

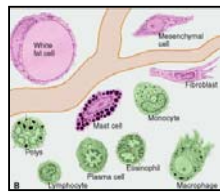
## Connective Tissues

### Connective tissues

- Tissues specialized for maintenance of integrity and support of organs
- Made from matrix proteins and cells in different composition and proportions
- Loose, dense or specialized such as bone or cartilage

### Two classes of connective tissue cells

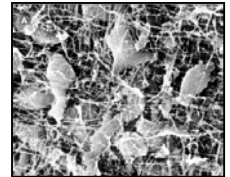
- Indigenous
- Immigrant



- Functions
  - Produce extracellular matrix
  - Defend against infections
  - Storage of foodstuffs in form of easily accessible fats

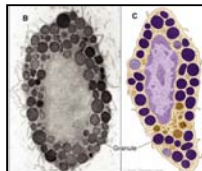
### Indigenous cells of connective tissue

- Undifferentiated mesenchymal cells
  - Proliferate and differentiate into fibroblasts, fat cells, chondrocytes
- Fibroblasts
  - Spindle shaped cells with big ER and Golgi
  - Synthesize most of ECM molecules (especially collagen)
  - Proliferate and migrate in response to tissue injury



### Indigenous cells of connective tissue

- Mast cells
  - Immune cells
  - Mediate immediate hypersensitivity reactions
  - Secrete histamine and proteases
    - Cause plasma extravasation (oedema), itching
  - Activated by IgE receptors crosslinked by antigen

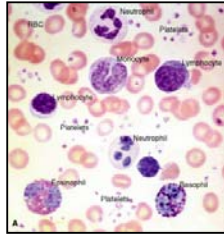


### Indigenous cells of connective tissue

- Adipocytes (white fat cells)
  - Mostly just under the skin
  - Store lipids in the form of single droplet
  - Effector cells for insulin
  - Take up glucose and synthesize triglycerides for storage in the lipid droplet
  - Also endocrine organ – secrete leptin, a hormone responsible for appetite regulation
- Different from brown fat cells that oxidize lipids to produce heat

## Immigrant cells of connective tissue

- Blood cells
  - Granulocytes
  - Monocytes and macrophages
  - Neutrophils
  - Lymphocytes
  - Basophils
  - Eosinophils
- All derive from a stem cell in bone marrow



## Loose connective tissue

- Underlies epithelia in “soft” places such as GI tract and lungs
- Found around organs
- Few fibers, some cells, sparse ECM
- ECM of hyaluronan and proteoglycans supported by collagen and elastic fibers
- Cells – mostly fibroblasts and migratory immune cells, adipocytes

## Vitreous body of the eye

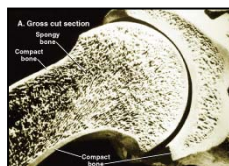
- A special case of very loose connective tissue
- Hyaluronan and proteoglycans supported by collagen II

## Dense connective tissue

- Lots of strong fibers, predominantly collagen
- Few cells, mostly fibroblasts
- Dependent on composition can be as hard as a bone or elastic as in skin
- Collagen can be arranged precisely such as in tendon or cornea or scattered as in skin
- Dense connective tissue can also be elastic (collagen and elastic fibers) as in skin or large arteries

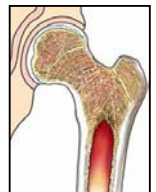
## Bone

- Connective tissue that provides mechanical support and protection
- Mostly calcified matrix with few cells
- Very important storage of calcium
- Mechanical strength derived both from composition and overall organization
- Spongy or compact



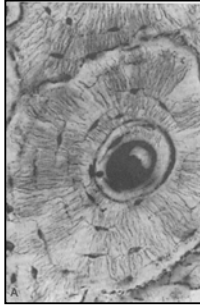
## Two components of the bone

- Compact = cortical Bone
  - Runs the length of the long bones, forming a hollow cylinder
- Spongy = trabecular bone
  - Has a light, honeycomb structure
  - Trabeculae are arranged in the directions of tension and compression
  - Occurs in the heads of the long bones
  - Also makes up most of the bone in the vertebrae



## Chemistry of the bone

- Cells
- Extracellular matrix
  - Osteoid – uncalcified bone matrix
  - Mineral
- Organized in rounded structures called osteons



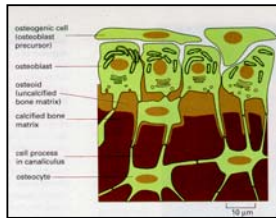
## Osteons

- Principal organizing feature of compact bone
- Haversian canal – place for the nerve blood and lymphatic vessels
- Lamellae – collagen deposition layers
- Osteocytes (bone cells) localized in lacunae



## Bone cells

- Osteocytes
- Osteoblasts and osteoclasts
  - Derived from osteoprogenitor cells



## Osteocytes

- Trapped osteoblasts
- Keep bone matrix in good condition and can release calcium ions from bone matrix when calcium demands increase
- Connected to each other by long filopodia that run through narrow channels in calcified matrix – canaliculi

## Osteoblasts

- Make collagen – well developed secretory organelles
- Activate crystallization of hydroxyapatite onto the collagen matrix, forming new bone
- As they become enveloped by the collagenous matrix they produce, they transform into osteocytes

## Osteoclasts

- Resorb bone matrix from sites where it is deteriorating or not needed
- Multinucleated giant cells
- Focal decalcification and extracellular digestion by acid hydrolases and uptake of digested material
- Attach to the surface of the bone via integrins
- Absorption by production of HCl by V-type proton pump and chloride channels

## Extracellular matrix of the bone - osteoid

- Collagen type I arranged in a mesh
- Layers of various orientations (add to the strength of the matrix)
- Other proteins 10% of the bone protein
  - Direct formation of fibers
  - Enhance mineralization
  - Provide signals for remodeling



## Mineral

- A calcium phosphate/carbonate compound resembling the mineral hydroxyapatite  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$
- Hydroxyapatite crystals
  - Imperfect
  - Contain Mg, Na, K



## Mineralization of the bone

- Calcification occurs by extracellular deposition of hydroxyapatite crystals
  - Trapping of calcium and phosphate ions in concentrations that would initiate deposition of calcium phosphate in the solid phase, followed by its conversion to crystalline hydroxyapatite
  - Mechanisms exist to both initiate and inhibit calcification



## Bone formation

- Osteoblast synthesize and secrete type I collagen
- Collagen molecules form fibrils
- Fibrils stagger and overlap themselves
- Mineral deposition
- Fibers join to form the framework



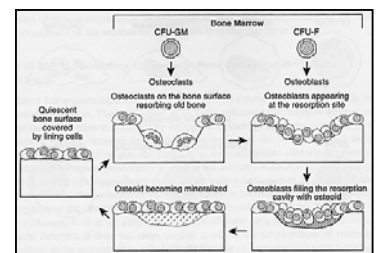
## Bone remodeling process

- Constant process
- Proceeds in cycles - first resorption than bone formation
- The calcium content of bone turns over with a half-time of 1-5 years



## Bone remodeling

- Sequential processes of resorption and formation



## Coordination of resorption and formation



- 3 phase process of bone remodeling
- Phase I
  - Signal from osteoblasts
  - Precursor stimulation to become osteoclasts
  - Process takes 10 days

## Coordination of resorption and formation



- Phase II
  - Osteoclast resorb bone creating a cavity
  - Macrophages clean up
- Phase III
  - New bone laid down by osteoblasts
  - Takes 3 months

## Diseases of bone remodeling



- Osteoporosis – too much resorption
- Osteopetrosis – failure of resorption – defective osteoclasts
- Osteogenesis imperfecta – multiple bone fractures due to defective bone formation

## What is osteoporosis?



- Defined as a condition characterized by low bone mass and deterioration of bone tissue, leading to enhanced bone fragility and an increase in fracture risk
- Mechanisms causing osteoporosis
  - Imbalance between rate of resorption and formation
  - Failure to complete 3 stages of remodeling
- Disease or not?
  - The bone composition is normal there is just less of it

## Did you know?



- Over 27 million or 1 of 3 women are affected with osteoporosis
- Over 5 million or 1 of 5 men are affected with osteoporosis

## WHO guidelines for determining osteoporosis



- Normal
  - Not more than 1 SD below the average for young adults
- Osteoporosis
  - More than 2.5 SD below the young adult average

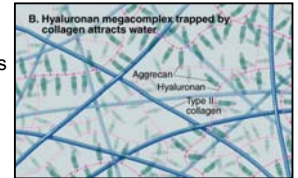
## Cartilage

- Very resilient connective tissue
- Covers the articular surfaces of joints
- Supports large airways, nose, ears etc
- Also embryonic precursor of bone during embryonic development
- Primarily glycosaminoglycans with few fibers and very few cells



## Cartilage

- ECM of collagen II crosslinked by collagen IX
- Lots of glycosaminoglycans and hyaluronan
  - Organized in megacomplexes
  - Hydration increases pressure resilience
- Cells – chondrocytes
  - Synthesize ECM
  - Limited turnover abilities



## Growth of cartilage

- Grows by expansion of extracellular matrix
- Chondrocytes trapped inside the cartilage can also divide
- Regulated by many growth factors and hormones



## “Elastic” cartilage

- Also called fibrocartilage
- Has elastic fibers in addition to collagen
- Supports structures that move
  - Larynx
  - External ear
- A lot of collagen fibers (as in dense connective tissue) and a glycosaminoglycan matrix (cartilage)

