WOUND HEALING

Phases of wound healing

- Wound healing occurs in 3 phases

1. Inflammatory phase
2. Proliferative phase
3. Remodeling phase

I. Inflammatory phase

A. Immediate to 2-5 days
B. Hemostasis
    1. Vasoconstriction – damaged blood vessels constrict
    2. Platelet aggregation – primary hemostasis
    3. Coagulation – fibrin – secondary hemostasis (clot – platelets + fibrin)
C. Inflammation
    A. Vasodilation
    B. Phagocytosis

II. Proliferative phase

A. 2 days to 3 weeks
B. Granulation
    I. Fibroblasts lay a bed of collagen to fill the defect
C. Angiogenesis
D. Contraction
    I. Wound edges pull together to reduce the defect
E. Epithelialization
    I. Epithelial cells migrate across the new tissue to form a barrier between the wound and the environment

III. Remodeling phase

A. 3 weeks to 2 years
B. New collagen forms which increases the tensile strength of the wound
C. Strength increases and becomes maximum but not as strong as original tissue
D. Scar tissue is only 80% of the strength of the original tissue

Wound healing

- Wound healing is accomplished in one of the following two ways:

1. **Healing by first intention (primary union)**
2. **Healing by second intention (secondary union)**

- Healing of skin wounds is a classical example

Healing by first intention (primary union)

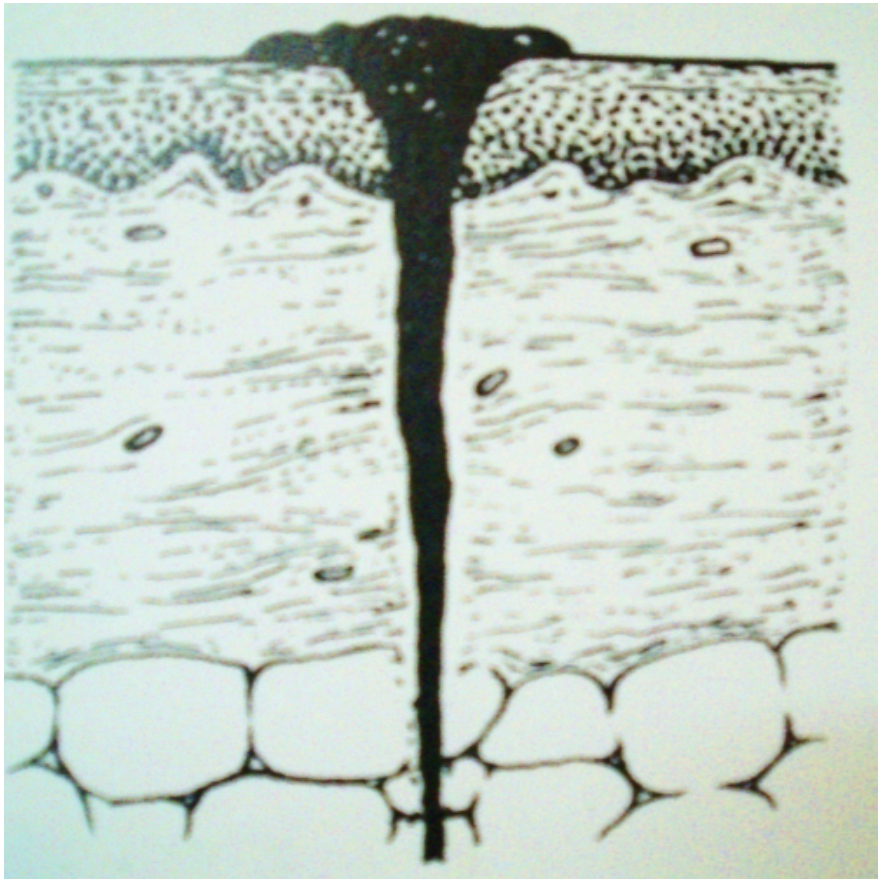
- Occurs in clean, incised wounds with good apposition of the edges – particularly planned surgical incisions
  - (clean wounds – no infections or foreign bodies)
- The incision causes only focal disruption of epithelial basement membrane continuity and death of a relatively few epithelial and connective tissue cells.
- As a result, epithelial regeneration predominates over fibrosis

Healing by first intention:

Sequence of events

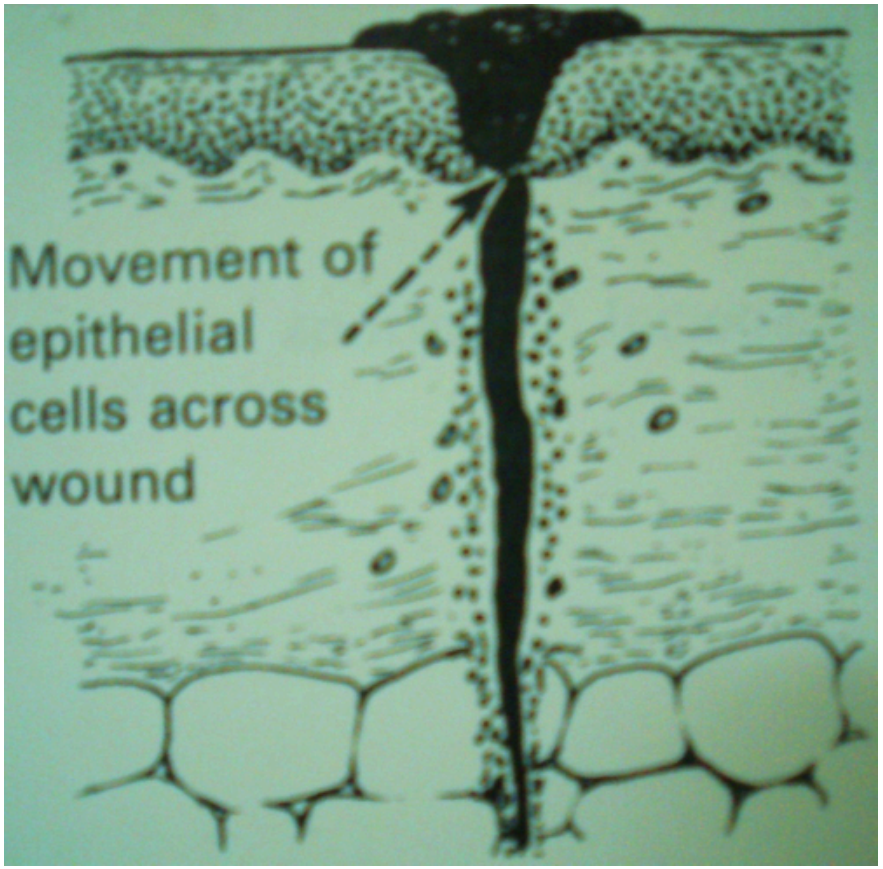
Immediate

- The narrow incisional space rapidly fills with fibrin clotted blood
- Dehydration at the surface produces a scab to cover and protect the healing repair site



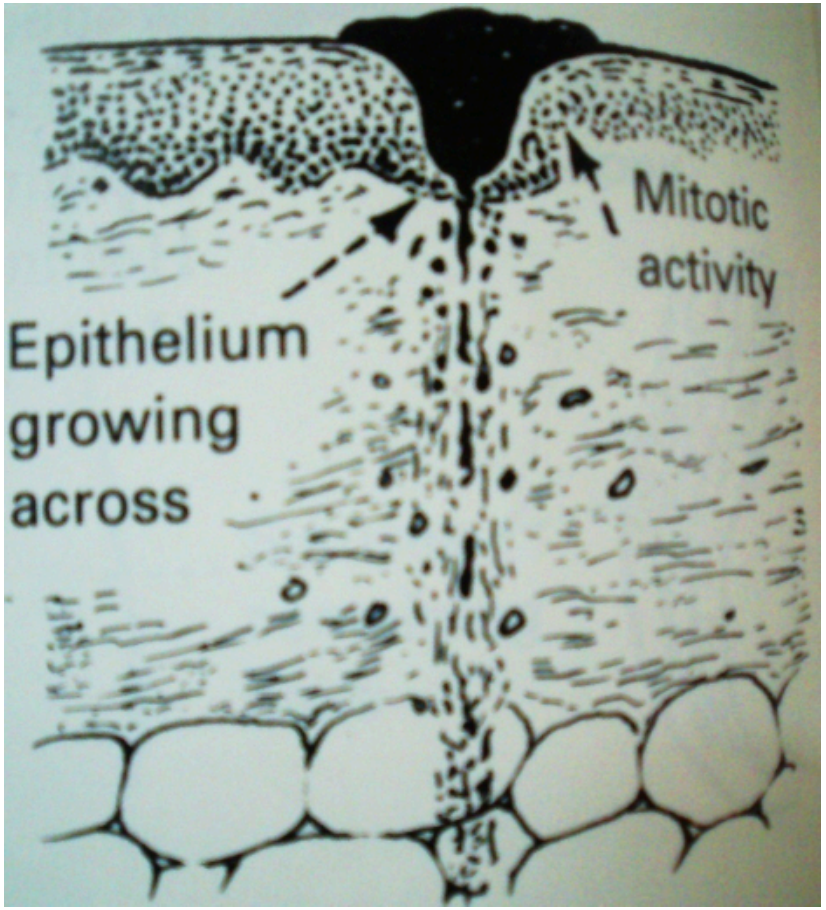
Within 24 hrs

- Movement and proliferation of epithelial cells across the wound resulting in a thin, but continuous epithelial layer
- Early inflammation close to the edges (neutrophils)



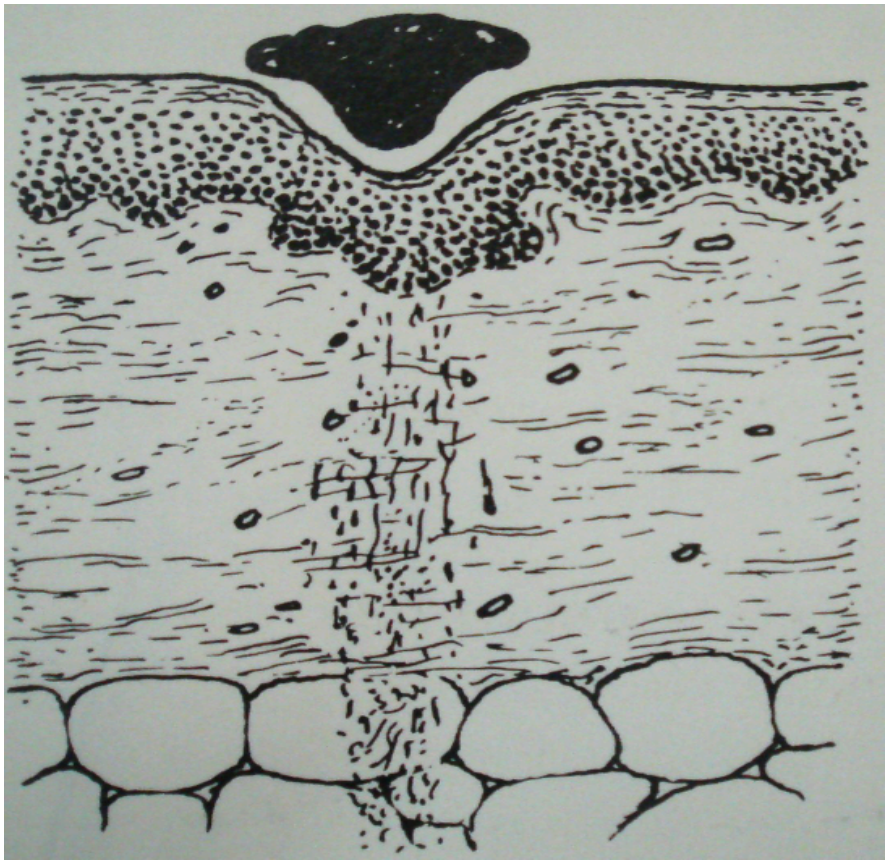
2-3 days

- Neutrophils replaced by macrophages
- Macrophages remove the blood clot
- Proliferation of epithelial cells
- Fibroblastic activity



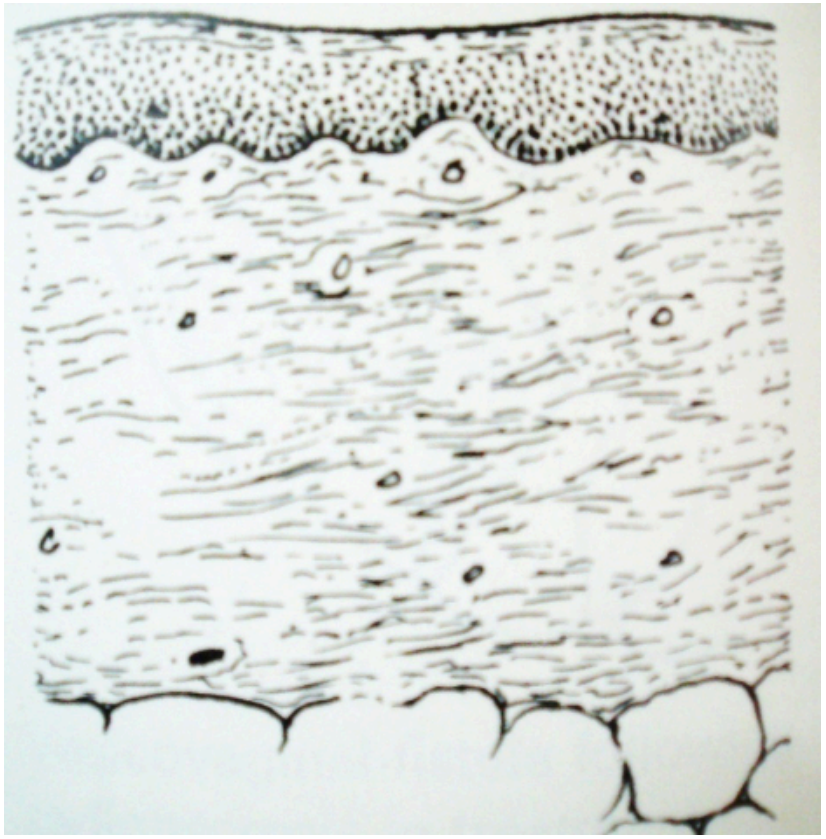
10-14 days

- *Scab loose* *(aka dry clot)*
- *Epithelial covering complete*
- *Fibrous union of edges*
- *Wound still weak*
- *vascularization*



By the end of the first month

- *Scar comprises of a cellular connective tissue devoid of inflammatory infiltrate, covered by intact epidermis*
- *Dermal appendages destroyed in the line of incision are permanently lost*
- *Tensile strength of the wound increases and reaches maximum*



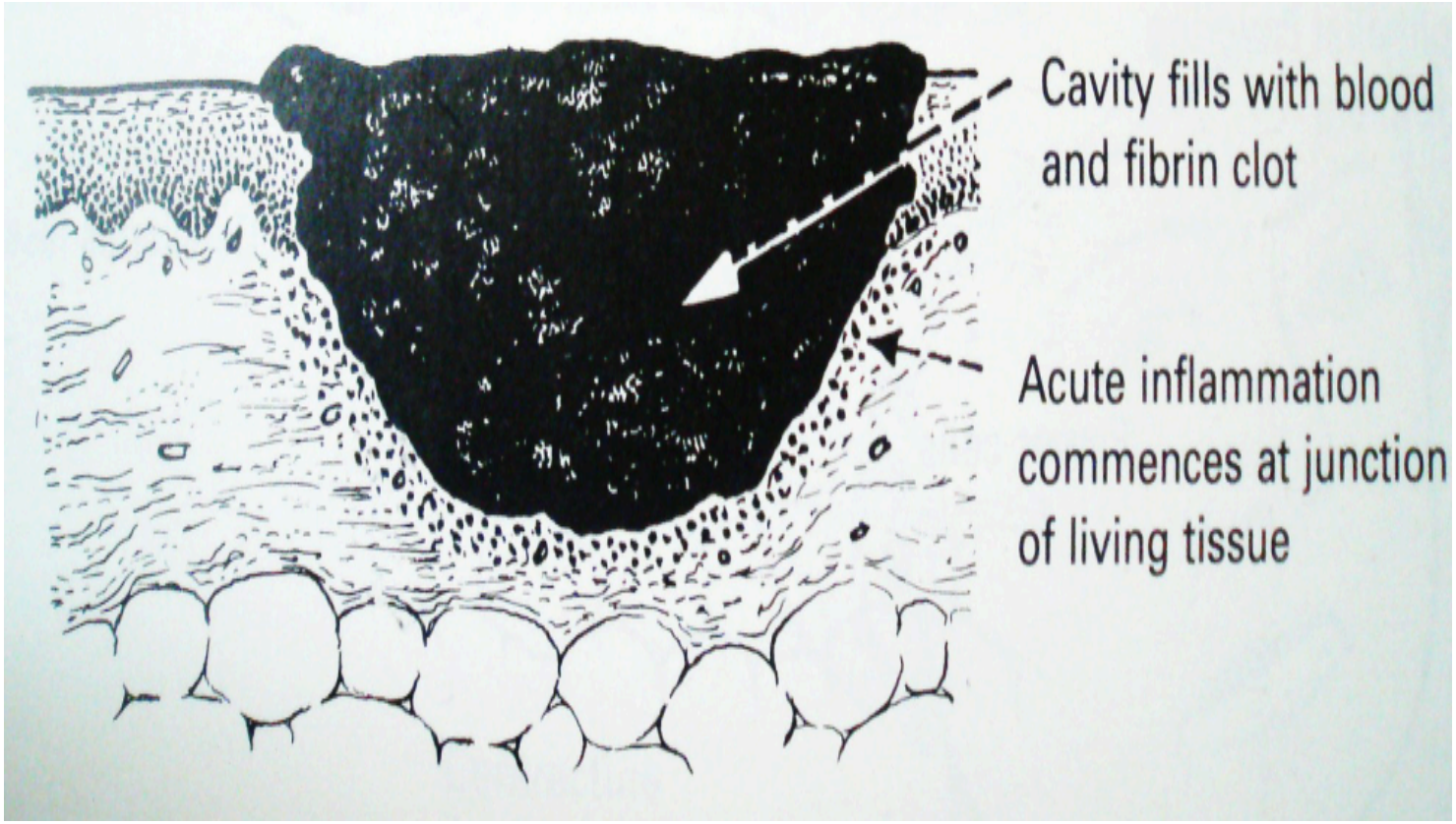
Healing by second intention (secondary union)

- This occurs in open wounds, particularly when there has been significant loss of tissue, necrosis or large wounds with irregular margins
- Regeneration of parenchymal cells cannot completely reconstitute the original architecture
- Abundant granulation tissue grows in from the margin to complete the repair
  - Granulation tissues consists of:
    - ECM fibroblasts
    - Macrophages, neutrophils
    - New blood vessels

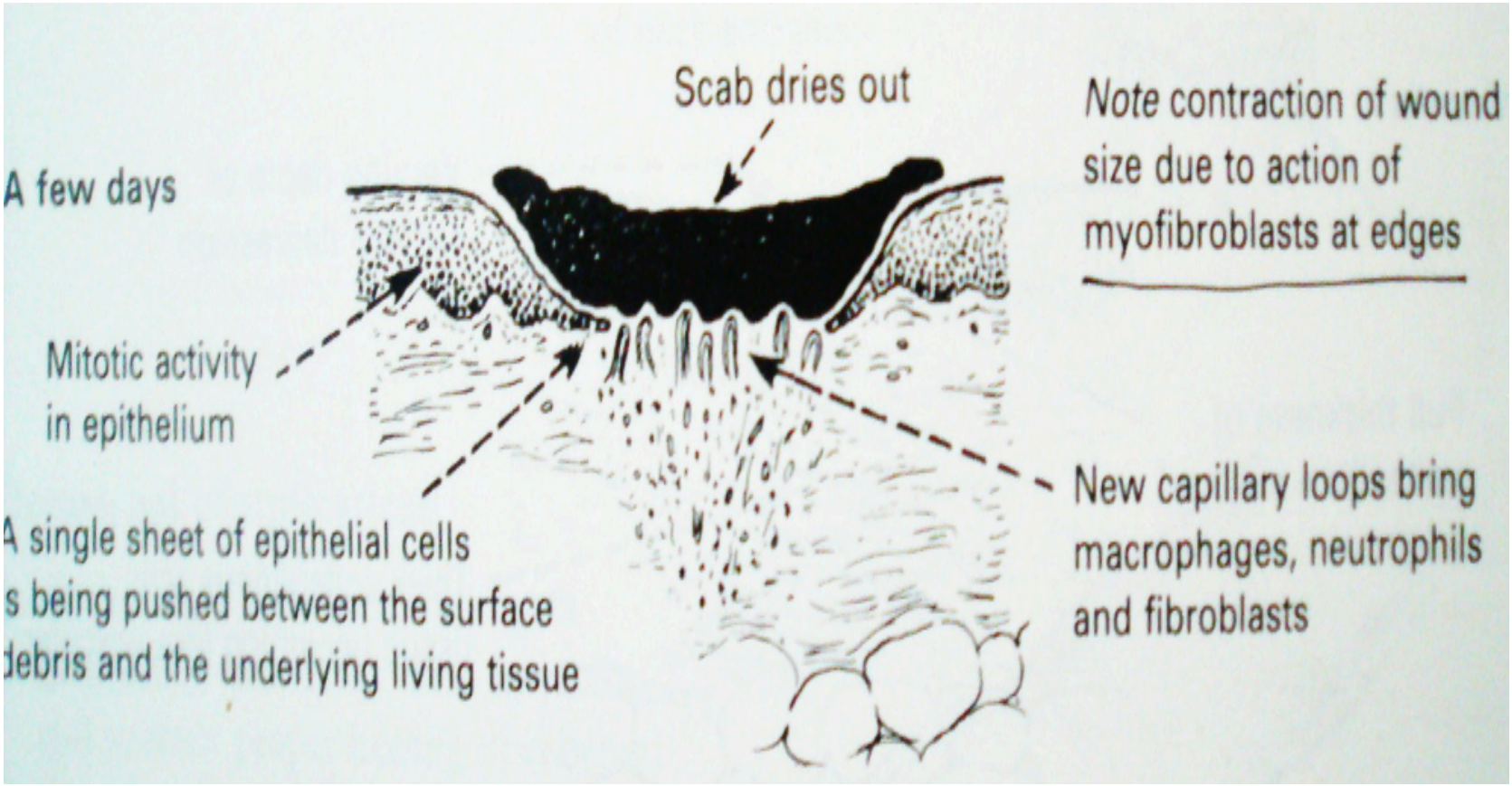
Healing by second intention (secondary union)

sequence of events

Early

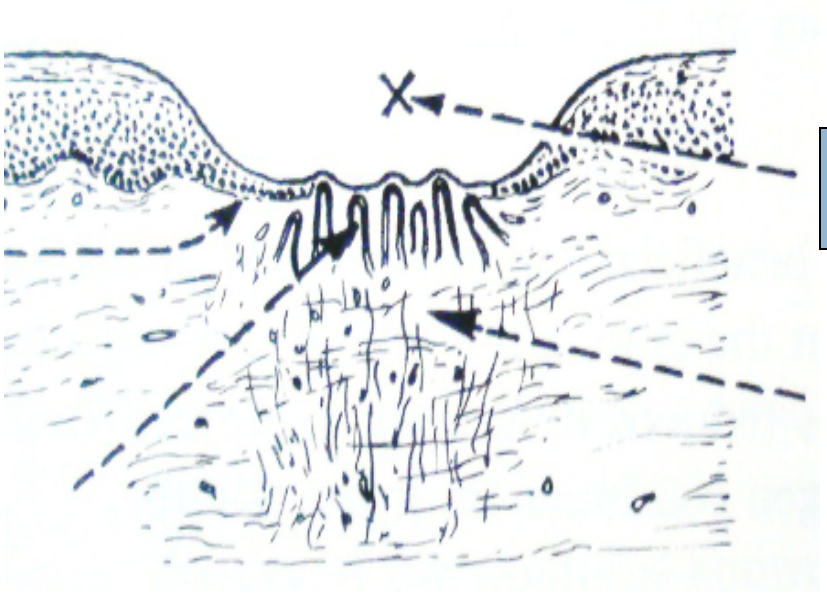

Cavity fills with blood and fibrin clot
Acute inflammation commences at junction of living tissue

A few days


Scab dries out
A few days
Note contraction of wound size due to action of myofibroblasts at edges
Mitotic activity in epithelium
New capillary loops bring macrophages, neutrophils and fibroblasts
A single sheet of epithelial cells
s being pushed between the surface
debris and the underlying living tissue

1 week

Epithelial proliferation

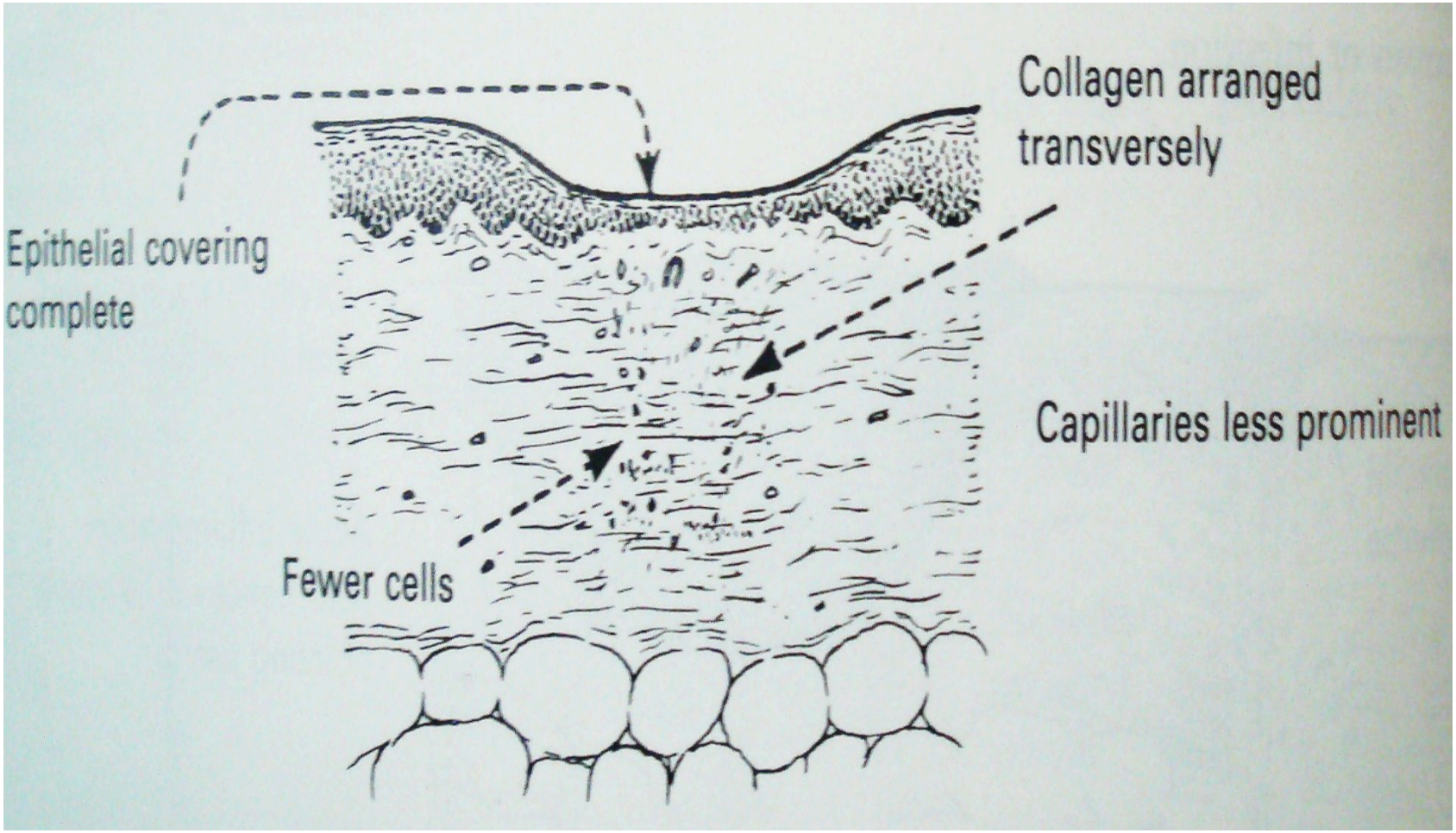


Scab shed

Loose connective Tissue formed by fibroblasts

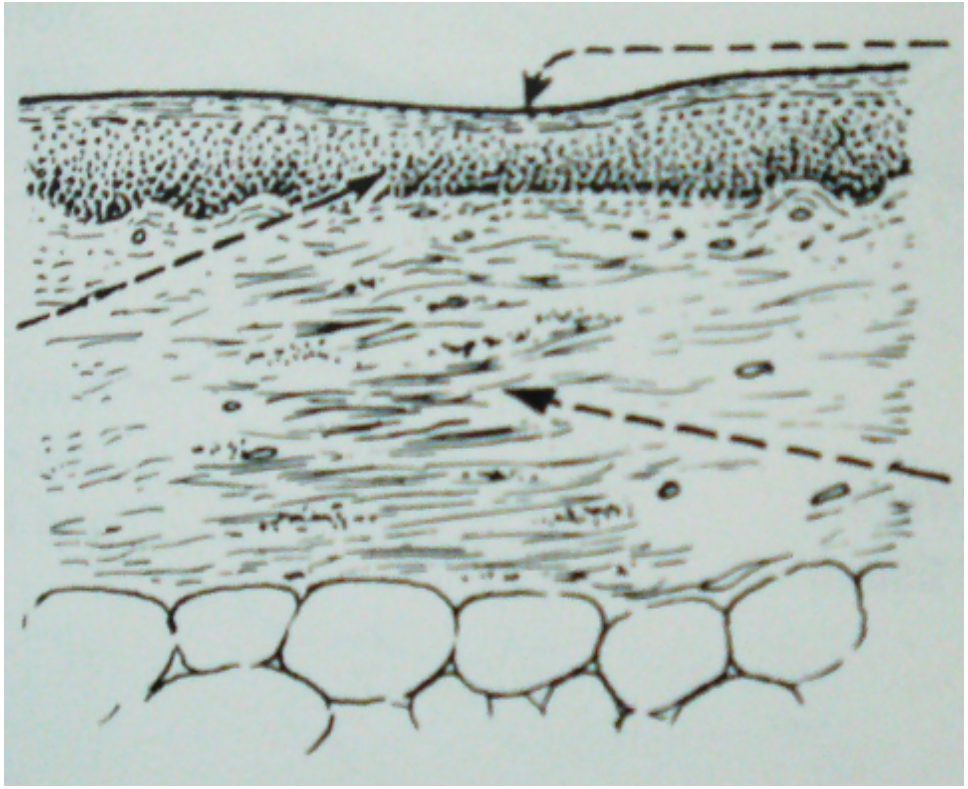
Capillary loops (granulations)

2 weeks onwards



Months

Full thickness of
Epithelium restored

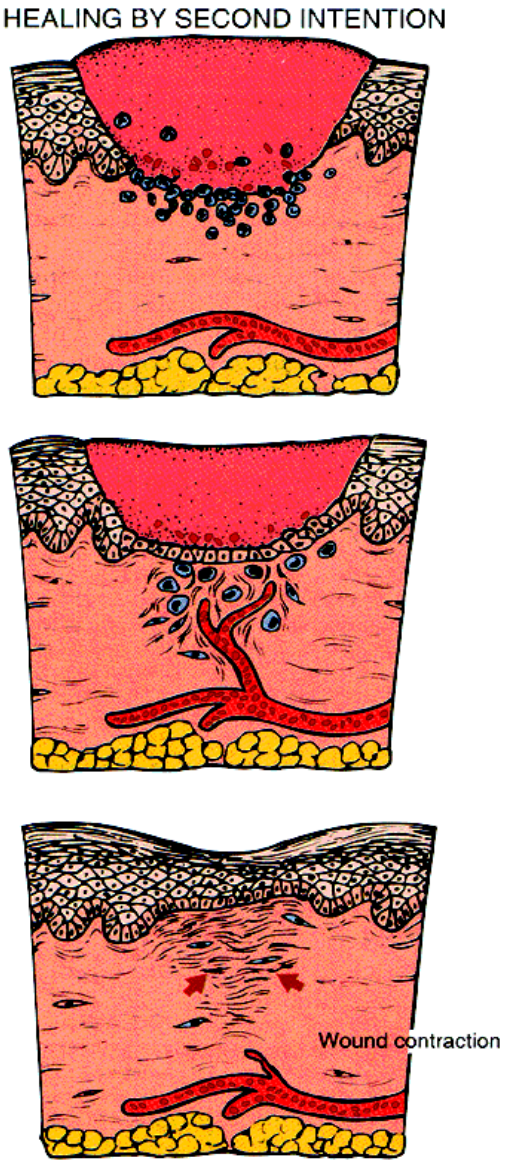


Varying depth of
Surface depression

Thick collagenous
Scar tissue becoming
Less vascular

Secondary union differs from primary union in several respects

1. inflammatory reaction is more intense
2. larger amounts of granulation tissue formation
3. larger scar
4. ***wound contraction
   - Myofibroblasts: modified fibroblasts with feature of SMC
   - defect significantly decreases in size as wound heals.



Wound Strength

- Skin wounds
  - 1 week old; 10% of unwounded skin
    - rapid increase in tensile strength as scar tissue accumulates over 2 months
  - Completely healed; 70-80% of unwounded skin
  - *Scar tissue is never as strong as the original tissue* !!

Factors that influence healing

- Classified as

A. Systemic

and

B. Local

Systemic Factors that Delay/Retard Wound Healing

- Nutrition
  - Protein deficiency, Vitamin C deficiency
    - inhibit collagen synthesis
  - Zn deficiency (cofactor in type III collagenase)
- Metabolic status
  - diabetes mellitus:
    - Susceptibility to infection caused by impaired circulation and increased glucose.
- Circulatory status
  - inadequate blood supply
    - atherosclerosis, vascular defects
- Hormones
  - glucocorticoids inhibit collagen synthesis, decrease inflammation

Local Factors that Delay/Retard Wound Healing

- Infection
  - most important cause of delayed wound healing
  - Persistent injury and inflammation
- Mechanical factors
  - motion early in healing
- Foreign material - like suture material and foreign bodies
- Size, location & type of wound
  - wounds in ↑ vascularized areas (face) heal faster than in poorly vasc areas (tendon, feet)
- small wounds heal faster than larger
  - incisions faster than blunt trauma (contusions)

Complications of wound healing

1. Deficient scar formation (most important)
2. Excessive formation of repair components
3. Exaggerated contraction

Deficient scar formation

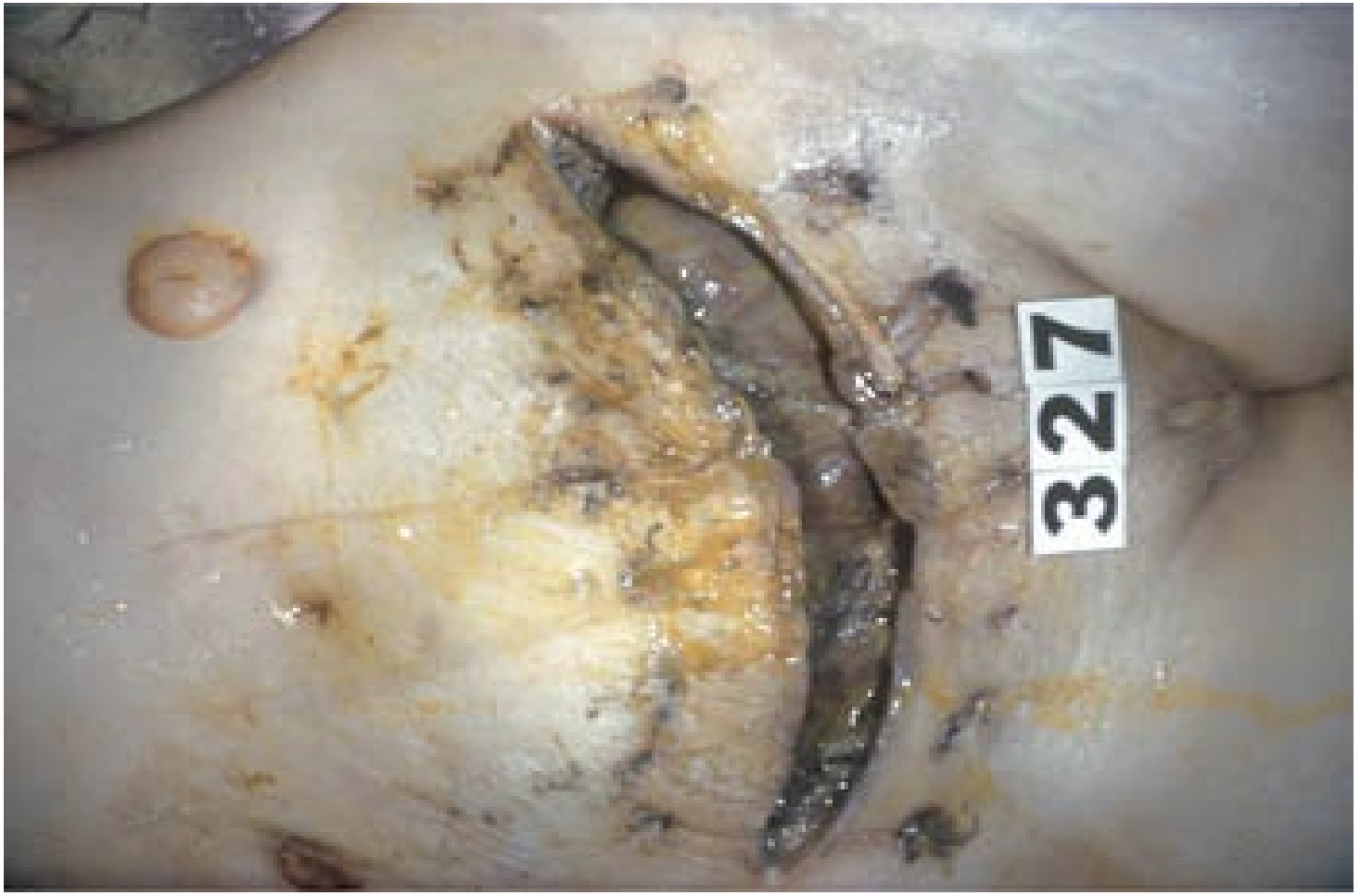
Can lead to two types of complications:

A. Wound Dehiscence (rupture of wound)

- most common after abdominal surgery
  - coughing, vomiting,

B. Ulceration - defect in the continuity

Wound Dehiscence



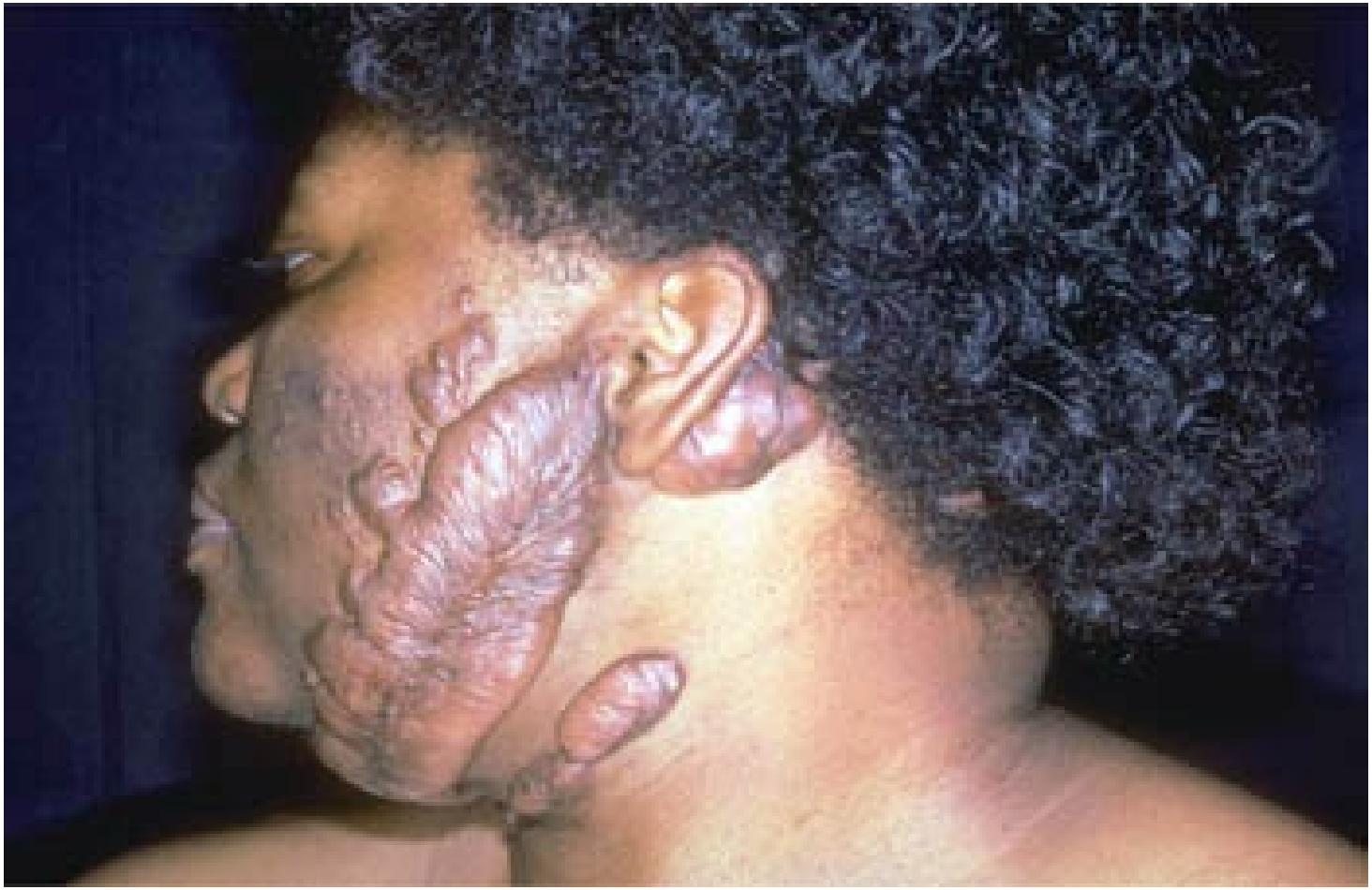
Excessive formation of repair components

1. Keloid / hypertrophic scar (excess collagen)
2. Exuberant granulation or proud flesh
   (excessive granulation tissue that protrudes above the level of the surrounding skin and impairs the growth of epithelium)

Keloid / hypertrophic scar

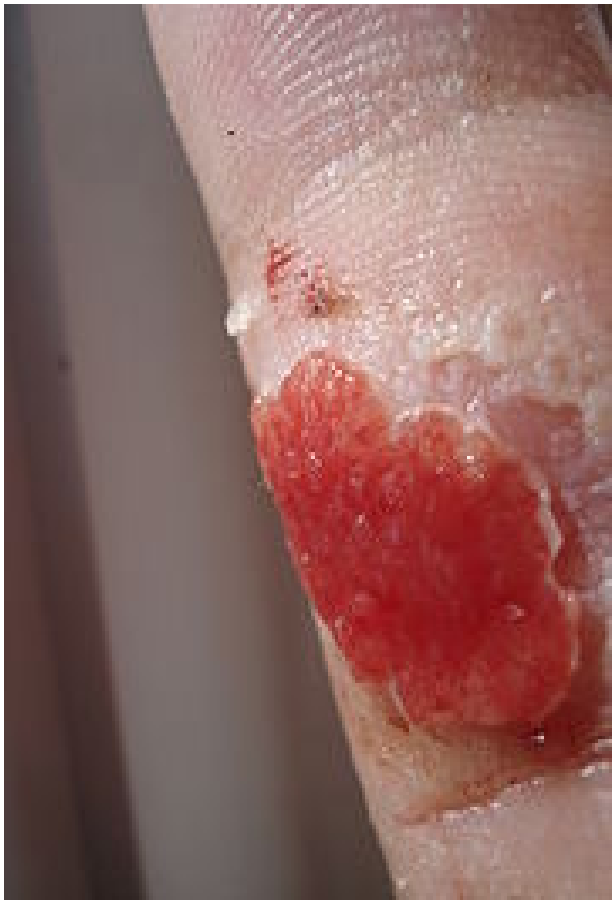
- Raised scars due to accumulation of excess amounts of collagen (type III – type I)
- Hypertrophic scars do not grow beyond the boundaries of the original wound
- Keloids grow beyond the boundaries of the original wound (more serious)
  - Can result from a surgery, an accident, body piercing or can be spontaneous
  - Genetic predisposition
  - More common in African – Americans
  - Commonly seen over face, shoulders and chest

Keloid



Exuberant granulation (proud flesh)

- Excessive granulation tissue
- Protrudes above surrounding skin
- Prevents re -epithelialization



Exaggerated contraction

- deformation of surrounding tissue or wound
- Can compromise the movement of joints.
- most common on
  - palms, soles, anterior thorax following severe burns

Important Growth factors responsible for wound healing

- Platelet derived growth factor:
  - Promotes migration and proliferation of fibroblasts
  - Is chemotactic for monocytes
- Epidermal growth factor
  - Promotes growth of endothelial, epithelial cells and fibroblasts

Growth factors in wound healing

- Fibroblast growth factor:
  - Promotes synthesis of ECM proteins including fibronectin.
  - Chemotactic for fibroblasts and endothelial cells
  - Promotes angiogenesis
- Vascular Endothelial Growth Factor (VEGF)
  - Angiogenesis
- Macrophage derived growth factors
  - IL-1 and TNF
    - Promote proliferation of fibroblasts and endothelial cells.