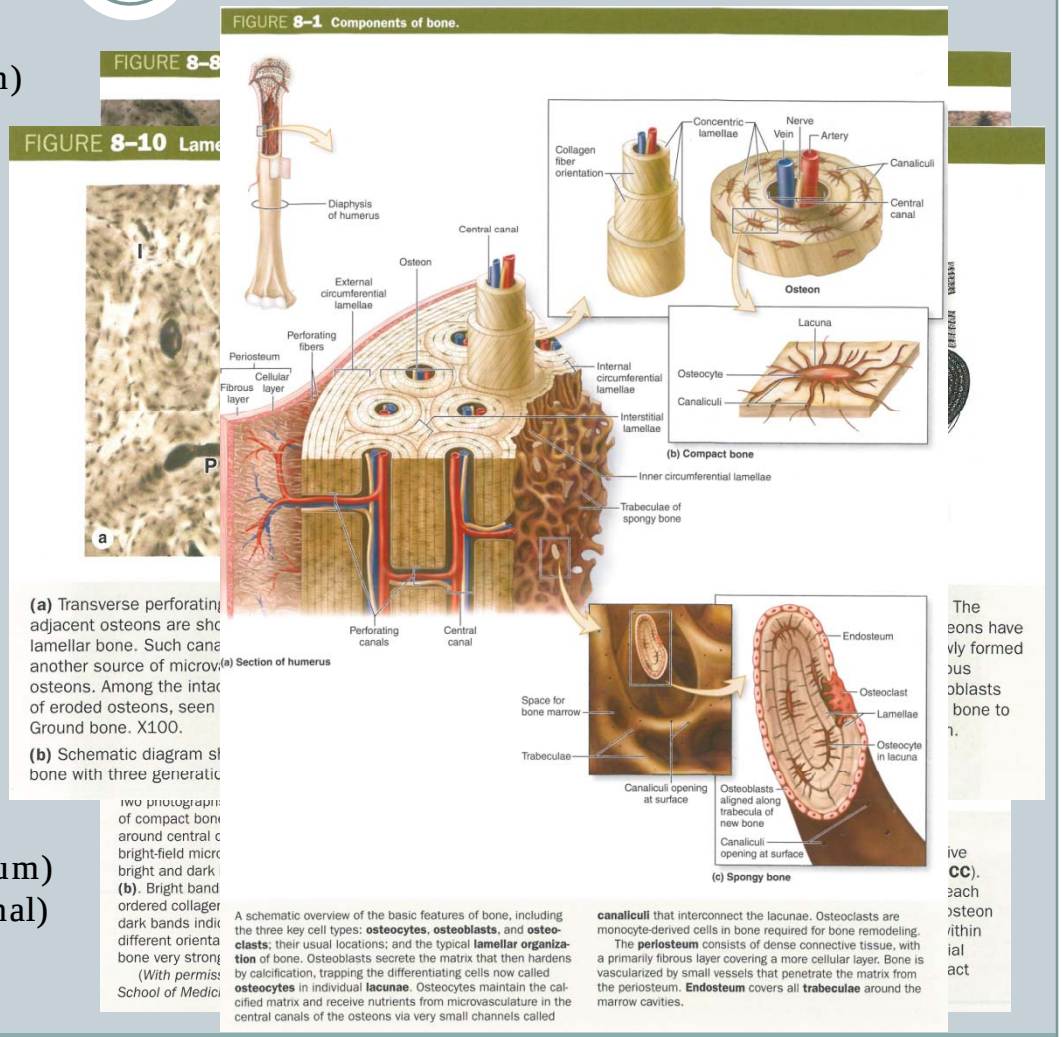
- Multiple layers around central canal
- With vessel & nerve
- Loose connective tissue
- Endosteum
- Outer boundry (cement line)

Rich collagen layer

Perforating (volkman) canal
Central canal no or less lamellar layer

Interstitial lamellae between osteons (old osteon)

In compact bone (diafhysis):
External circumferential lamellae (under periosteum)
Inner circumferential lamellae (around central canal)



Bone remodeling

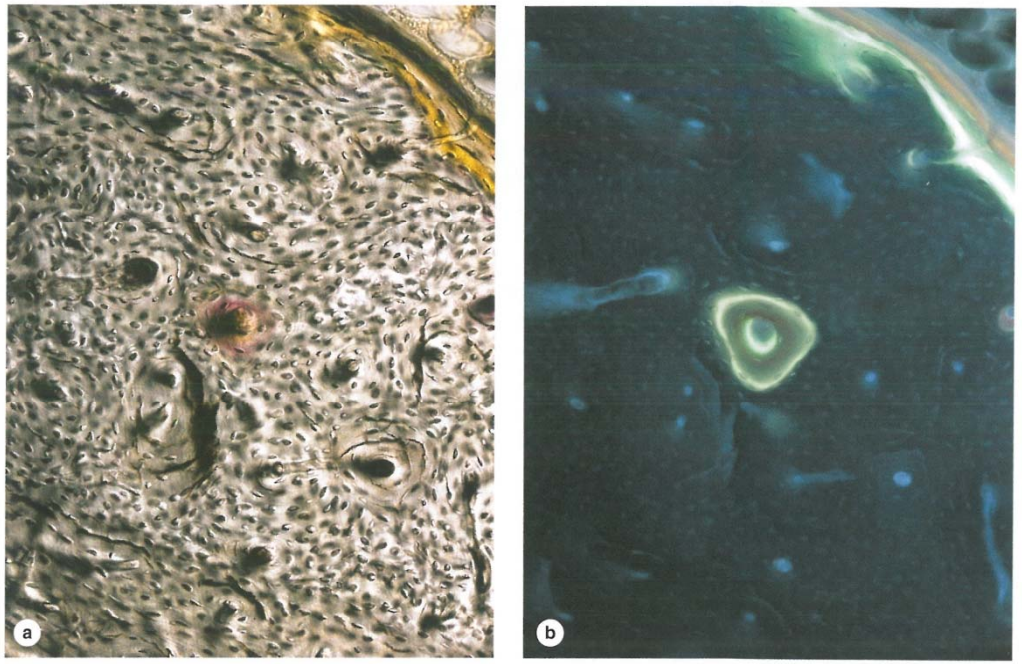
- Continuous bone absorption & formation
- In adults (5-10%)
- Osteoclasts
- New osteon

- Tetracycline

>> MEDICAL APPLICATION

The antibiotic **tetracycline** is a fluorescent molecule that binds newly deposited osteoid matrix during mineralization with high affinity and specifically labels new bone under the UV microscope (Figure 8–12). This discovery led to methods for measuring the rate of bone growth, an important parameter in the diagnosis of certain bone disorders. In one technique tetracycline is administered twice to patients, with an intervening interval of 11-14 days. A bone biopsy is then performed, sectioned without decalcification, and examined. Bone formed while tetracycline was present appears as fluorescent lamellae and the distance between the labeled layers is proportional to the rate of bone appositional growth. This procedure is of diagnostic importance in such diseases as **osteomalacia**, in which mineralization is impaired, and **osteitis fibrosa cystica**, in which increased osteoclast activity results in removal of bone matrix and fibrous degeneration.

FIGURE 8- FIGURE **8–12** **Tetracycline localization of new bone matrix.**



Newly formed bone can be labeled with the molecule tetracycline, which forms fluorescent complexes with calcium at ossification sites and provides an in vivo tracer to localize bone formation. A group of osteons in bone after tetracycline incorporation in vivo seen with bright-field **(a)** and fluorescent microscopy **(b)** reveals active ossification in one osteon and the external circumferential lamellae (upper right).
(With permission, from Dr Matt Allen, Indiana University School of Medicine, Indianapolis.)

Histology of Spongy Bone

Trabeculae instead of osteons

- lattice of spines, rods, plates
- Develop along lines of stress
- Still lamellar, but no central canals

Bone marrow

- In space between trabeculae
- Osteocytes are close to marrow blood supply

Found

in ends of long bones and inside flat bones such as the hipbones, sternum, sides of skull, and ribs.

Woven bone

- Nonlamellar
- Collagen I fibers (random disposition)

- First bone tissue:

Embryonic development
Fracture repair

Temporary tissue

In adults only in:
Near sutures of calvaria
Insertion of some tendons

Less organic substace
More osteocytes