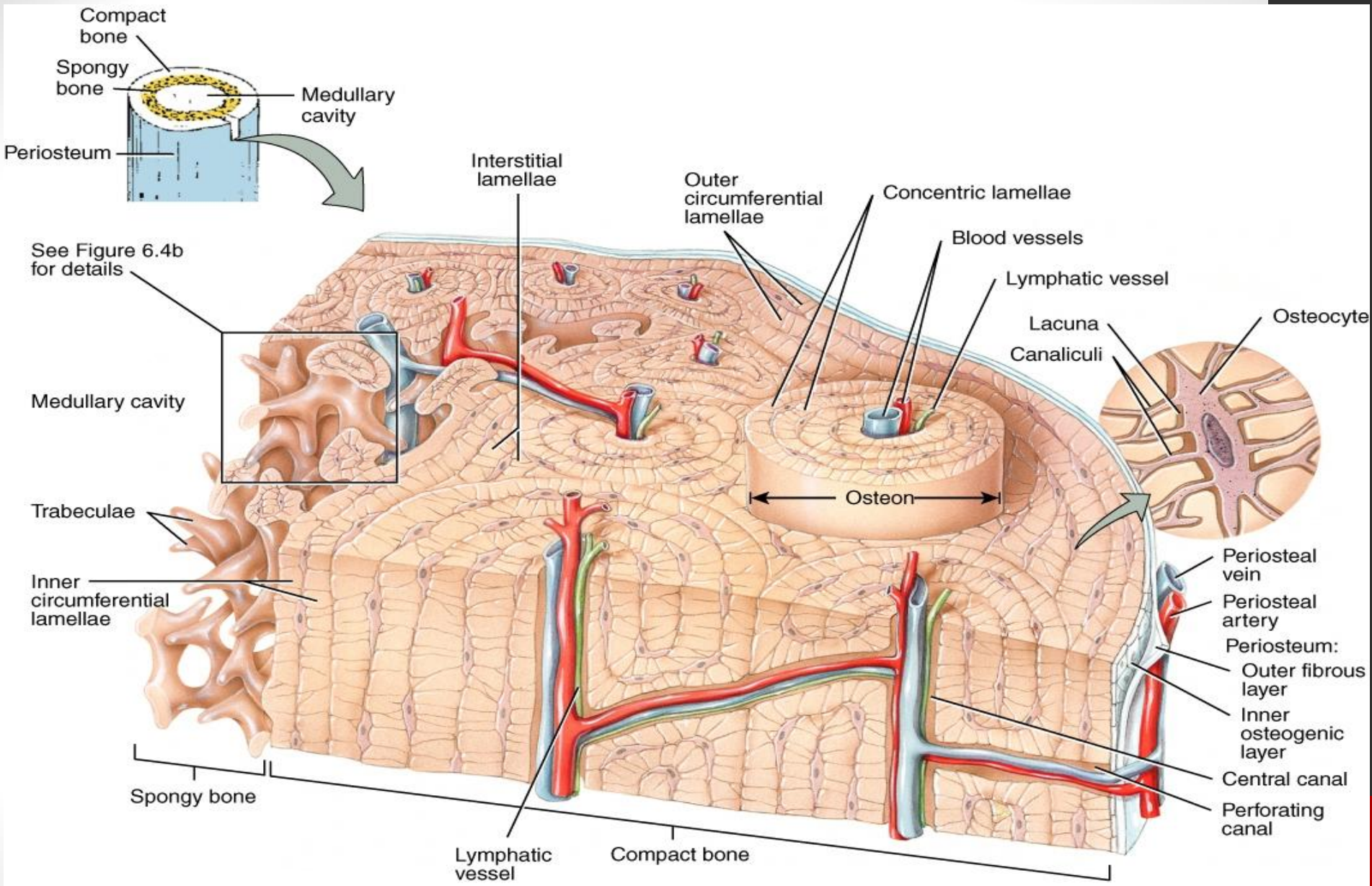
PLEASE CLICK ON THE FOLLOWING LINK TO WATCH THE LECTURE

ONLINE:-

https://www.youtube.com/watch?v=rK2-ikS0-Yg&list=PLuBRb5B7fa_eyBVgz4xb_AqlGcXLIEyRA&index=17

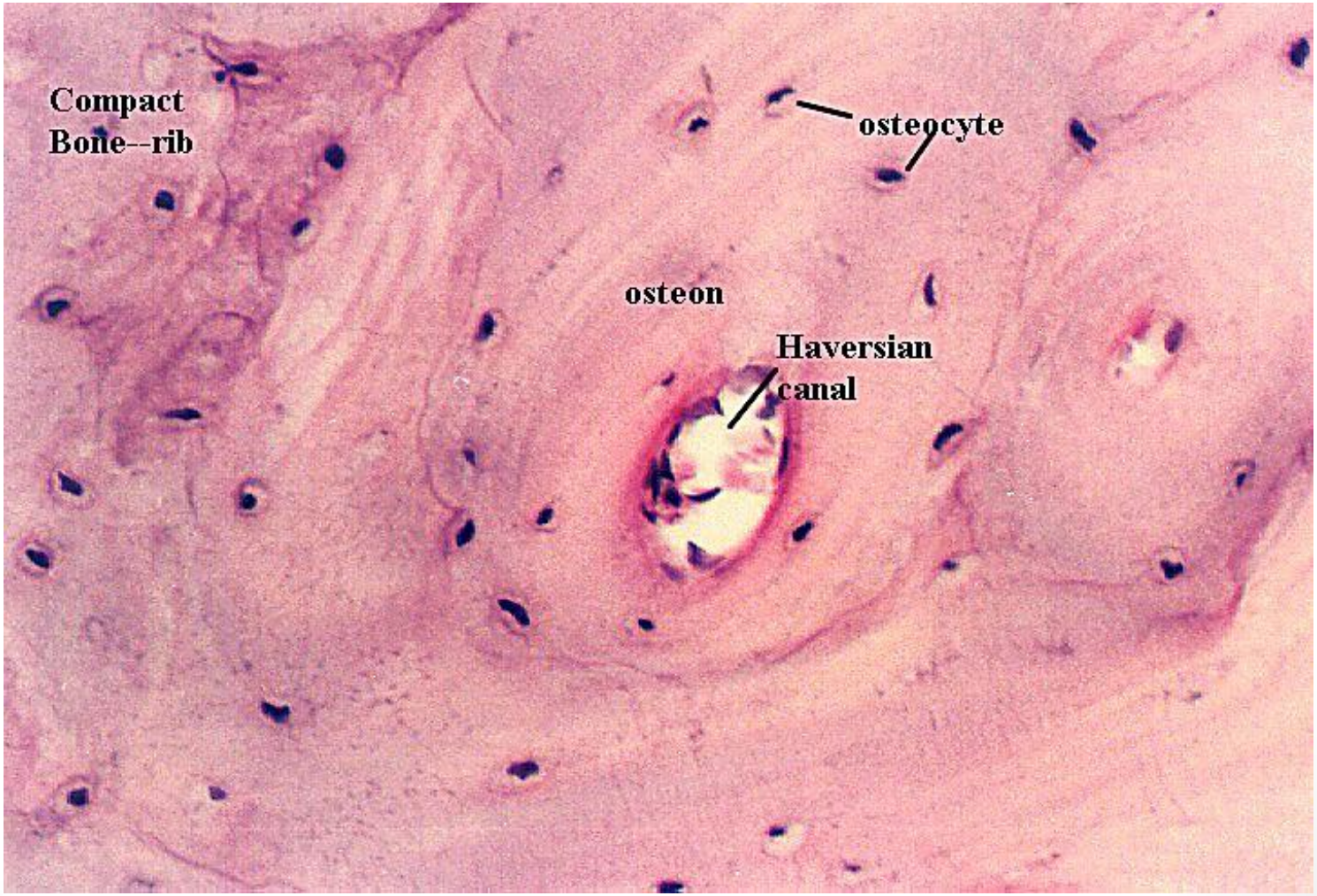
Biology of bone healing

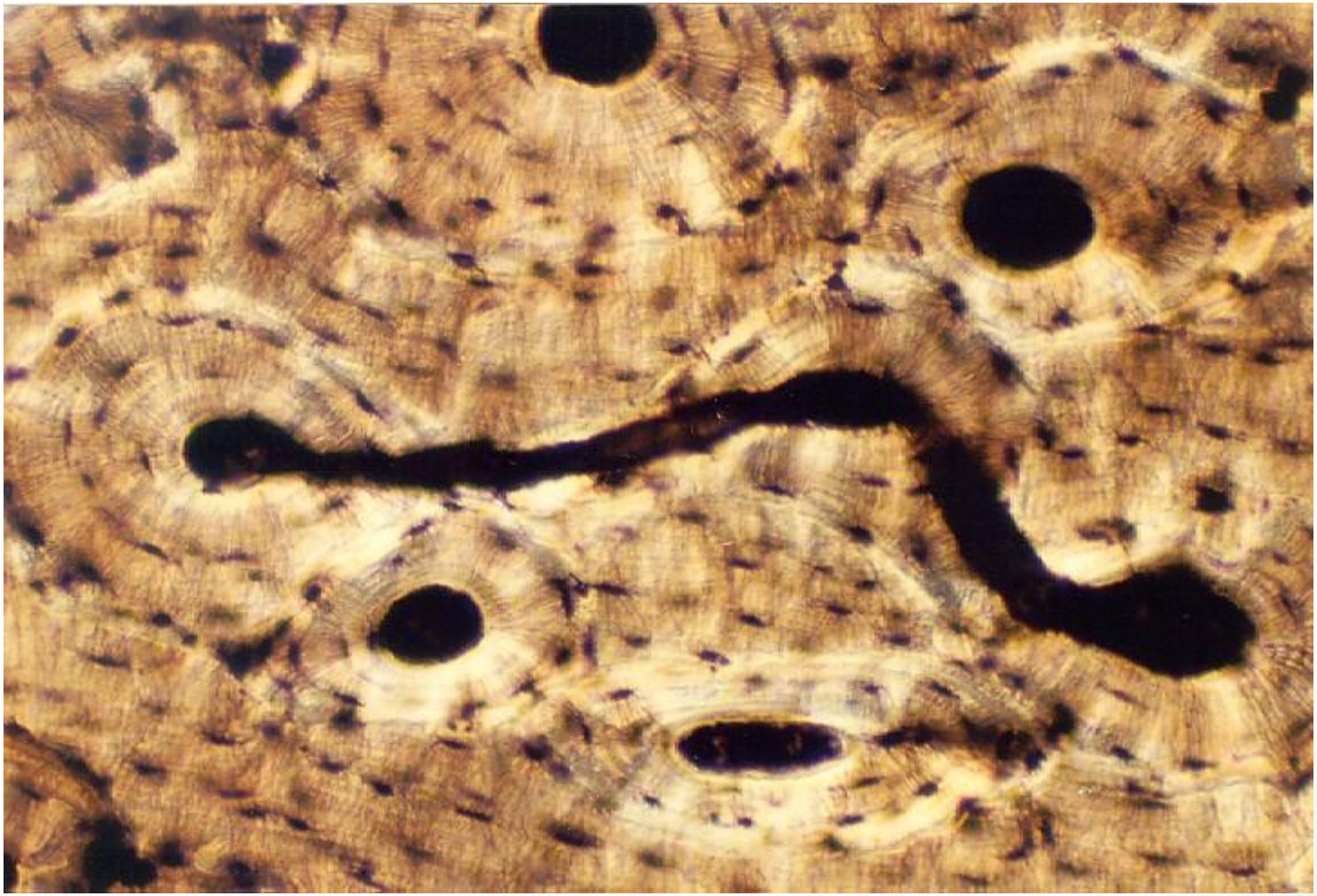
MOHAMMAD ALSAAIDEH



Osteons (Haversian systems) in compact bone and trabeculae in spongy bone

06.03


Compact
Bone--rib
osteocyte
osteon
Haversian
canal

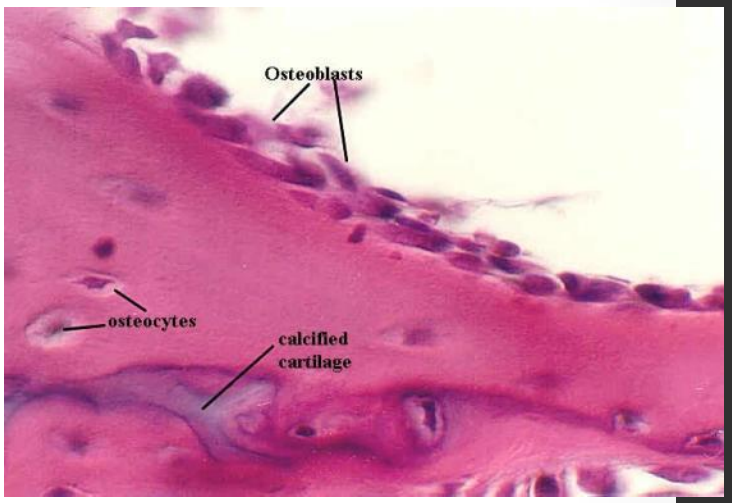


Bone Composition

- Cells
  - Osteocytes
  - Osteoblasts
  - Osteoclasts
- Extracellular Matrix
  - Organic (35%)
    - Collagen (type I) 90%
    - Osteocalcin, osteonectin, proteoglycans, glycosaminoglycans, lipids (ground substance)
  - Inorganic (65%)
    - Primarily hydroxyapatite $Ca_5(PO_4)_3(OH)_2$

Osteoblasts

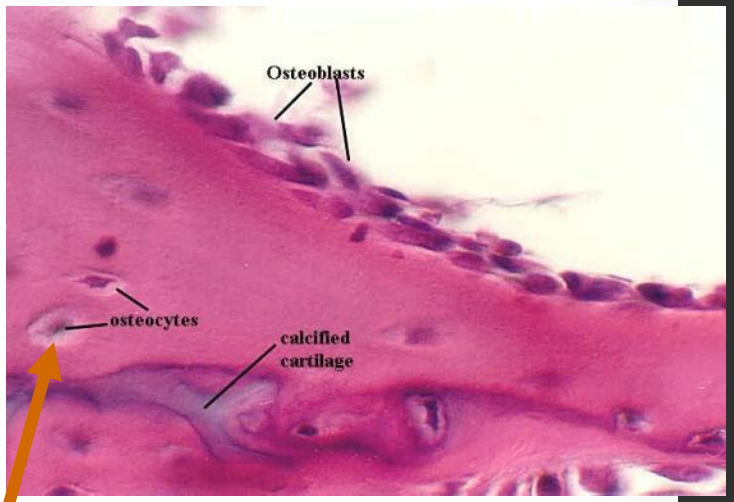
- Derived from mesenchymal stem cells
- Line the surface of the bone and produce osteoid
- Immediate precursor is fibroblast-like preosteoblasts



Picture courtesy Gwen Childs, PhD.

Osteocytes

- Osteoblasts surrounded by bone matrix
  - trapped in lacunae
- Function poorly understood
  - regulating bone metabolism in response to stress and strain



Picture courtesy Gwen Childs, PhD.

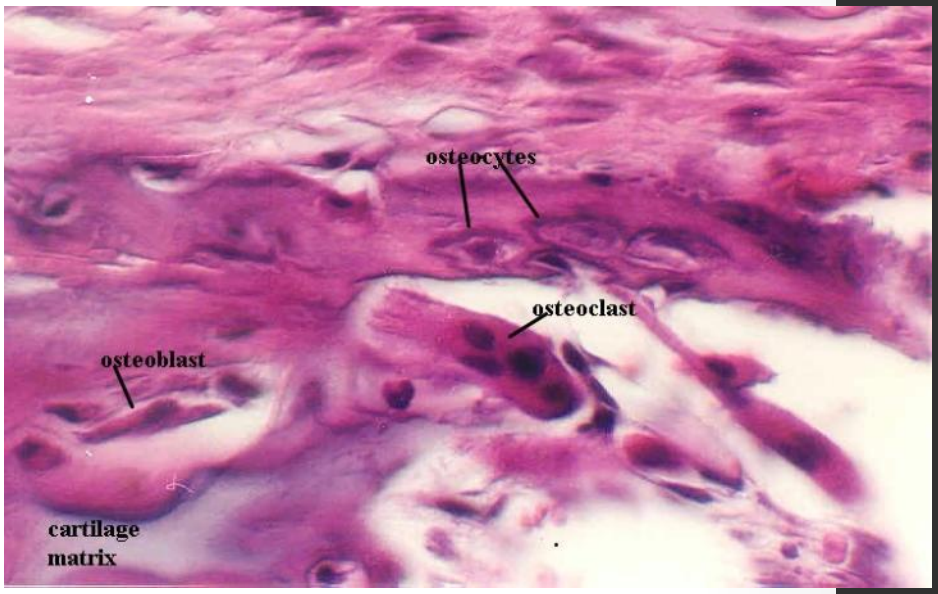
Osteocyte Network

- Osteocyte lacunae are connected by canaliculi
- Osteocytes are interconnected by long cell processes that project through the canaliculi

- Network probably facilitates response of bone to mechanical and chemical factors

Osteoclasts

- Derived from hematopoietic stem cells (monocyte precursor cells)
- Multinucleated cells whose function is bone resorption
- Reside in bone resorption pits (Howship's lacunae)
- Parathyroid hormone stimulates receptors on osteoblasts that activate osteoclastic bone resorption



Picture courtesy Gwen Childs, PhD.

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The healing potential of bone is influenced by a variety of biochemical, biomechanical, cellular, hormonal, and pathological mechanisms.

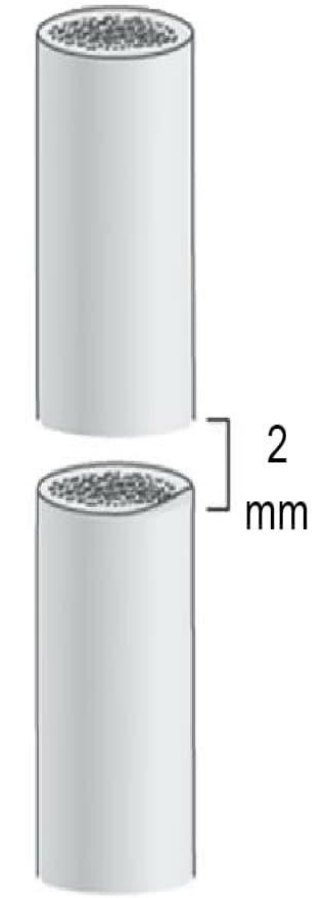
Prerequisites for Bone Healing

- Adequate blood supply
- Adequate mechanical stability

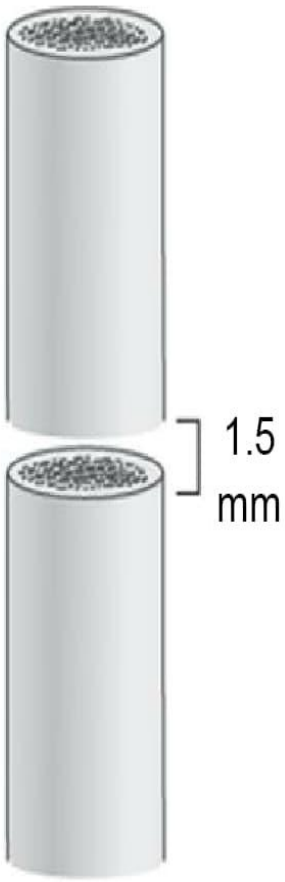
- Fracture stability dictates the type of healing that will occur

- mechanical stability governs the mechanical strain

Strain



Original
width = 2 mm



Width after
load = 1.5 mm

$$\text{Strain} = \frac{\text{Change in gap width (.5 mm)}}{\text{Original width (2 mm)}} = 25\%$$

Modes of bone healing

- primary bone healing (strain is < 2%)
- Secondary bone healing (strain 2% - 10 %)

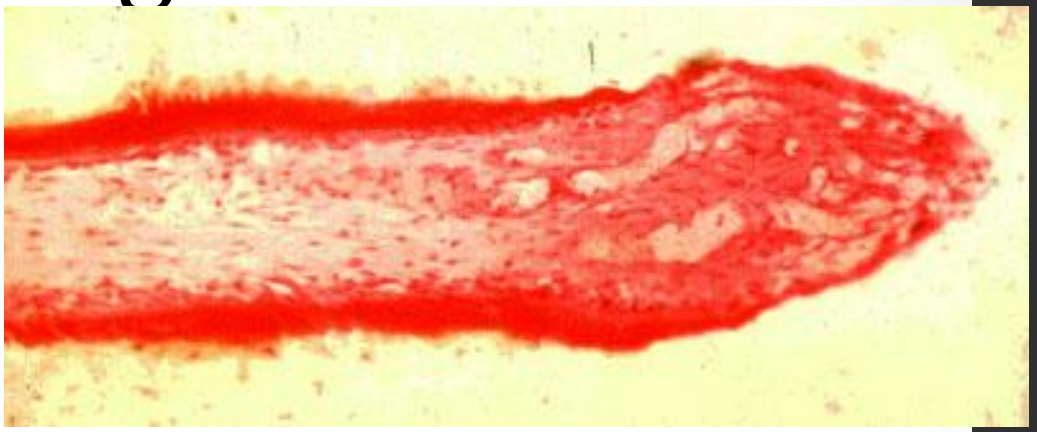
Primary bone healing

- contact healing (cutting cones)

- Gap healing

Cutting Cones

- Primarily a mechanism to remodel bone
- Osteoclasts at the front of the cutting cone remove bone
- Trailing osteoblasts lay down new bone



Courtesy Drs. Charles Schwab and Bruce Ma

Primary bone healing

- Intramembranous Bone Formation

  - Mechanism by which a long bone grows in <u>width</u>
  - Osteoblasts differentiate directly from preosteoblasts and lay down lines of osteoid
  - Does NOT involve cartilage anlage

Primary bone healing

- occurs via Haversian remodeling
- occurs with absolute stability constructs

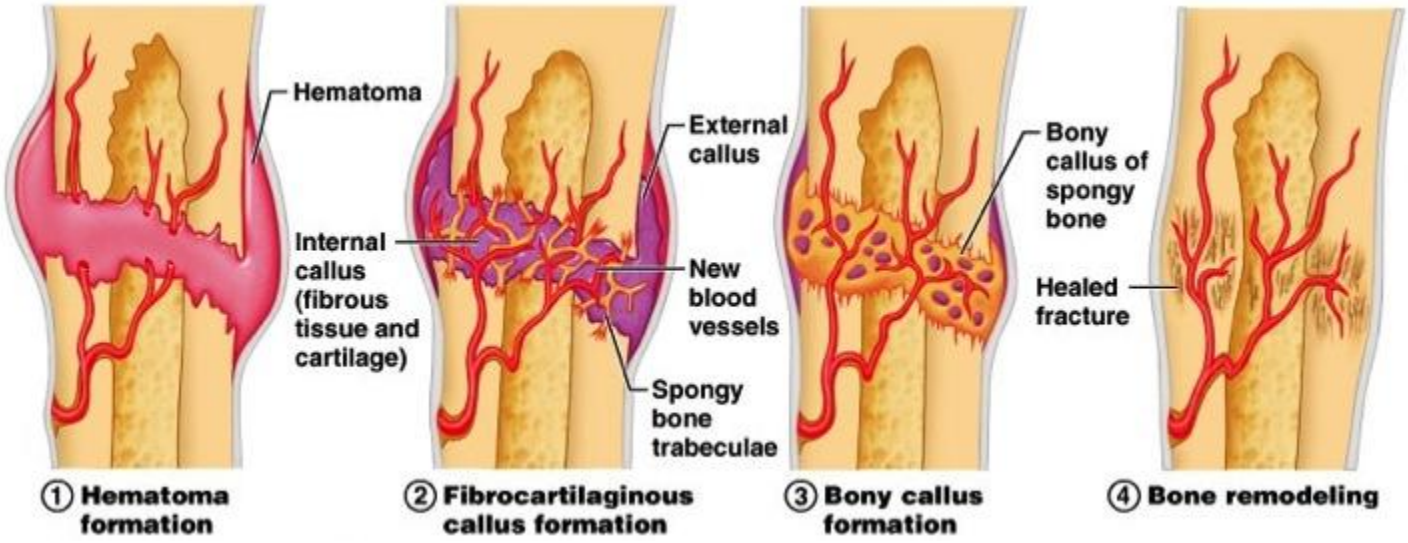
Secondary bone healing

- occurs with non-rigid fixation, as fracture braces, external fixation, bridge plating, intramedullary nailing, etc.

Secondary bone healing

- ENCHONDRAL BONE HEALING
  - Mechanism by which a long bone grows in <u>length</u>
  - The chondrocytes hypertrophy, degenerate and calcify (area of low oxygen tension)
  - Vascular invasion of the cartilage occurs followed by ossification (increasing oxygen tension)

Secondary bone healing



Secondary bone healing

- Inflammation
- Repair
- Remodelling

Secondary bone healing

- Inflammation
- Hematoma forms and provides a source of hematopoietic cells capable of secreting growth factors.
- fibroblasts and mesenchymal cells migrate to fracture site and granulation tissue forms around fracture ends

Secondary bone healing

- Repair

- Primary callus forms within two weeks
- endochondral ossification converts soft callus to hard callus
- Cartilage production provides provisional stabilization
- Type II collagen (cartilage) is produced early in fracture healing and then followed by type I collagen (bone)

Secondary bone healing

- Remodelling
- Begins in middle of repair phase and continues long after clinical union

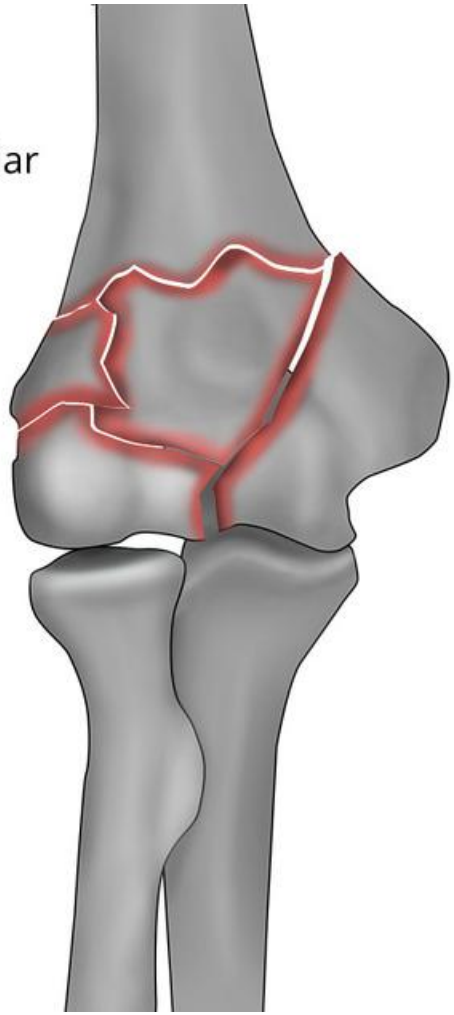
- Newly formed bone (woven bone) is remodeling via organized osteoblastic/osteoclastic activity

- Inadequate stabilization may result in excessive deformation at the fracture site interrupting tissue differentiation to bone .

- bone healing may occur as a combination of the above two process depending on the stability throughout the construct

C2

Complete articular
Fragmentary
metaphyseal



FACTORS AFFECTING FRACTURE HEALING

- blood supply

- initially the blood flow decreases with vascular disruption
- after few hours to days, the blood flow increases
- this peaks at 2 weeks and normalizes at 3-5 months
- un-reamed nails maintain the endosteal blood supply

Hormones

- Estrogen
  - Stimulates fracture healing through receptor mediated mechanism
- Thyroid hormones
  - Thyroxine and triiodothyronine stimulate osteoclastic bone resorption
- Glucocorticoids
  - Inhibit calcium absorption from the gut causing increased PTH and therefore increased osteoclastic bone resorption

Hormones (cont.)

- Parathyroid Hormone
  - Intermittent exposure stimulates
    - Osteoblasts
    - Increased bone formation
- Growth Hormone
  - Mediated through IGF-1 (Somatomedin-C)
  - Increases callus formation and fracture strength

Local Anatomic Factors That Influence Fracture Healing

- Soft tissue injury
- Interruption of local blood supply
- Interposition of soft tissue at fracture site
- Bone death caused by radiation, thermal or chemical burns or infection

Systemic factors affecting healing

- Diet
- nutritional deficiencies
- vitamin D and calcium
- as high as 84% of patients with nonunion were found to have metabolic issues
- greater than 66% of these patients had vitamin D deficiencies

Systemic factors affecting healing

- Diabetes mellitus
- affects the repair and remodeling of bone
- decreased cellularity of the fracture callus
- delayed endochondral ossification
- diminished strength of the fracture callus

- fracture healing takes 1.6 times longer in diabetic patients versus non-diabetic patients

Systemic factors affecting healing

- nicotine
- decreases rate of fracture healing
- inhibits growth of new blood vessels as bone is remodeled
- increase risk of nonunion (increases risk of pseudoarthrosis in spine fusion by 500%)
- decreased strength of fracture callus
- smokers can take ~70% longer to heal open tibial shaft fractures versus non-smokers

Systemic factors affecting healing

- bisphosphonates are recognized as a cause of osteoporotic fractures with long term usage

- recent studies demonstrated longer healing times for surgically treated wrist fractures in patients on bisphosphonates

- long term usage may be associated with atypical subtrochanteric/femoral shaft fractures
-

Systemic factors affecting healing

- systemic corticosteroids

- studies have shown a 6.5% higher rate of intertrochanteric fracture non unions

Systemic factors affecting healing

- NSAIDs
- prolonged healing time becaue of COX enzyme inhbition

- quinolones
- toxic to chondrocytes and diminishes fracture repair

Low Intensity Pulsed Ultrasound (LIPUS)

- exact mechanism for enhancement of fracture healing is not clear
- alteration of protein expression
- INCREASE in vascularity
- accelerates fracture healing and increases mechanical strength of callus

THANK YOU