Wound Healing

South College PA Course
University of Tennessee Medical Center at Knoxville

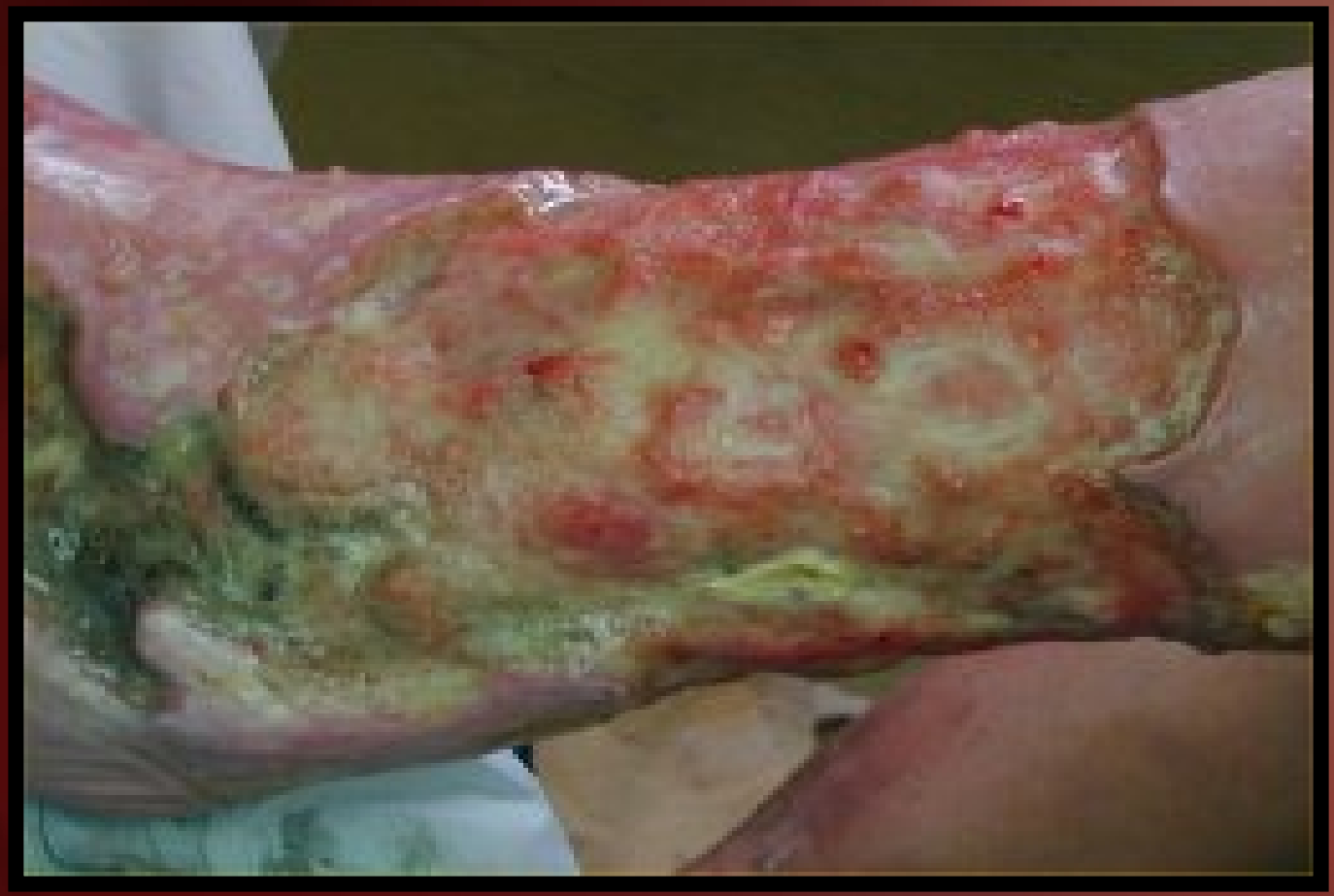
Wound Healing

"For I am fearfully and wonderfully made…that my soul knoweth right well"

~ Ps. 139 :14~

Wound Healing

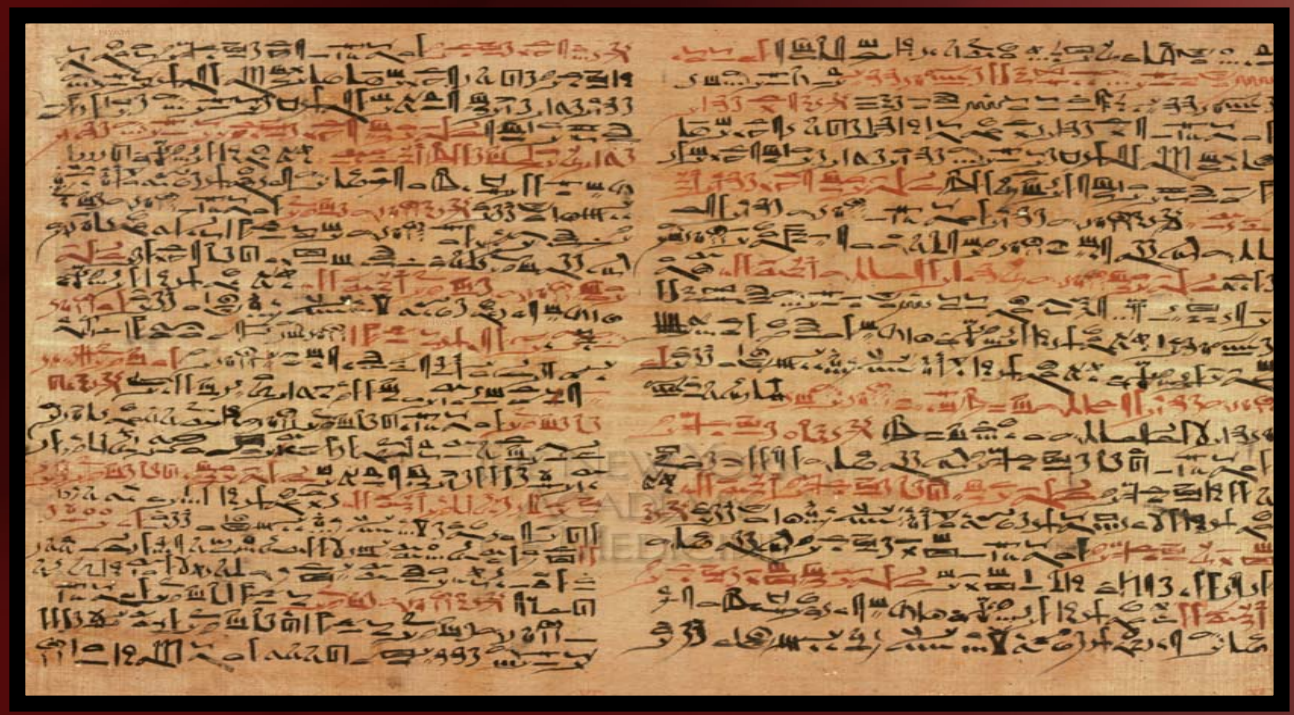
Wound Healing



Wound Healing

Edwin Smith Papyrus

~ 1650 B.C.



Wound Healing

Ebers Papyrus

~ 1550 B.C.

Wound Healing

1. **Classification**
   - *Acute vs chronic*
2. **Phases of Healing**
   - *Coagulation*
   - *Inflammation*
   - *Proliferation*
   - *Maturation*
3. **Components of healing**
   - *Cellualar/mechanical constituents*
     - Neutrophils
     - Macrophages
     - Fibroblasts
     - Collagen
   - *Chemical/cytokine constituents*
4. **Factors Affecting Wound Healing**
   - *Extrinsic*
   - *Instrinsic*
5. **Pathologic States**
   - *Impaired vs excessive healing*
   - *Organ specific problems*
   - *Genetic abnormalities*
6. **Treatment Options**
   - *Local wound care*
   - *Skin replacement/ adjuncts*
   - *New horizons*

Wound Healing

- **Acute Wounds**

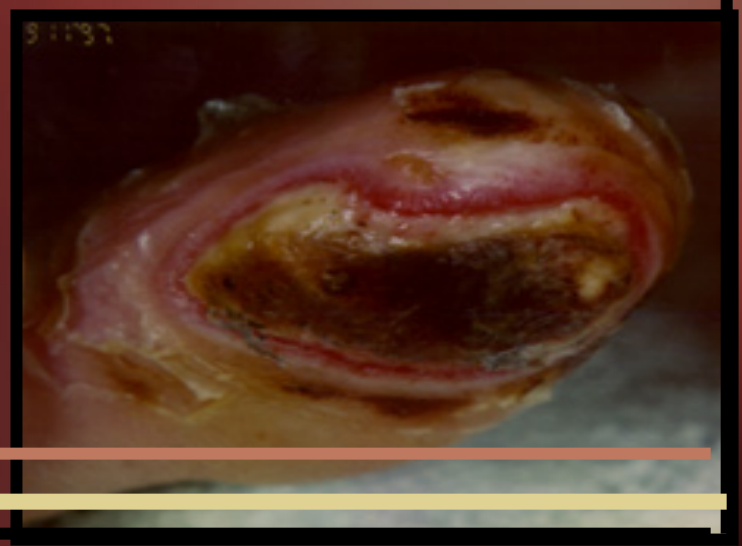
- **Chronic Wounds**
  - ***Diabetic***
  - ***Arterial***
  - ***Venous***
  - ***Pressure related***

Wound Healing

- **Chronic Wounds**
  - **>3 mos. to heal**
  - **repeated trauma/ poor perfusion/ ongoing inflammation**
  - **Potential for malignant degeneration (i.e. Marjolin's ulcer)**

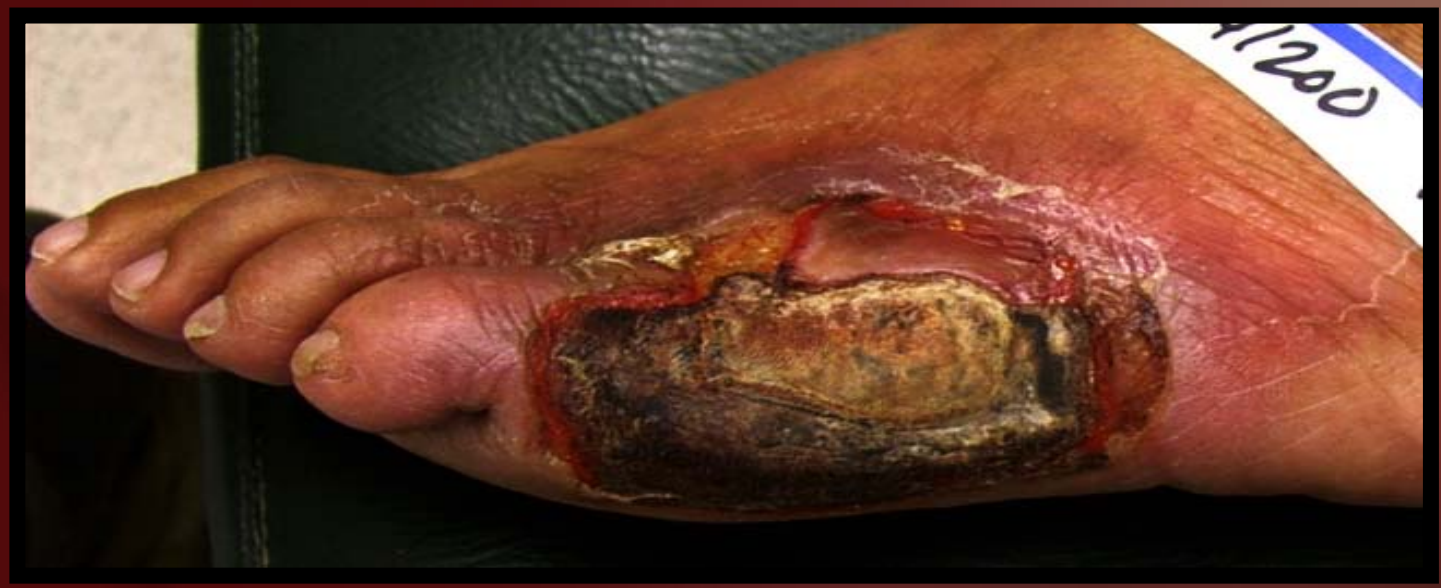
Wound Healing

- **Chronic Wounds/ Diabetic**
  - *Etio: Ischemia, neuropathy (motor/sensory), deformity (e.g. Charcot's foot)*
  - *Tx: blood Glucose control, R/O osteo, off load deformities, adequate debridement*



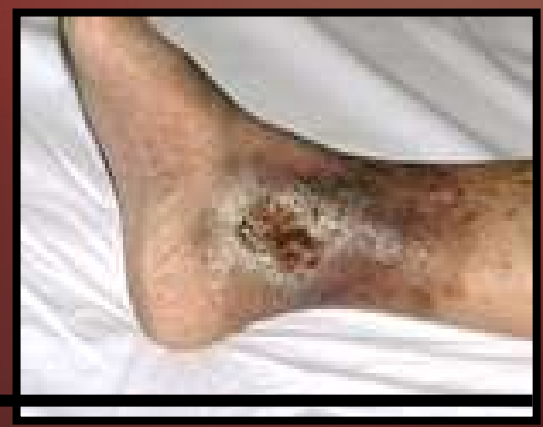
Wound Healing

- **Chronic Wounds/ Arterial**
  - *Etio: inadequate perfusion*
  - *S/S: Painful, dry, punctate vs. venous stasis*
  - *Tx: Restablishment of adequate flow + wound care*



Wound Healing

- **Chronic Wounds/ Venous**
  - *Etio: Hydrostatic pressure/ transudation/ fibrin polymerization/ "perivascular cuffing"*
  - *S/S: Medial ankle, moist, superficial, diffuse vs arterial*
  - *Tx: Elevation/ compression/ pain control (catecholamine response)*



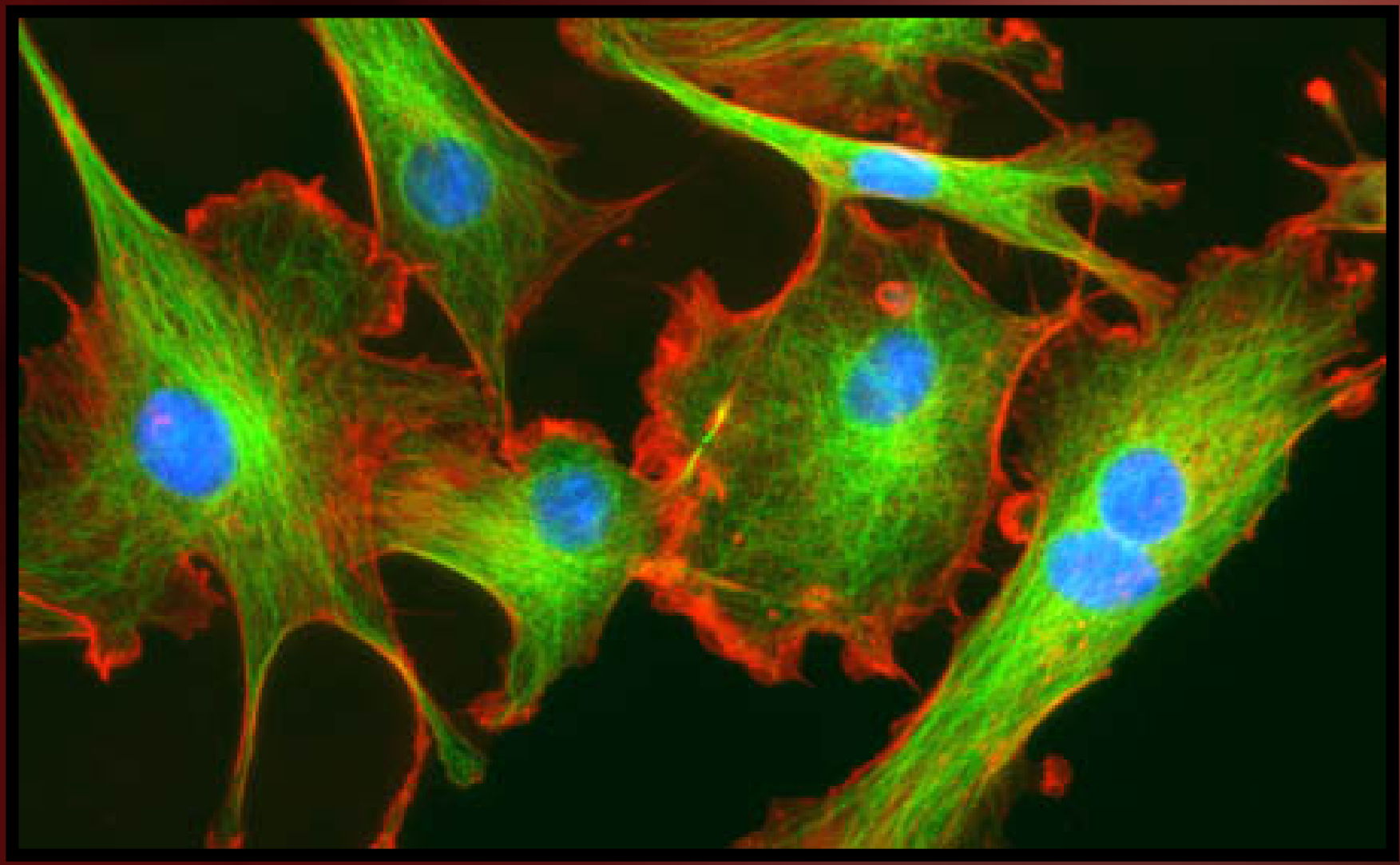
Wound Healing

- **Chronic Wounds/ Pressure sores**
  - ***Etio: capillary compression***
  - ***Classification*** *NatnL. Pressure Ulcer Advisory Panel*
    - ***Stage I*: skin intact**
    - ***Stage II*: epidermal/dermal skin breakdown**
    - ***Stage III*: ST loss down to but not through fascia**
    - ***Stage IV*: extensive destruction through fascial plane**
  - ***Tx: debridement, wound care, offloading pressure, grafting/flaps***

Wound Healing

- **Fibroblasts**
  - –Migration by 3rd day/ dominant cell by 5th day
  - –GAG synthesis
  - –Collgaen synthesis
  - –Elucidate MMPs

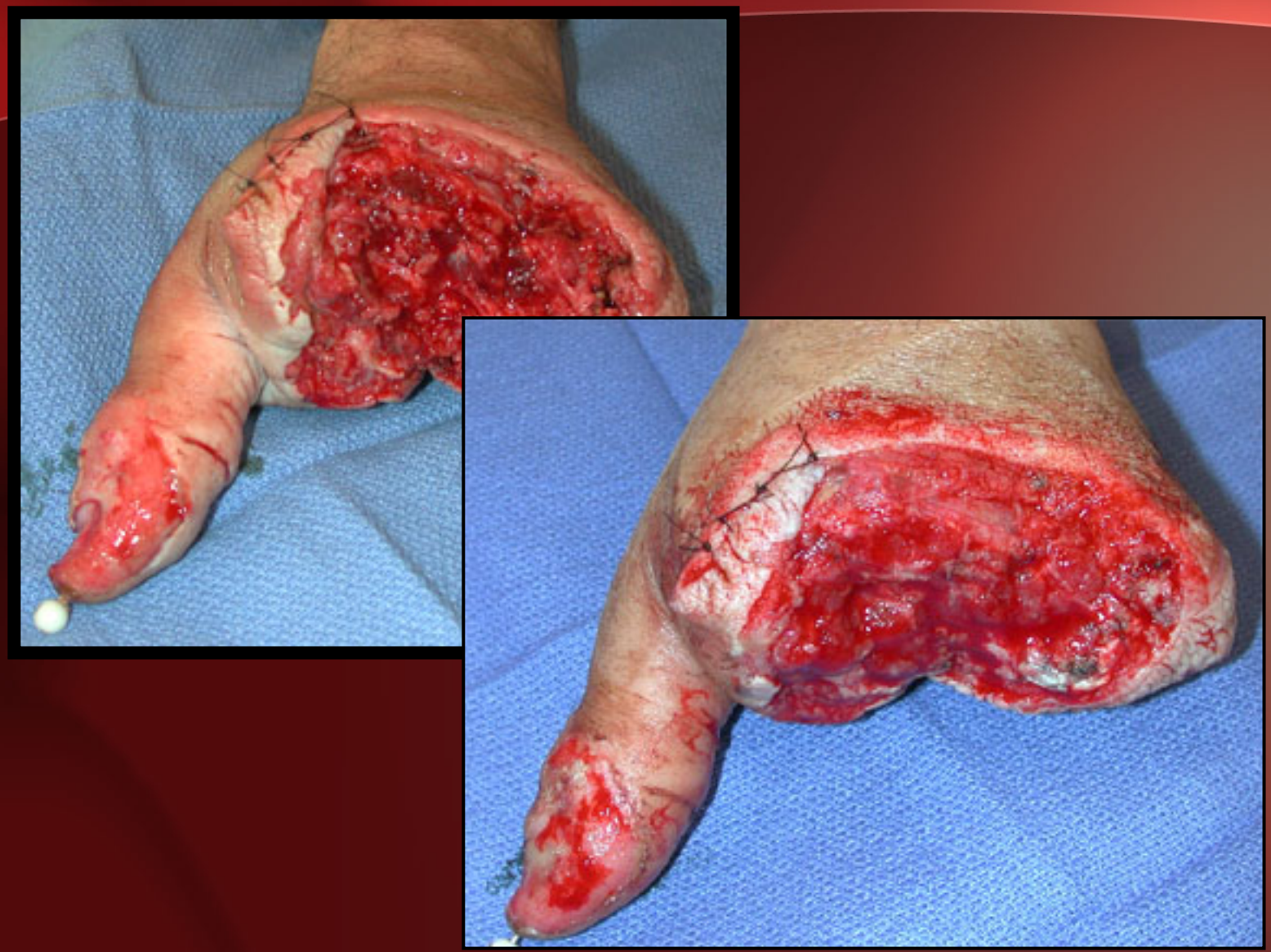
Wound Healing



Wound Healing

- **Angiogenesis**
  - –Low O_2tension/ elevated lactic acid concentration
  - –VGEF, aFGF & bFGF as per macrophages/endothelial cells/ fibroblasts
  - –Endothelial migration in accord w/ chemotactic gradient by collagenases
  - –Organization / Type IV collagen / basement membrane est./ granulation tissue formation/ ground substance & high HA content

Wound Healing

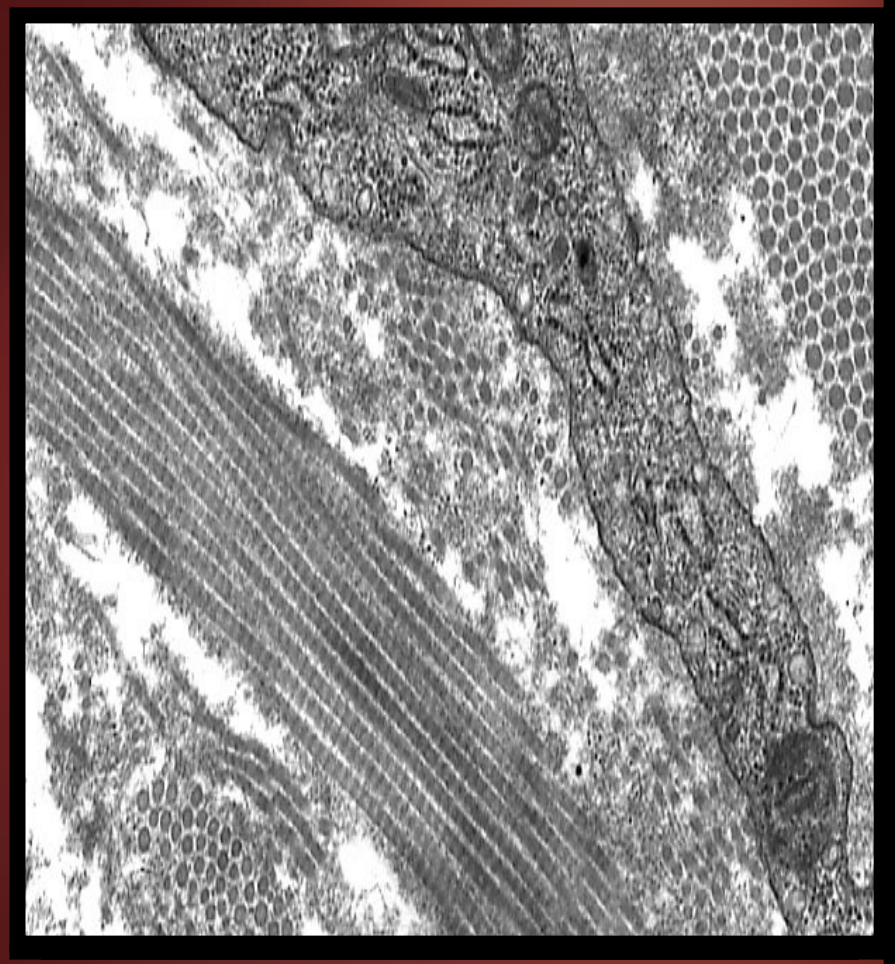


Wound Healing

- **Phases of Healing/ Proliferation (3 days-3 weeks)**
  - **Fibroblast migration**
    - **Via PDGF/TGF-B direction**
    - **ECM interplay facilitated by fibronectin**
    - **Heralds transition from inflammatory to reconstructive phase**
  - **Collagen Synthesis**
    - **Properties**
    - **Process**
    - **Regulation**

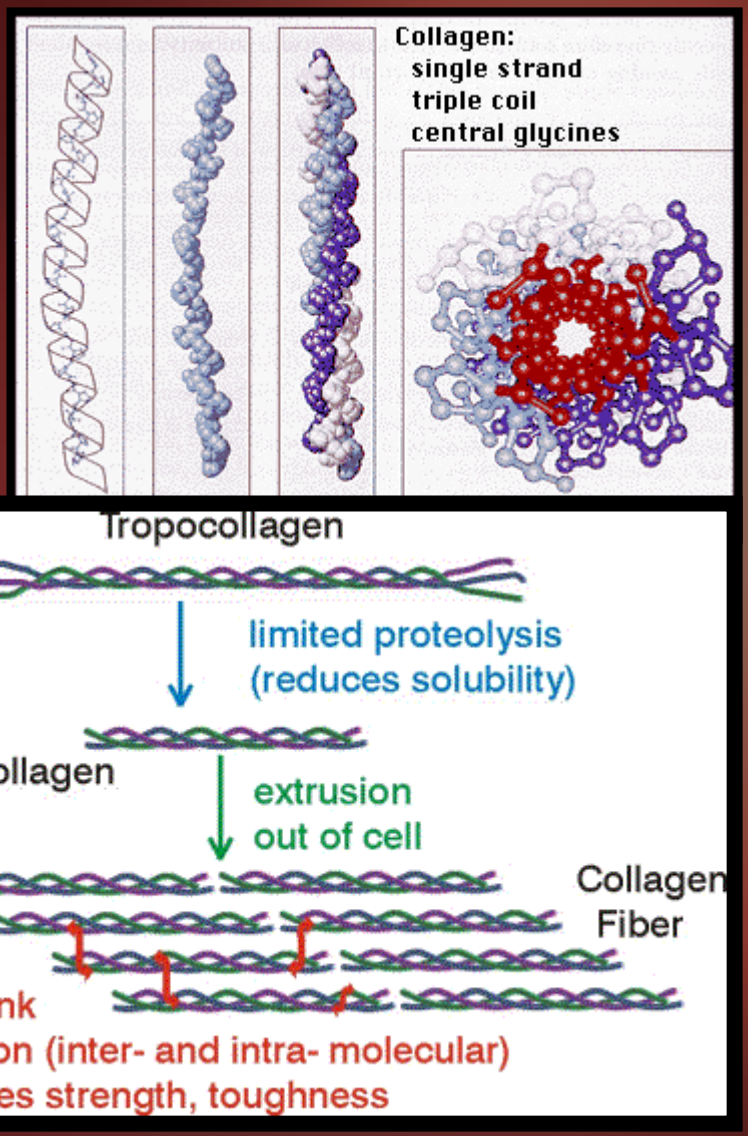
Wound Healing

- Collagen Properties
  - Most abundant protein in body
  - 19 variants w/ Type I predominant
  - Types II, III, IV, V
  - High glycine content (q3)
  - Unique AA's
    - 4-hydroxyproline
    - 5-hydroxylysine



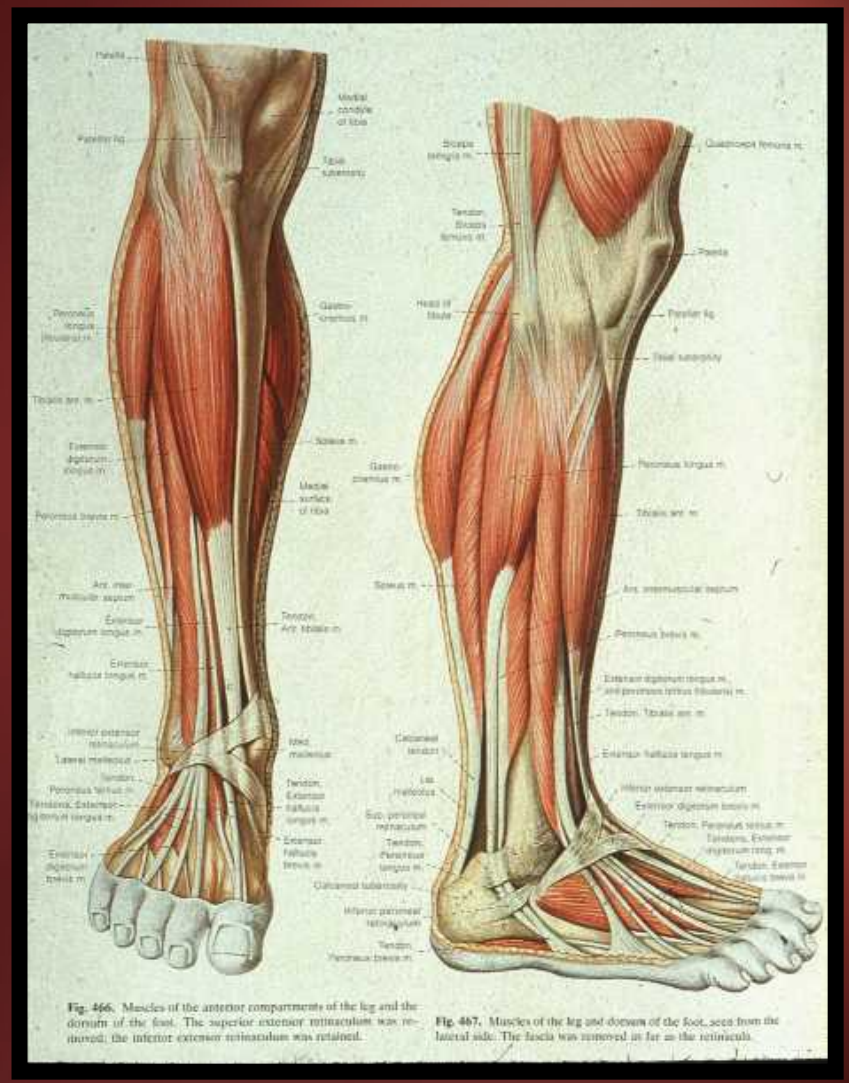
Wound Healing

- **Collagen Synthesis/ Regulation**
  - **Intracellular synthesis**
    - **Triple ą helix w/ H bond linking**
  - **Post trans oxidation proline lysine**
    - **Vit C crucial for prolyl/lysyl hydroxylase**
  - **Propeptide prevention of aggregation**
  - **EC secretion of procollagen**
  - **Terminal propeptides cleaved→tropocollagen**
  - **Tropocollagen limking→ collagen**
    - **Via Cu-dependent lysine oxidase**



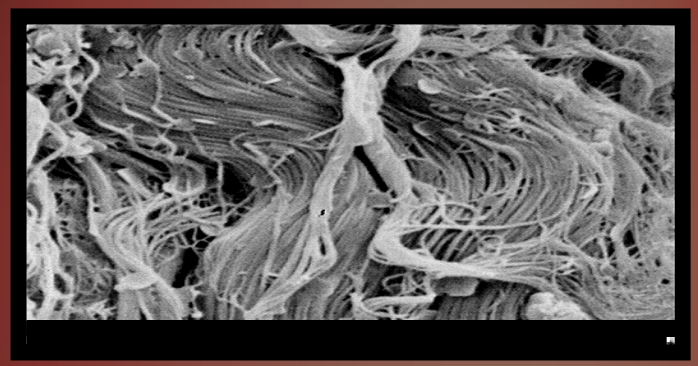
Wound Healing

- Collagen Synthesis Regulation
  - Max accumulation by 2-3 wks
  - total content = after 3 wks
  - Pro:
    - Acidemia
    - TGF-B
    - Hypoxia
  - Inhibitory:
    - NAD+/ ADP ribose



Wound Healing

- **Phases of Healing/ Maturation (3 weeks-6 months)**
  - **Tensile strength:**
    - Per fibril cross-linking
    - 50% @ 6 wks
    - eventually ~70-80% @ ≥ 6 months



  - **Contraction:**
    - myofibroblast /actin fibers w/in → 30-90% reduction in CSA
    - Max rate 0.75 mm/ day
  - **Reepithelialization:**
    - facilitated by contraction
    - from peripheral basal margins inward
    - Type IV collagen/basement membrane per keratinocytes
    - Max rate 1-2mm/day

Wound Healing

Cytokines

TABLE 5.1. GROWTH FACTORS IN WOUND HEALING

Growth Factor	Cell Source	Function
PDGF	Macrophages Platelets Endothelial cells Epithelial cells Fibroblasts Others	Stimulates fibroblast and smooth muscle cell chemotaxis and proliferation, neutrophil and macrophage chemotaxis, collagen synthesis, proteoglycan synthesis, collagenase activity, fibronectin synthesis
TGF-β	Platelets Macrophages Lymphocytes Fibroblasts Keratinocytes Others	Stimulates fibroblast chemotaxis and proliferation (dose dependent), collagen synthesis, proteoglycan synthesis, fibronectin synthesis, angiogenesis, wound contraction
EGF	Macrophages Platelets Epithelial cells Others	Stimulates epithelial cell chemotaxis and proliferation, fibroblast chemotaxis and proliferation, endothelial cell proliferation
FGF-2	Macrophages Endothelial cells Fibroblasts	Stimulates fibroblast proliferation, epithelial cell proliferation, endothelial cell proliferation and migration, collagen synthesis, proteoglycan synthesis, fibronectin synthesis, angiogenesis, wound contraction
TGF-α	Macrophages Platelets Keratinocytes	Same as EGF
IL-1	Macrophages	Stimulates inflammatory cell chemotaxis, epithelial cell chemotaxis, fibroblast proliferation, collagen synthesis, collagenase activity
VEGF	Fibroblasts Macrophages Endothelial cells Epithelial cells	Stimulates endothelial cell proliferation and migration, angiogenesis
KGF (FGF-7)	Fibroblasts	Stimulates epithelial cell proliferation and migration
IGF	Fibroblasts Macrophages	Stimulates fibroblast proliferation, collagen synthesis, proteoglycan synthesis

EGF, epidermal growth factor; FGF, fibroblast growth factor; IGF, insulin-like growth factor; KGF, keratinocyte growth factor; PDGF, platelet-derived growth factor; VEGF, vascular endothelium growth factor; TGF, transforming growth factor.

Modified from Peacock JL, Lawrence WT, Peacock EE Jr. Wound healing. In: O'Leary JP, ed. *The physiologic basis of surgery.* 1st ed. Baltimore: Williams & Wilkins, 1993.