Wound Healing

Wound Healing

- After Injury to cells and tissues, series of events take place to initiate the healing process. Healing process can be divided into 3 types:
  - Regeneration
  - Repair
  - Fibrosis

Wound Healing

- **Regeneration**:
  - Refers to the proliferation of cells and tissues to replace the lost structure essentially return to a normal state. It occurs by proliferation of cells that survive after injury and retain the capacity to proliferate.
  - Example: in the rapidly dividing epithelia of the skin and intestines, and in some parenchymal organs, like the liver.
  - In other cases, tissue stem cells may contribute to the restoration of damaged tissues.
  - But in lower animals like salamanders and fish that regenerate entire limbs or appendage and mammals have a limited capacity to regenerate damaged tissues and organs.

Wound Healing

- **Repair**:
  - Replacement of lost tissue by granulation tissue that matures to form scar tissue. This occurs when the surrounding specialized cells do not possess the capacity to proliferate and replace the lost tissue. Like in muscle and neurons.
  - **Regeneration** occurs in labile cells & **repair** occurs in permanent cells.

- **Fibrosis**:
  - Extensive deposition of collagen that occurs due to persistent injury in chronic inflammatory process or disease. E.g: cirrhosis of liver, kidney, lungs etc.

Wound Healing

- If the supporting structures of the tissue are severely damaged then repair occurs by the laying down of connective (fibrous) tissue & this process may result in formation of a scar.
- Although the fibrous scar is not normal, it provides enough structural stability that the injured tissue is usually able to function.

Types of cells on the basis of regeneration capacity

1. Labile cells (continuously dividing types of cells)
2. Quiescent (stable cells)
3. permanent cells(non dividing types of cell)

1. Labile cells (continuously dividing cells):

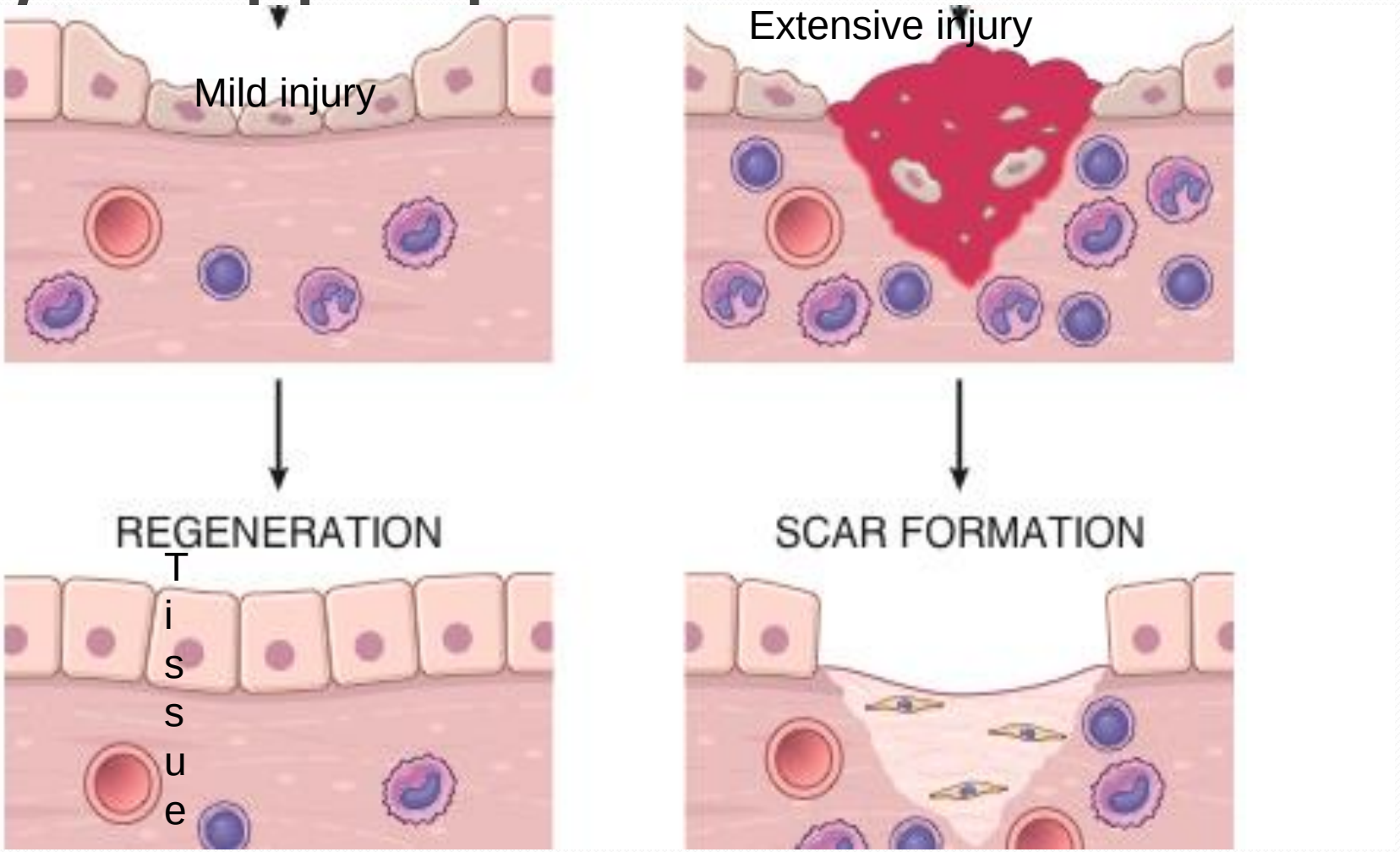
- These cells Proliferate throughout life replacing those tissue that are destroyed. E.g.
  - Stratified squmaous epithelium of the skin, oral cavity, vagina, cervix, the lining mucosa all excretory ducts of glands (salivary gland, pancreas, biliary tree etc)
  - The columnar epithelium of gastrointestinal tract
  - Transitional epithelium of urinary tract.
  - Cells of bone marrow and hematopoietic tissues.

2. Stable cells(Quiescent cells):

- Normally they have low capacity of replication, however can undergo rapid division in response to stimuli. e.g.
  - Parenchymal cells of liver, kidney and pancreas
  - Mesenchymal cells such as fibroblast and smooth muscle
  - Vascular endothelial cells
  - With exception of liver, stable cells have limited capacity to regenerate after injury.

3. Non dividing (permanent cells):

- Actually these types of cell have no capacity to proliferate. So regeneration occur by scar formation.
- Example: Neurons, and cardiac muscle, skeletal muscle.



NotesMed.com

Wound healing

- If repair can't be accomplished by tissue regeneration it occurs by replacement of injured cells by connective tissue(fibers) leading to formation of scar.

- Or by combination of regeneration of some residual cells and formation of scar.

Steps in scar formation

a. *Angiogenesis*: formation of new blood vessels(VEGF) from existing one.
b. *Formation of granulation tissue*: it is immature mesenchymal (connective) tissue with proliferation of fibroblast with macrophase and the formation of new blood vessels . The term granulation tissues derives from its pink, soft, granular appearance on the surface of wounds.

- This tissue progressively invades the site of injury & the amount of granulation tissue that is formed depends on the size of the tissue deficit created by the wound and the intensity of inflammation.

c. *Remodeling of connective tissue*

- Maturation and organization of connective tissue producing a stable fibrous scar. Wound strength increases because of cross-linking of collagen and increased size of collagen fibers. In addition, there is a shift of the type of collagen deposited, from type III collagen early in repair to more resilient type I collagen

Wound healing

1. Primary healing/healing by first intention
2. Secondary healing/ healing by second intention

1.Primary healing/healing by first intention

Healing of clean, uninfected surgical incision approximated by surgical sutures referred as healing by first intention.

Sequences of events in primary wound healing

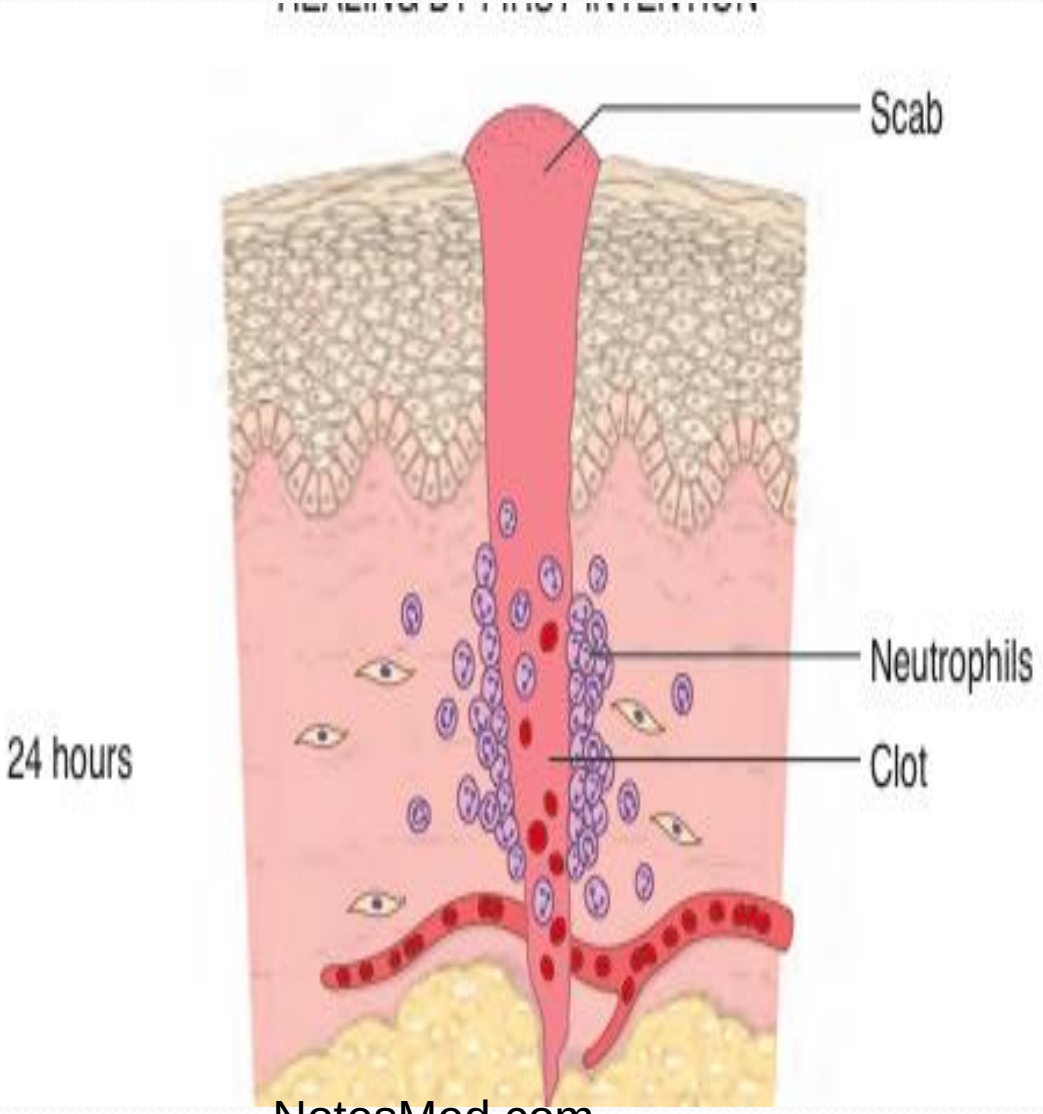
1. Blood clot formation
2. Granulation tissue formation
3. Cell proliferation and collagen deposition
4. Scar formation
5. Wound contraction
6. Recovery of strength

Healing by first intention (cutaneous wound)

a. Formation of blood clot(within 24 hr):

-Rapid activation of coagulation pathways, results in formation of blood clot.

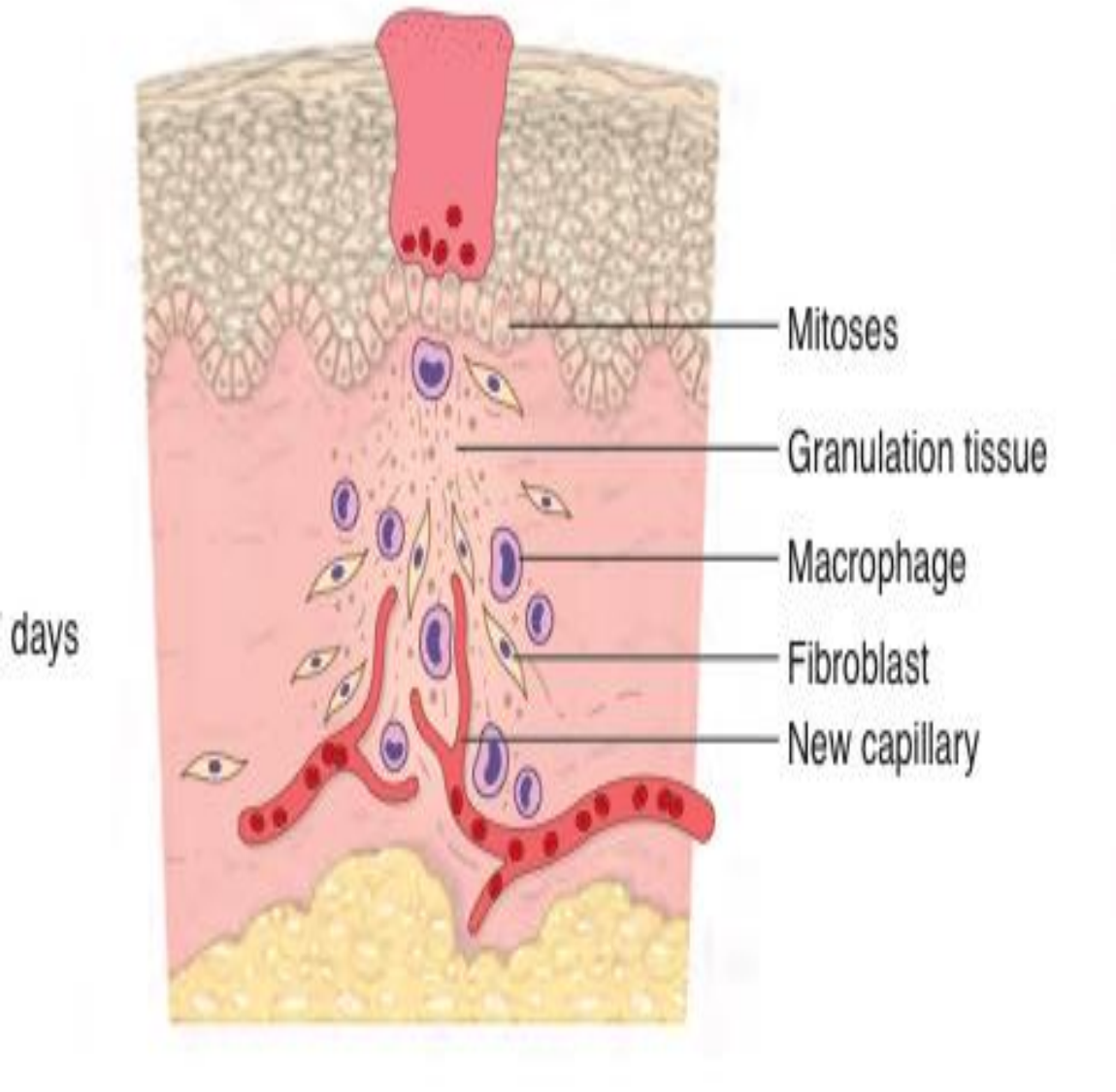
-neutrophils appear at margin of the incision. They release proteolytic enzymes that clean out debris and bacteria and formation of scab that covers the wound.



b. Granulation tissue formation(3-7 days):

-Fibroblasts and vascular endothelial cells proliferation called granulation tissue which invades the incision space.

-By 5-7 days, granulation tissue fills the wound area and neovascularization is maximal



Day3- 5th: Cell proliferation and collagen deposition:

-Neutrophils replaced by macrophages (by 48-96 hrs) which promotes angiogenesis,fibroblastic proliferation and extracellular matrix deposition(ECM),

-Collagen fibers bridge the incision

-Epithelial cells proliferate and fuse beneath the surface scab

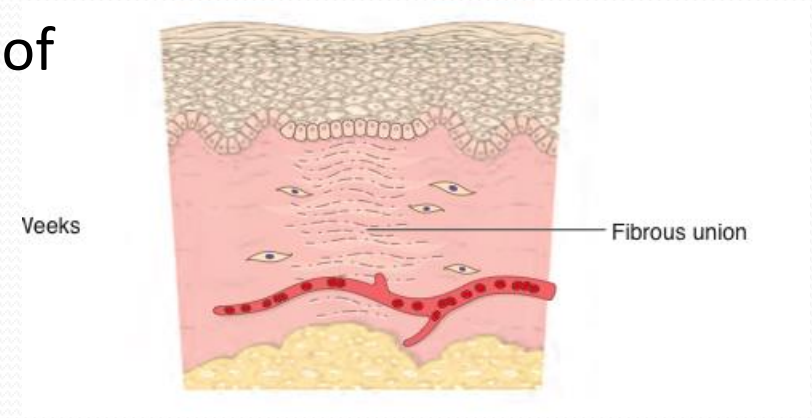
-The epidermis recovers its normal thickness and architecture

c.Weeks(month): scar formation.

Continue accumulation of fibrocollagenous tissue.

Disappearance of leukocyte infiltrate and edema.

-Formation of scar by connective tissue



Wound contraction follows

2.Secondary healing/healing by second intention

Healing by secondary intention occurs when cell or tissue loss is more extensive, ulceration, ischemic necrosis(infarction) in parenchymal organs, the repair is more complex and involves a combination of regeneration as well as scarring.

Secondary healing differs from primary healing in followings:

- Larger tissue defects generate a larger fibrin clot that fills the defect. (hematoma formation)
- The inflammatory reaction is more intense.
- Granulation tissue formation: more
- Wound contraction: more by action of myofibroblast.
- Scar formation

Factors affecting wound healing

A. systemic:

1. **Nutrition**: protein deficiency and vitamin C deficiency and trace elements such as copper and zinc deficiency - inhibit collagen synthesis and impairs wound healing.
2. **Age:** Wound healing is rapid in young age people compared to in aged people
3. **Metabolic states**: e.g. Diabetes mellitus is associated with delay wound healing due to microangiopathy
4. **Circulatory status**: inadequate blood supply (e.g. arteriosclerosis) or venous abnormalities (e.g. vericose veins) that retard venous drainage and that impairs wound healing

Factors affecting wound healing

A. Systemic factors

5. **Hormones**: steroids have anti-inflammatory effects and inhibits collagen synthesis, thereby inhibits wound healing
6. Hematological abnormalities: qualitative or quantitative defects in neutrophils and bleeding abnormalities may delayed healing process.

Factors affecting wound healing

B. Local factors

1. **Infection**: cause delay wound healing
2. **Mechanical factor**: movement impairs wound healing. E.g: at joints
3. **Size,location and type of wound:**
   - Highly vascularized area (face) heal faster than those in poorly vascularized area(foots).
   - Small incisional injuries heal faster that large excisional wounds
4. Foreign bodies: inessential sutures or foreign bodies (fragment of steel, glass), or even bone can dealy the wound healing.
5. Ionizing radiation may decreases repair process
6. Complications may delayed wound healing.

Complication of wound healing

A. Deficient scar formation
B. Excessive formation of the repair components
C. Formation of contracture
D. Others
    A. Epidermal cysts
    B. Pigmentation
    C. Infection of wound by different microbes
    D. Neoplasia: e.g. Squamous cell carcinoma (SCC) may develop in Marjolin's ulcer.
E. Fibrosis: excessive deposition of ECM and collagen.

A. Defective scar formation

- Inadequate formation of granulation tissue or assemmbly of scar can lead to

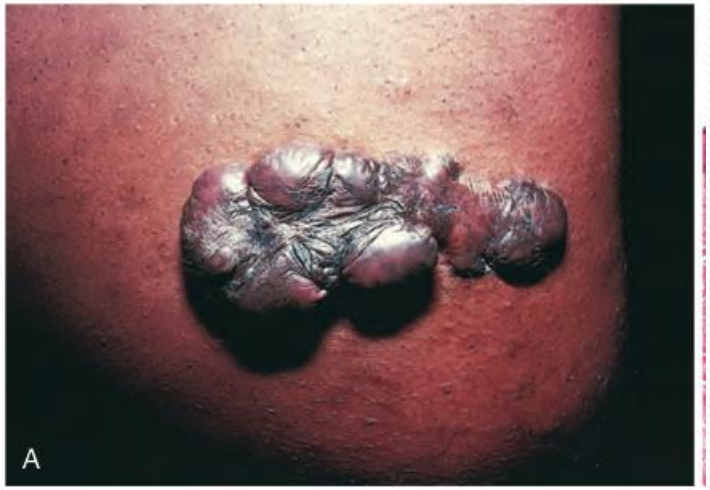
1. **Wound dehiscence**:
   - Dehiscence or rupture of wound is common like after abdominal surgery due to increased abdominal pressure. Mechanical stress on abdominal wall: e.g. vomiting and coughing or ileus.
2. **Ulceration**:
   - Inadequate blood supply during healing: peripheral vascular disease
3. **Incisional hernia:**
   - It is due to insufficient deposition of extracellular matrix or inadequate cross-linking in the collagen matrix.

Excessive formation of the repair component

1. **Hypertrophied scar**: Accumulation of excess amounts of collagen
2. **Exuberant granulation**: formation of excessive amount of granulation of tissue which protrudes above the skin surface level . E.g.
    1. Pyogenic granuloma or granuloma pyogenicum or proud flesh
    2. Desmoid or aggressive fibromatoses: usually occurs in the anterior abdominal wall.

3. Keloid:

- If the scar tissue grows beyond the boundaries of original wound and doesn't regress it is called keloid.(excessive ECM production or excessive deposition of type III collagen) and more common in dark skinned persons.



Contraction

- Exaggeration of contraction at wound site is called contracture resulting in deformities of wound and surrounding tissues. E.g. in burns
- Site of contracture: Palm, sole and anterior aspect of the thorax.
- Consequences of contractures:
  - Compromise movements: burns and joint movements.
  - Obstruction: e.g. stricture