Fracture Healing

Dr Rodney Itaki

Anatomical Pathology Discipline

University of Papua New Guinea
School of Medicine & Health Sciences
Division of Pathology

Types of fractures

- Depends on magnitude and direction of force
- Closed
  - Bone fragments do not pierce skin
- Open/compound
  - Bone fragments pierce skin
- Displaced or undisplaced
- Pathological Fracture
- Stress Fracture – slowly and due to increased physical activity

Prerequisites for Bone Healing

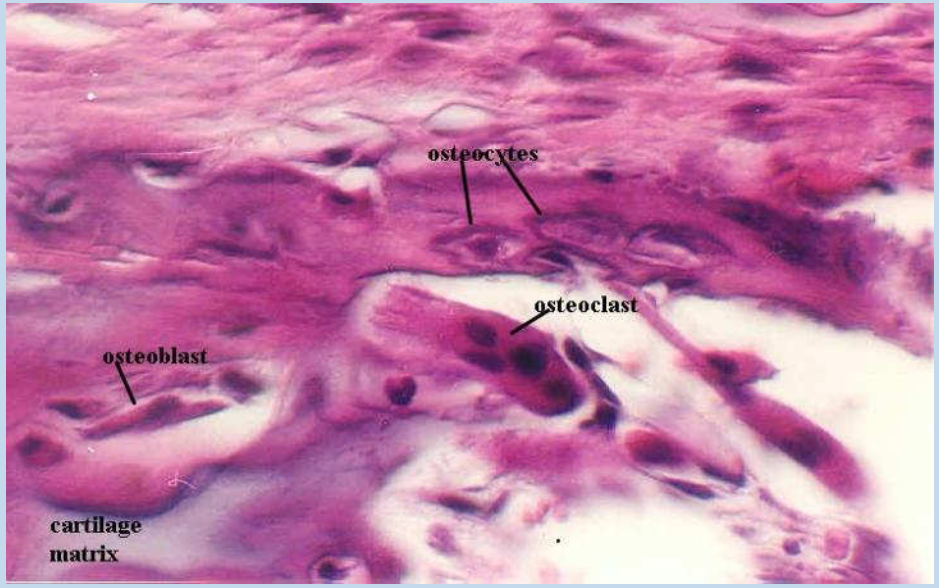
- Adequate blood supply
- Adequate mechanical stability

Cells Involved in Fracture Healing

- Inflammatory Cells – various white blood cells
- Platelets
- Osteoblasts
- Osteoclasts
- Osteocytes

Osteoclasts

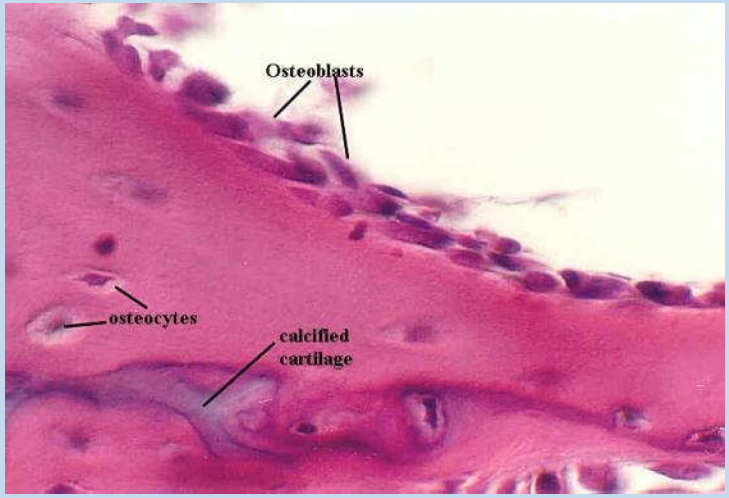
- Breakdown bone
- Derived from hematopoietic stem cells (monocyte precursor cells)
- Multinucleated cells whose function is bone resorption
- Reside in bone resorption pits (Howship's lacunae)
- Parathyroid hormone stimulates receptors on osteoblasts that activate osteoclastic bone resorption



Picture courtesy Gwen Childs, PhD

Osteoblasts

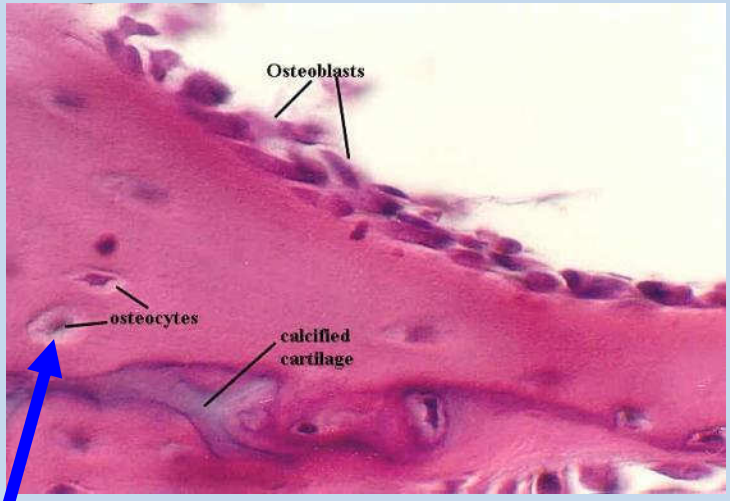
- Bone forming cells
- Derived from mesenchymal stem cells
- Line the surface of the bone and produce osteoid
- Immediate precursor is fibroblast-like preosteoblasts



Picture courtesy Gwen Childs, PhD

Osteocytes

- Osteocytes 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
- Preosteoblasts also have connections via canaliculi with the osteocytes
- Network probably facilitates response of bone to mechanical and chemical factors

Mechanisms of Bone Formation

- Cutting Cones
- Intramembranous Bone Formation
- Endochondral Bone Formation

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 Martin

Intramembranous (Periosteal) Bone Formation

- Mechanism by which a long bone grows in width
- Osteoblasts differentiate directly from preosteoblasts and lay down seams of osteoid
- Does NOT involve cartilage precursors

Endochondral Bone Formation

- Mechanism by which a long bone grows in length
- Osteoblasts line a cartilage precursor
- The chondrocytes hypertrophy, degenerate and calcify (area of low oxygen tension)
- Vascular invasion of the cartilage occurs followed by ossification (increasing oxygen tension)

Response To Fracture

- Cellular Response
- Vascular Response

Stages of Fracture Healing

- Inflammation
- Repair
- Remodeling

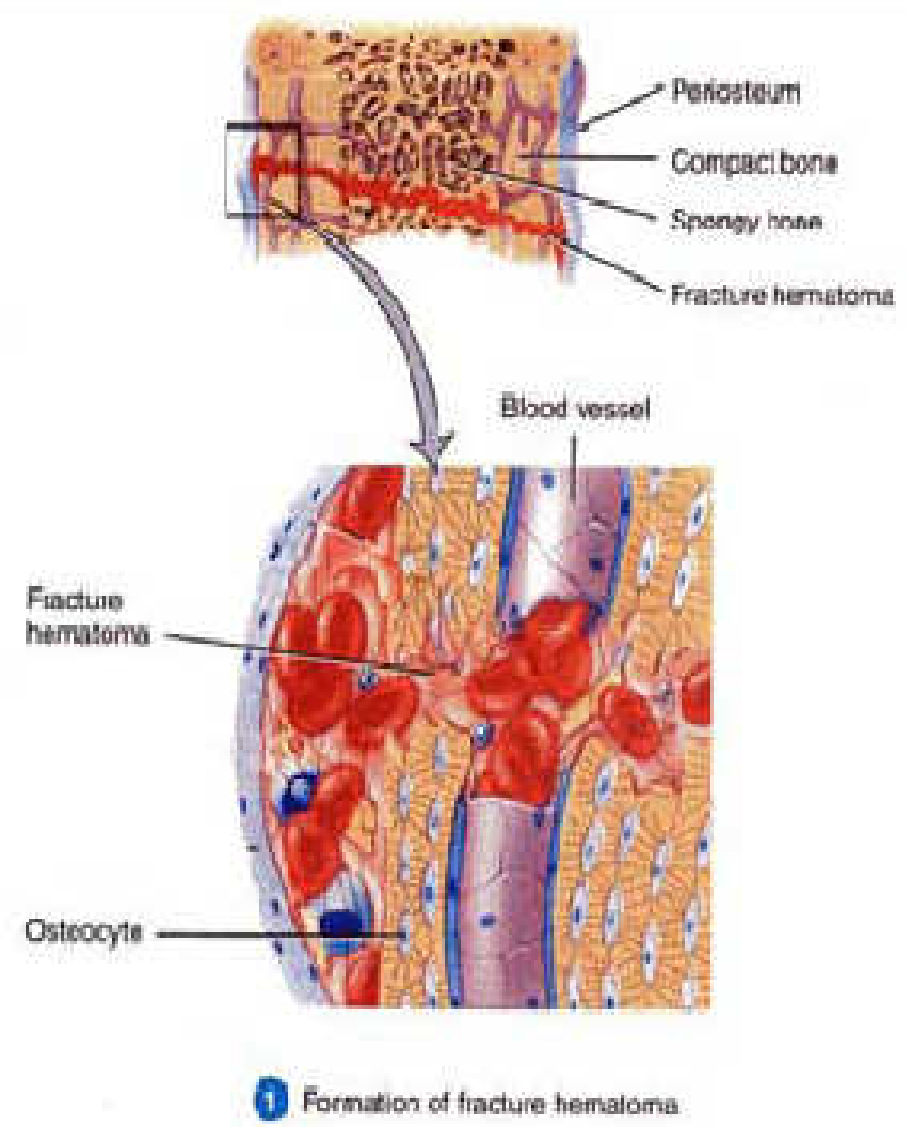
Bone Healing

1. Fracture hematoma

– blood from broken vessels forms a clot.

– 6-8 hours after injury

– swelling and inflammation to dead bone cells at fracture site



Fracture Healing

- Immediately after a facture is haematoma formation (vascular response)
- Fibrin mesh deposited to helps to seal off fracture site
- Serves as framework for influx of inflammatory cells and ingrowths of fibroblasts and new capillary vessels
- Simultaneously release of mediators from degranulated platelets

Fracture Healing

Mediators from degranulated platelets release mediators critical for healing process

Mediators	Function
Platelet Derived Growth Factor (PDGF)	Angiogenesis, cell growth and cell division
Transforming Growth Factor –β (TGF–β)	Proliferation and cell differentiation
Fibroblast Growth Factor (FGF)	Proliferation & Differentiation of cells
Various Interleukins	Signaling proteins and involved in promote development and differentiation of T & B lymphocytes

Fracture Healing

- Released mediators induce an inflammatory response
- Activation of progenitor cells in periosteum, medullary cavity and surrounding soft tissue
- Stimulate production of osteoclastic and osteoblastic activity

Fracture Healing

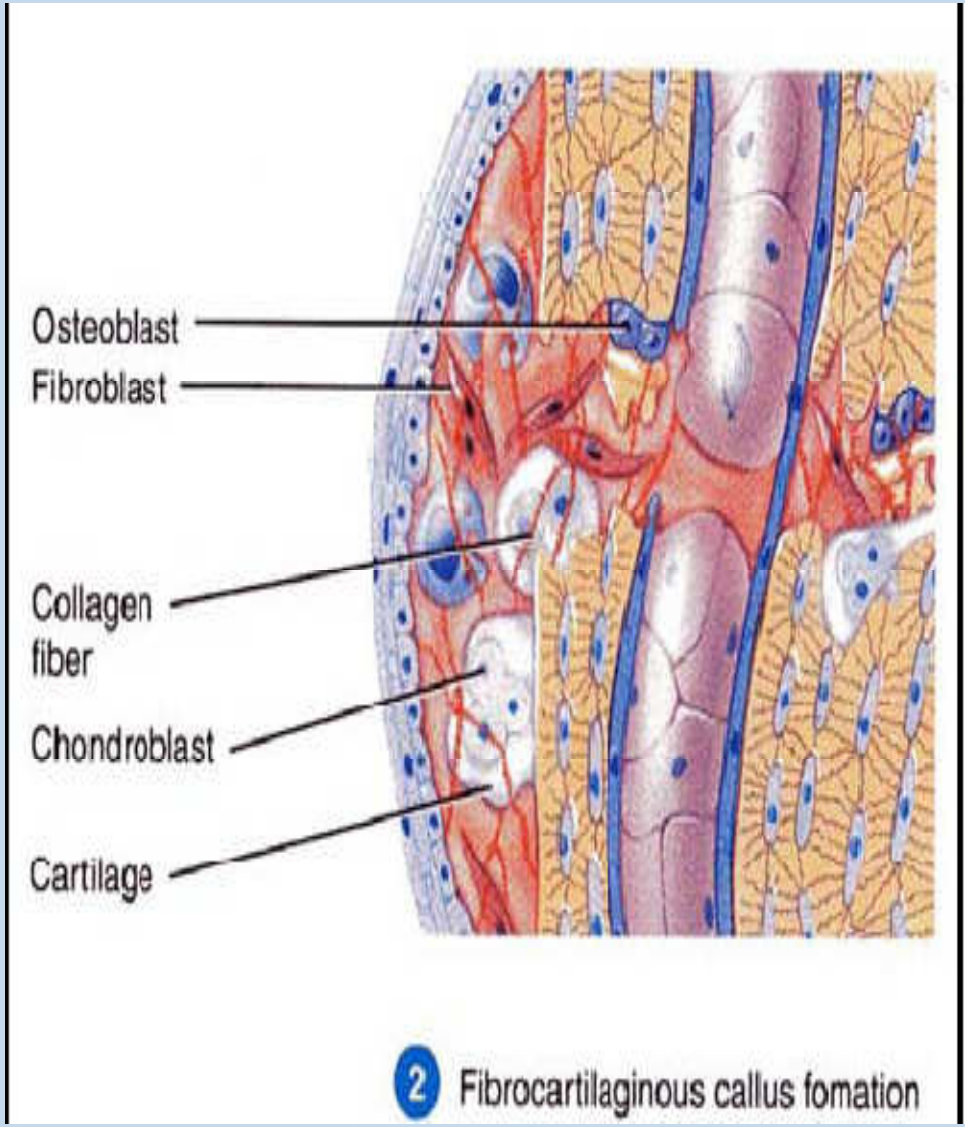
- End of 1st week: organisation of haematoma
- Formation of uncalcified tissue between fractured ends – *procallus* or *soft tissue callus*
- Procallus provides anchorage between fractured ends

Fracture Healing

- Activated osteoprogenitor cells deposit subperiosteal trabeculae of woven bone
- Woven bone is perpendicular to cortical axis & within medullary cavity
- Activated mesenchymal cells surrounding fracture differentiate into chondoblasts and deposit fibrocartilage & hyaline cartilage.
- *Not all fracture types will contain cartilage as part of healing*

2. **Fibrocartilaginous callus**

- (lasts about 3 weeks (up to 1st Month))
  – new capillaries organise fracture hematoma into granulation tissue - ‘procallus’
  – Fibroblasts and osteogenic cells invade procallus.
  – Make collagen fibres which connect ends together
  – Chondroblasts begin to produce fibrocatilage,



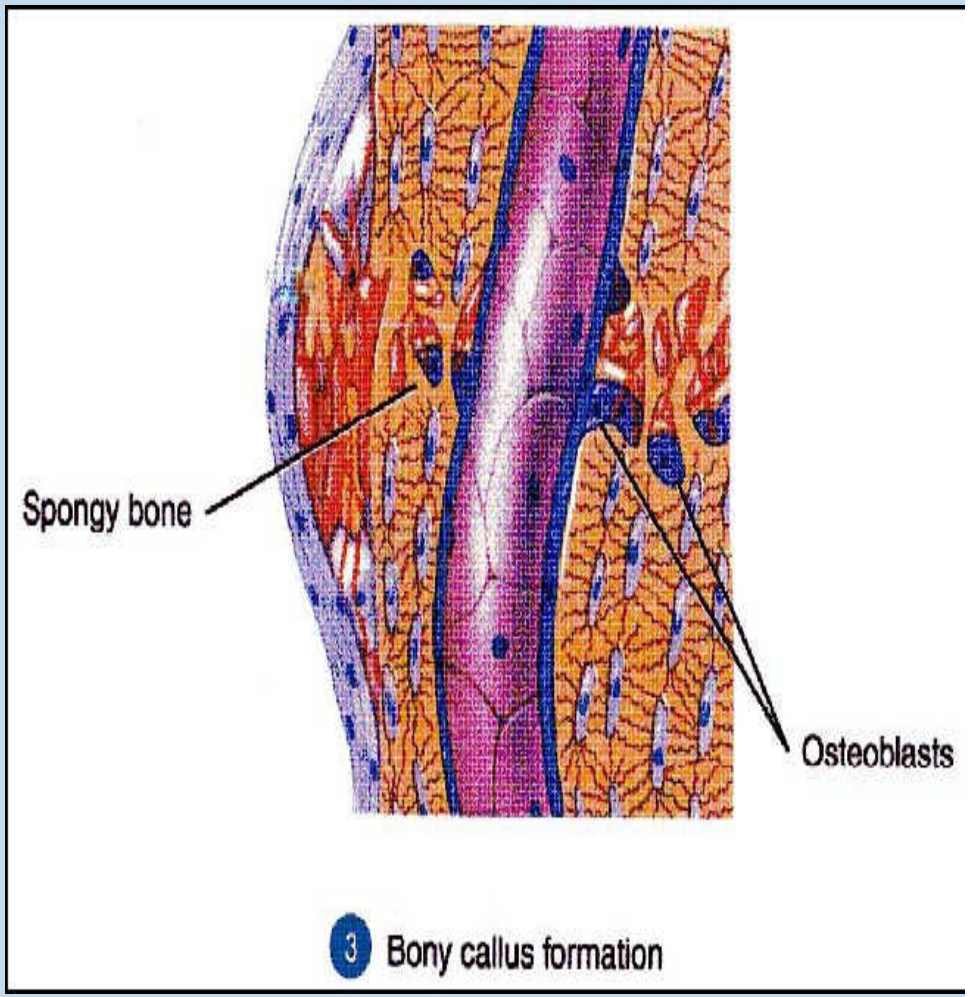
Fracture Healing

- Newly formed cartilage undergo enchondral ossification as intramedullary and subperiosteal reactive woven bone reach newly formed cartilage
  - Similar to what occurs at growth plates
- Ultimately results in formation of a *bony callus*
- *Bone callus* increases in strength and stiffness as it mineralizes and able to bear weight

3. **Bony callus**

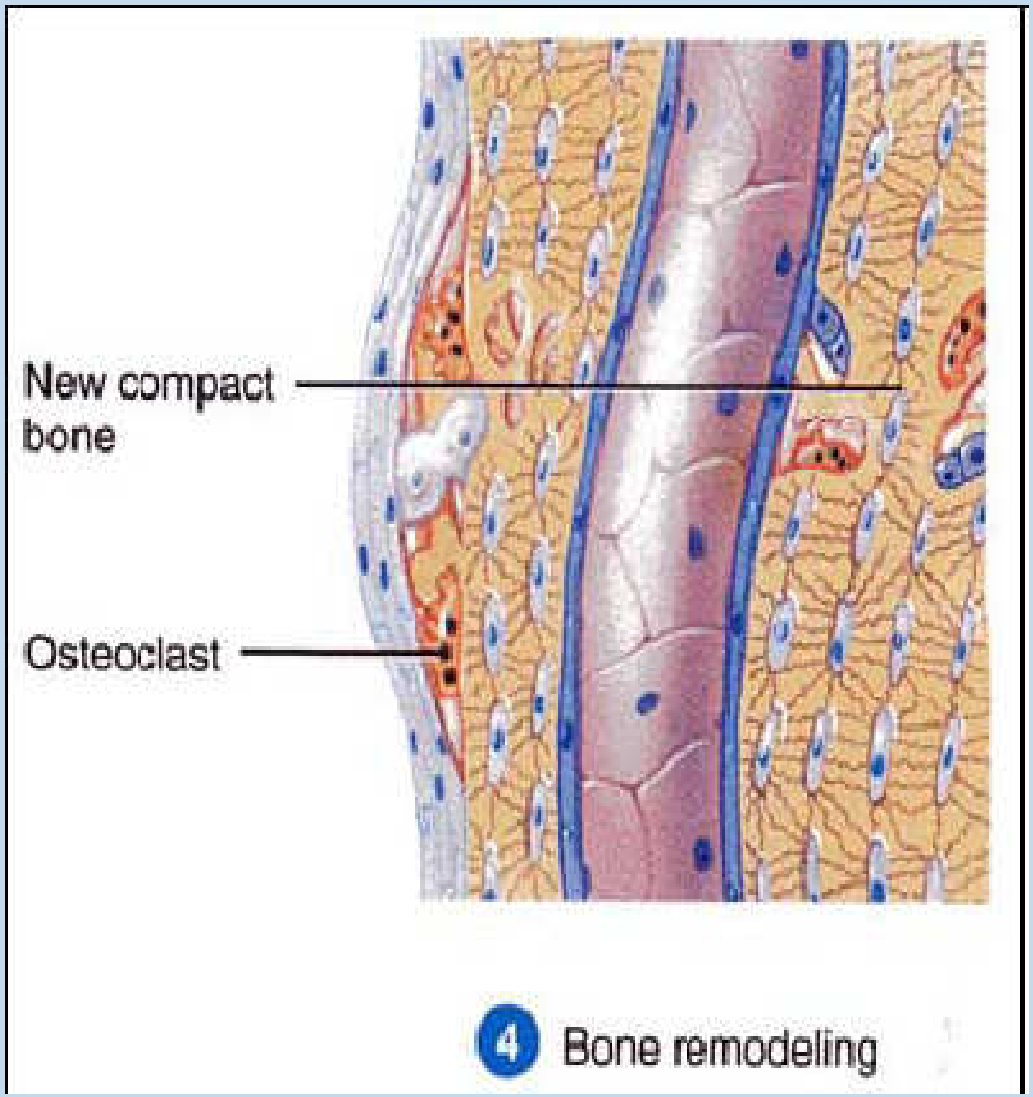
- (after 3 weeks and lasts about 3-4 months)

  – osteoblasts make woven bone.



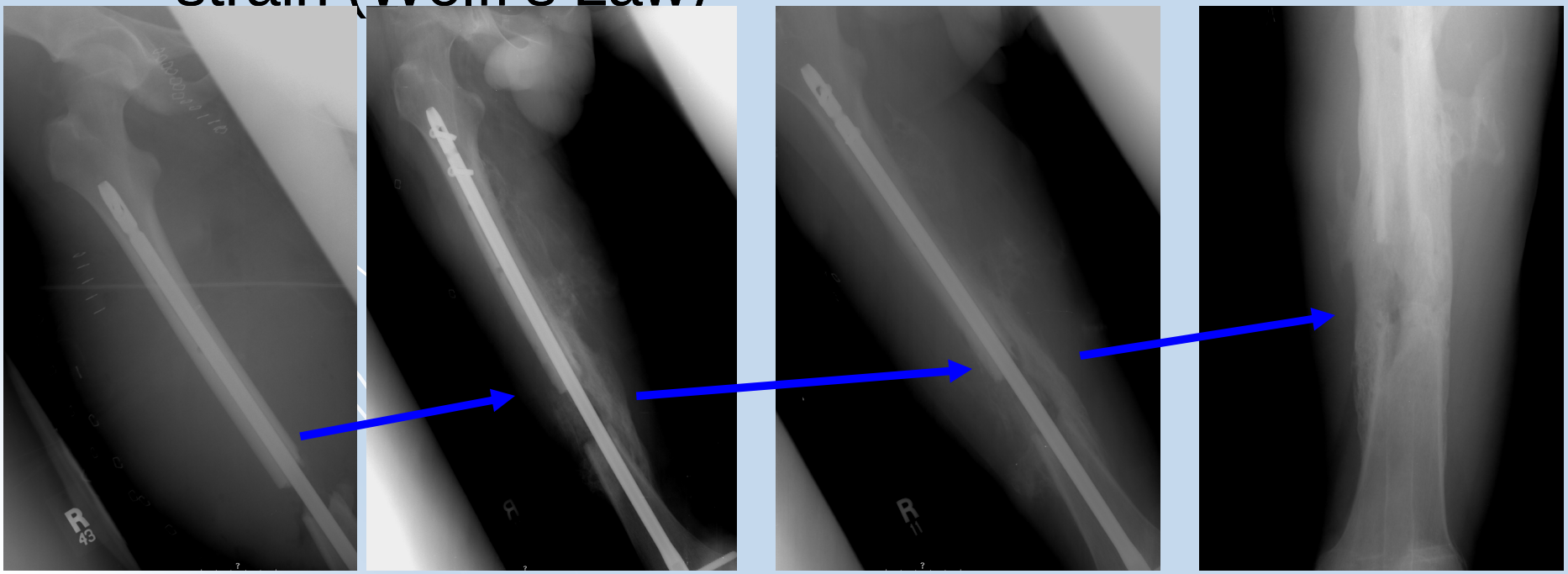
4. **Bone Remodeling**

- Osteoclasts remodel woven bone into compact bone and trabecular bone
  - Often no trace of fracture line on X-rays.



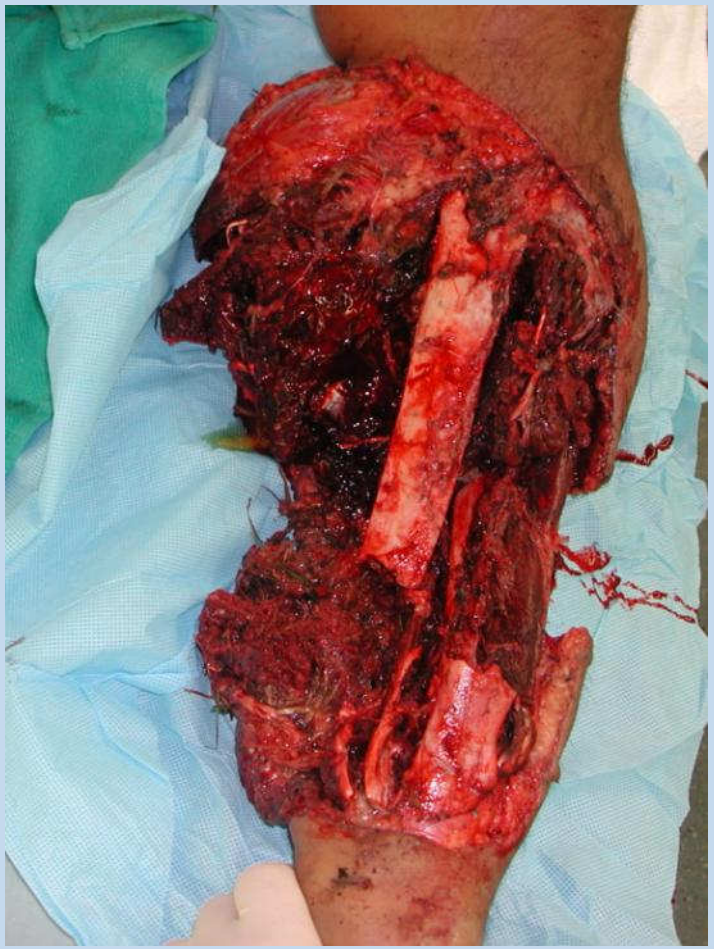
Remodeling

- Woven bone is gradually converted to lamellar bone
- Medullary cavity is reconstituted
- Bone is restructured in response to stress and strain (Wolff's Law)



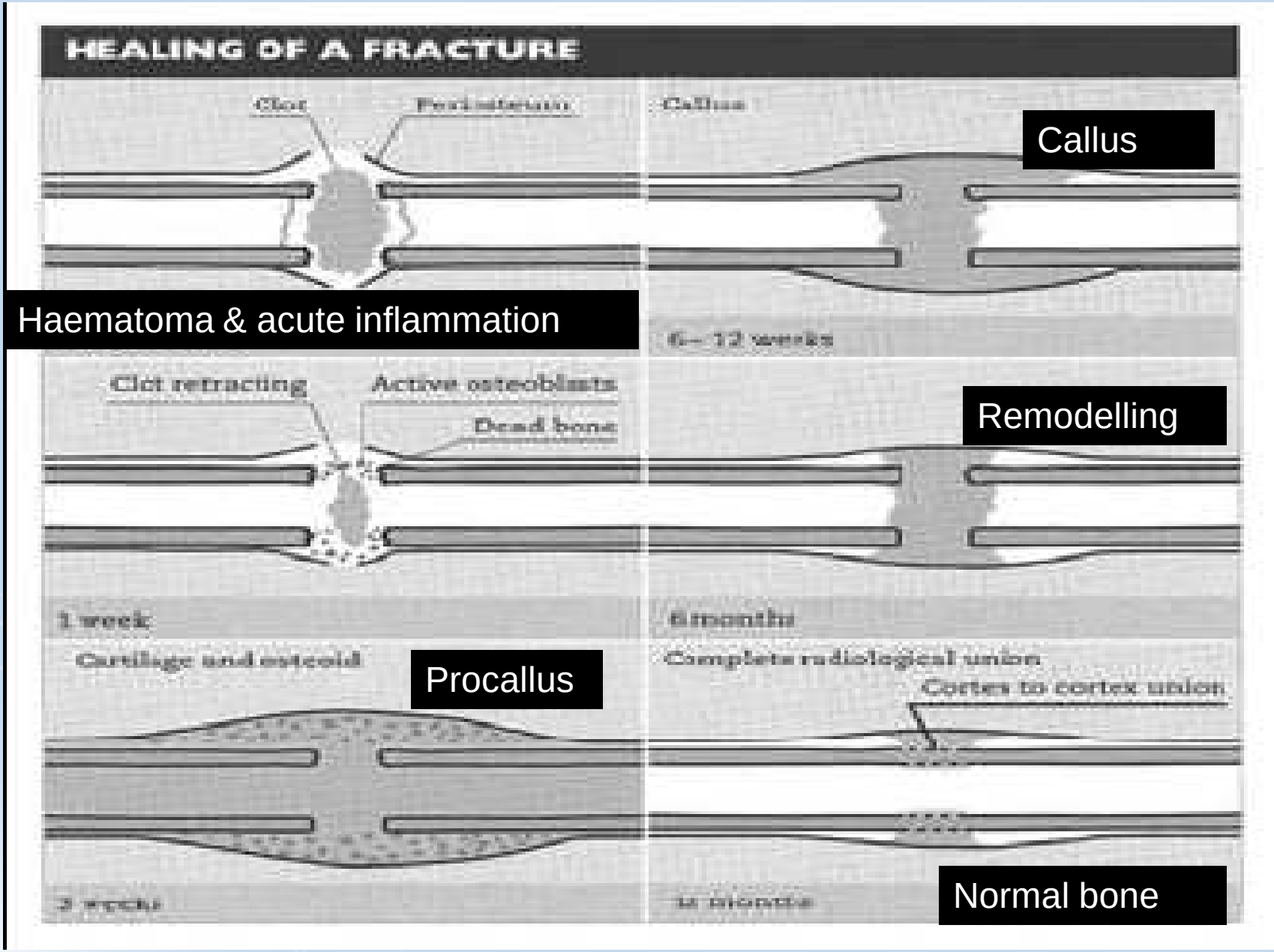
Local Anatomic Factors That Influence Fracture Healing

- 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 That Decrease Fracture Healing

- Malnutrition
  - Reduces activity and proliferation of osteochondral cells
  - Decreased callus formation
- Smoking
  - Cigarette smoke inhibits osteoblasts
  - Nicotine causes vasoconstriction diminishing blood flow at fracture site
- Diabetes Mellitus
  - Associated with collagen defects including decreased collagen content, defective cross-linking and alterations in collagen sub-type ratios
- Anti-Inflammatory Medications
  - Cause (at least a temporary) reduction in bone healing


HEALING OF A FRACTURE
Clot
Periosteum
Callus
Haematoma & acute inflammation
Callus
6–12 weeks
Clot retracting
Active osteoblasts
Dead bone
Remodelling
1 week
6 months
Cartilage and osteoid
Procallus
Complete radiological union
Cortex to cortex union
Normal bone

Reference: Robins Pathological Basis of Diseases

Download seminar notes: www.pathologyatsmhs.wordpress.com

END