Bone Formation, Growth, and Remodeling
Pre-natal Ossification

Embryonic skeleton:

- fashioned from fibrous membranes or cartilage to accommodate mitosis.

- 2 types of pre-natal **ossification** (bone formation)

1. **Intramembranous**
   - Bone develops from fibrous membrane
   - Forms bones of skull and clavicle (all flat bones)
   - Begins at 8 weeks of development

2. **Endochondral**
   - Bone develops from hyaline cartilage
   - Forms all bones below base of skull
   - Begins 2nd month of development
Intramembranous Ossification
(prenatal)

Mesenchymal cells create fibrous CT framework for ossification

Some mesenchymal cells differentiate into osteoblasts in an ossification center

Osteoblasts secrete bone matrix, osteoid
Intramembranous Ossification
(prenatal)

Mineralization and calcification of osteoid

Trapped osteoblasts become osteocytes
Intramembranous Ossification (prenatal)

Osteoid accumulates in between embryonic blood vessels, creating trabeculae of woven bone.

Mesenchyme on bone face condense and differentiate into periosteum.
Intramembranous Ossification
(prenatal)

A bone collar of thickly woven osteoid forms around trabeculae and ossifies into compact bone.

Spongy bone (diploë) cavities made up of trabeculae fill with red marrow created from vessels (vascular tissue).
Endochondral Ossification

Bone collar formed around diaphysis by osteoblasts located on inner side of periosteum
Endochondral Ossification

Cartilage in primary ossification center calcifies, then the cells die and cavities form (cavitates)

Bone collar provides stability during cavitation

Cartilage elsewhere continues to elongate
Endochondral Ossification

Periosteal bud (lymph, blood vessels, nerves, red marrow, osteoblasts and osteoclasts) enters cavity and builds spongy bone.
Endochondral Ossification

Osteoclasts dissolve spongy bone to create medullary cavity

Secondary Ossification Center forms in epiphysis
Endochondral Ossification

Hyaline only remains on epiphyseal surface (articular cartilage) and at diaphysis and epiphysis junction, to form the epiphyseal plates.

Secondary Ossification Center does NOT calcify. Spongy bone retained.
Endochondral Ossification:
the process by which most bones in the body grow.

Growing taller throughout childhood!
Growing Taller!
(A closer look at the epiphyseal plate)

Lots of activity!
Growing Taller!
(A closer look at the epiphyseal plate)

- rapidly mitotic cartilage, lengthening bone; **chondrocytes** form columns

- enlarging size of chondrocytes (hypertrophy)

- matrix of cartilage calcifies and cells die forming spiky tips

- spiky calcified cartilage reshapes into spongy bone, converted into medullary cavity or compact bone later as bone grows.
When does lengthening stop?

- End of adolescence - lengthening stops
  - Chondrocytes stop mitosis.
  - Plate thins out and replaced by bone
  - Diaphysis and epiphysis fuse to be one bone
  - Epiphyseal plate closure (18 yr old females, 21 yr old males)

- Thickening of bone continuous throughout life
Bone growth regulated by hormones

- **Human Growth Hormone (HGH):** from pituitary gland in brain promotes epiphyseal plate activity
- **Thyroid hormones:** regulate HGH for proper bone proportions
- **Puberty:** **Testosterone** or **Estrogen** cause adolescent growth spurt and skeletal differences between the sexes:
  - Wider shoulders, larger bones, narrow pelvis in men
  - Wider hips, smaller upper body in women
- **Excesses in any hormones can cause abnormal skeletal growth**
  - Ex. gigantism or dwarfism
Robert Wadlow, world's tallest man 8 ft 11 inches

Yao Defen, gigantess currently in treatment for pituitary tumor in China. 7 ft 7 inches 396 lbs
Bone Remodeling

• While bone is getting longer, the epiphysis has to continually be reshaped to maintain proportions

• Involves:
  – Dissolving/destroying bone
  – New bone growth

more specific details on how this happens later…
Bone is Dynamic!
Bone is constantly remodeling and recycling

- Coupled process between:
  1. Bone deposition (by osteoblasts)
  2. Bone destruction/resorption (by osteoclasts)
- 5-7% of bone mass recycled weekly
- All spongy bone replaced every 3-4 years.
- All compact bone replaced every 10 years.

Prevents mineral salts from crystallizing; protecting against brittle bones and fractures
Bone Resorption

- Osteoclasts are related to macrophages:
  - secrete lysosomal enzymes and HCl acid
- Move along surface of bone, dissolving grooves into bone with acid and enzymes
- Dissolved material passed through osteoclasts and into bloodstream for reuse by the body
Bone Deposition

• Thin band of osteoid (unmineralized bone) laid down by osteoblasts, located on inner surface of periosteum and endosteum.

• Mineral salts (Ca$^{2+}$ and Pi) are precipitated out of blood plasma and deposited amongst the osteoid fibers.

  - Requires proper Ca$^{2+}$ and Phosphate ion concentration
  - Vitamin D, C, A, and protein from diet

(Poor nutrition will negatively affect bone health)
Bone is a reservoir for Calcium

- Constant supply of Ca$^{2+}$ in the blood stream needed for:
  - Transmission of nerve impulses
  - Muscle contraction
  - Blood coagulation
  - Cell division
- A narrow range of 9-11 mg Ca/100 ml blood maintained at all times.
- Bone remodeling = key in maintaining proper blood calcium levels
Control of Remodeling/Resorption

2 methods

1. (-) feedback, hormonal controls maintain [Ca2+] in blood
2. Mechanical/Gravitational forces on bone
Hormonal Control of Blood Calcium

- $[Ca^{2+}]$ controlled by negative feedback loop

Control of Bone Deposition

Control of Bone Resorption

Calcium homeostasis of blood: 9–11 mg/100 ml
Response to Mechanical/Gravitational Forces

• **Wolff’s Law:**
  – Bones respond to muscles pulling on them (mechanical stress) and to gravity by keeping the bones strong where they are being stressed.

• weight bearing activities → stronger projections where muscles/ligaments attach and thicker bones where there is compression.

• High rate of bone deposition in specific areas.
Do your push-ups...

...to make strong bones!

But don't ever get THIS ridiculous, although I probably have some mighty bones!
Periosteum: double-layered membrane on external surface of bones

**Outer layer:** protective, fibrous dense irregular connective tissue

**Inner layer:** osteogenic stem cells that differentiate (specialize) into bone cells like osteoblasts (bone forming) or osteoclasts (bone dissolving) cells.

Periosteum (review)