

HEALING AND REPAIR

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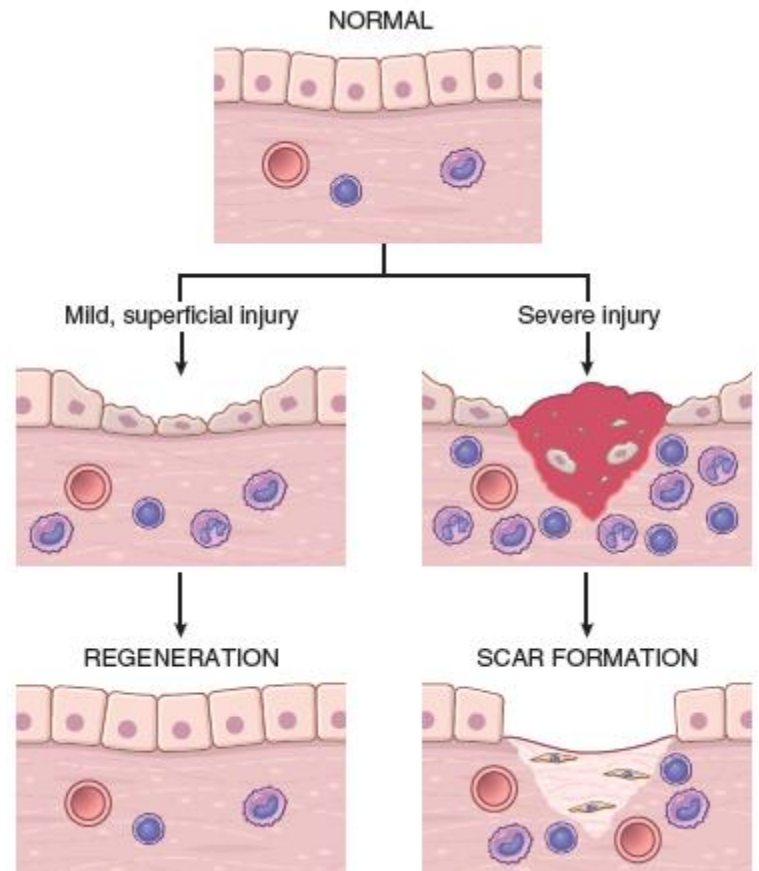
1. Definition of tissue repair
2. Types of tissue repair
3. Proliferative capacity of tissue
4. Consequences of disordered tissue repair

Repair: Definition

- Repair aka healing, refers to the restoration of tissue architecture and function after an injury

Two methods

- Repair of damaged tissues occurs by two types of reactions:
 - REGENERATION by proliferation of residual (uninjured) cells and maturation of tissue stem cells, and
 - the DEPOSITION OF CONNECTIVE TISSUE to form a scar



Clinical application

- *Fibrosis*: extensive deposition of collagen that occurs in....as a consequence of chronic inflammation, or in the myocardium after extensive infarction
- If fibrosis develops in a tissue space occupied by an inflammatory exudate, it is called *organization* (as in *organizing pneumonia* affecting the lung).

REPAIR BY REGENERATION

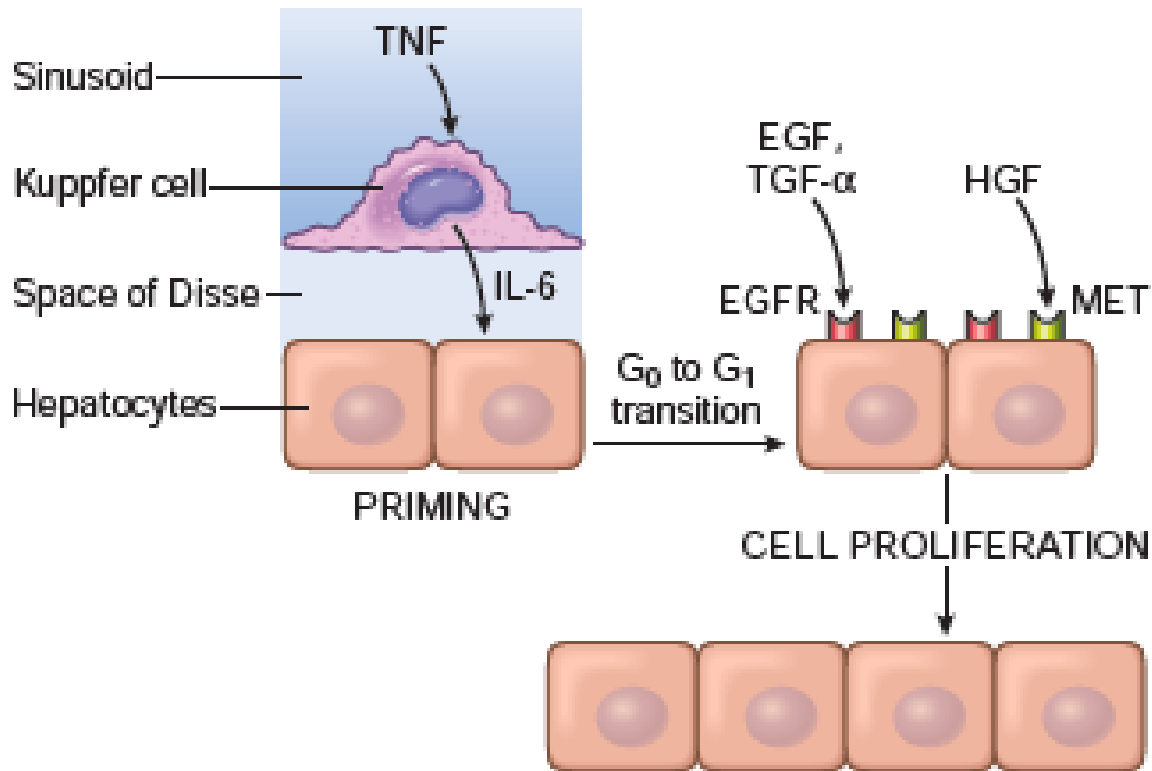
Proliferative capacity of tissues

- **Labile**
 - Continuously dividing
 - Eg. Surface epithelium such as skin, bone marrow, duct, columnar (GIT)
- **Stable**
 - Quiescent (G0 of cell cycle)
 - liver, kidney, and pancreas, other (fibroblasts, endothelial cells, muscle)
- **Permanent**
 - Terminally differentiated
 - Neurons and muscle

Cell proliferation

- Cell proliferation is driven by signals from GFs and from the EC matrix.
 - GFs activate signaling pathways that induce production of proteins involved in driving cells through the cell cycle and other proteins that release blocks on the cell cycle (checkpoints)
 - Cells use integrins to bind to ECM proteins, and signals from the integrins stimulate cell proliferation

Liver regeneration



**REPAIR BY CONNECTIVE TISSUE
DEPOSITION**

Repair by connective tissue deposition

1. If repair cannot be accomplished by regeneration alone it occurs by replacement of the injured cells with connective tissue.

- Scar formation

Steps in scar formation

1. Angiogenesis

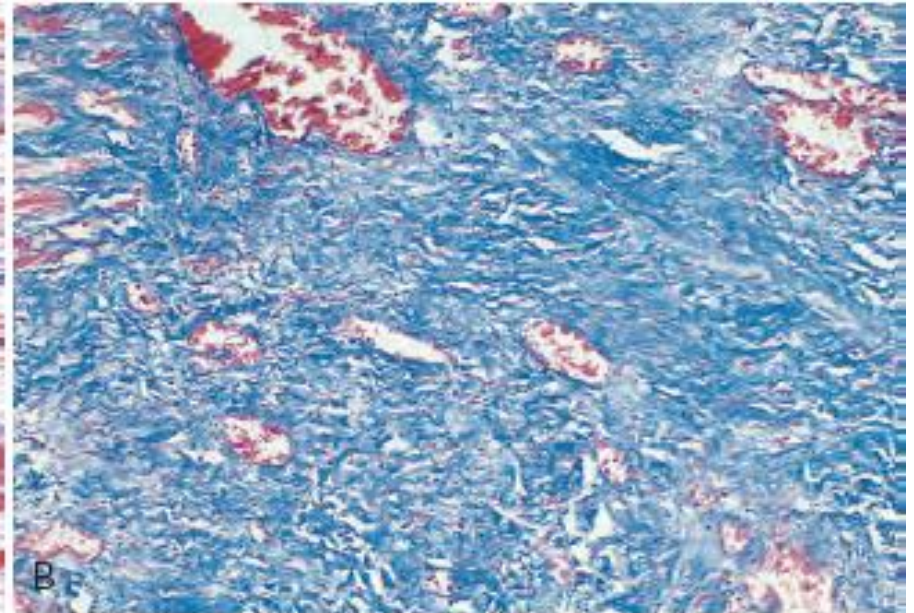
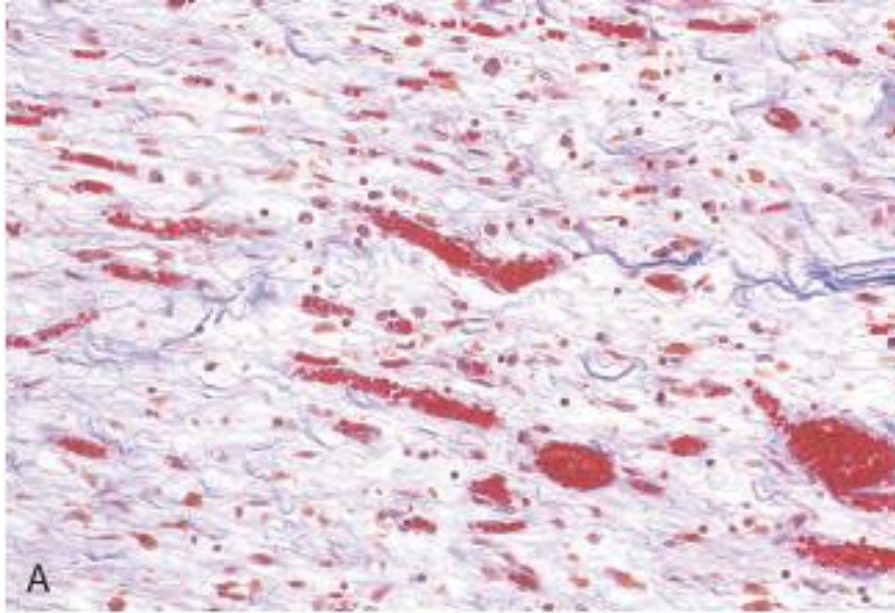
- VEGF

2. Formation of granulation tissue

- fibroblasts and loose connective tissue, new blood vessels and interspersed WBCs

3. Remodeling of connective tissue

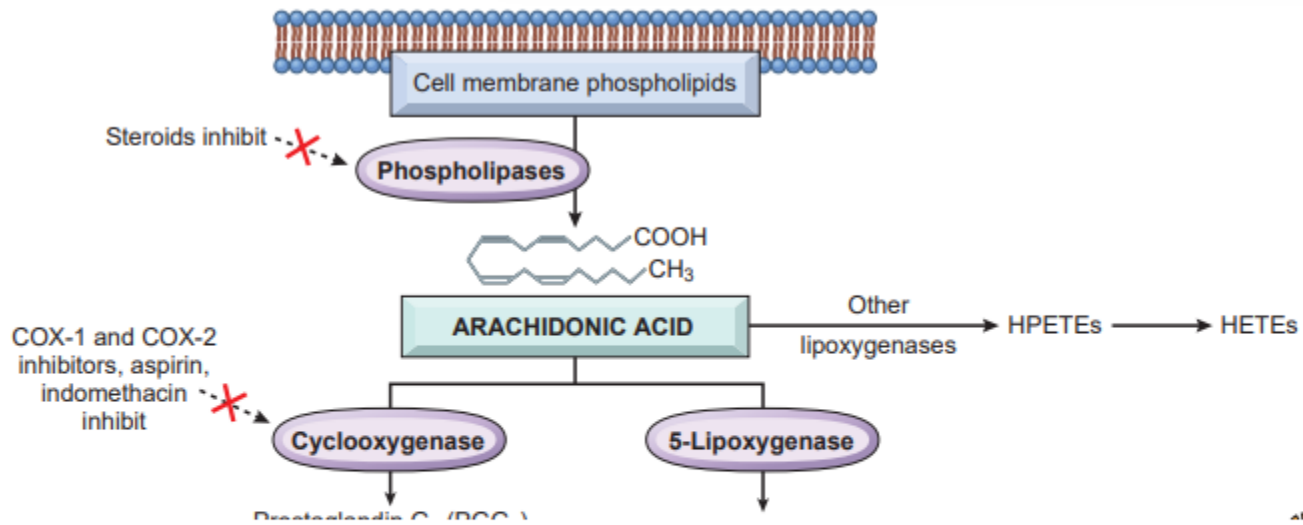
- Maturation and reorganization of the connective tissue (remodeling) produces the stable fibrous scar.



- Macrophages are a key player in healing
- Alternatively activated (M2) macrophages responsible for tissue healing by fibrosis

Factors that influence tissue repair

1. Infections
2. Diabetes
3. Nutritional status
4. Glucocorticoid (steroid)
5. Mechanical factors
6. Poor perfusion
7. Foreign bodies
8. Type and extent of injury
9. Location of injury



Healing of Skin Wounds

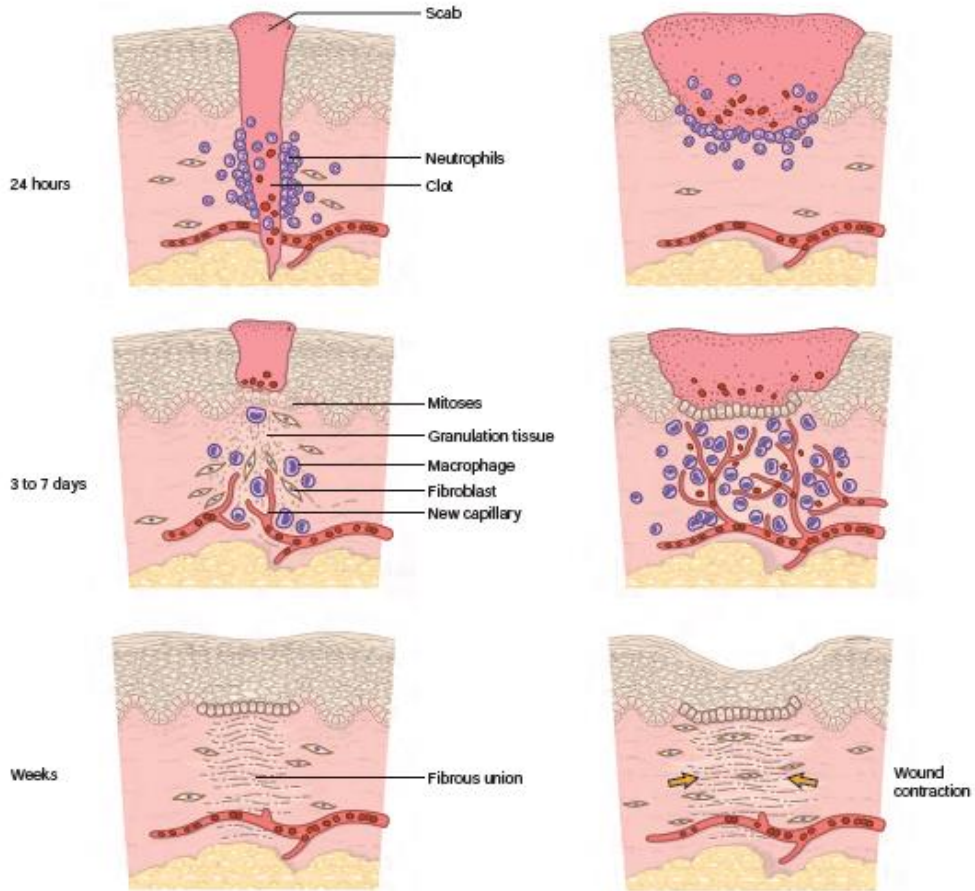
- Healing by first intention
- Healing by secondary intention

Healing by first intention

- **When the injury involves only the epithelial layer, the principal mechanism of repair is epithelial regeneration, also called *primary union* or *healing by first intention***
- ***Example: clean surgical scar***
- ***Steps: inflammation, proliferation* of epithelial and other cells, and *maturation* of the connective tissue scar**

HEALING BY FIRST INTENTION

HEALING BY SECOND INTENTION

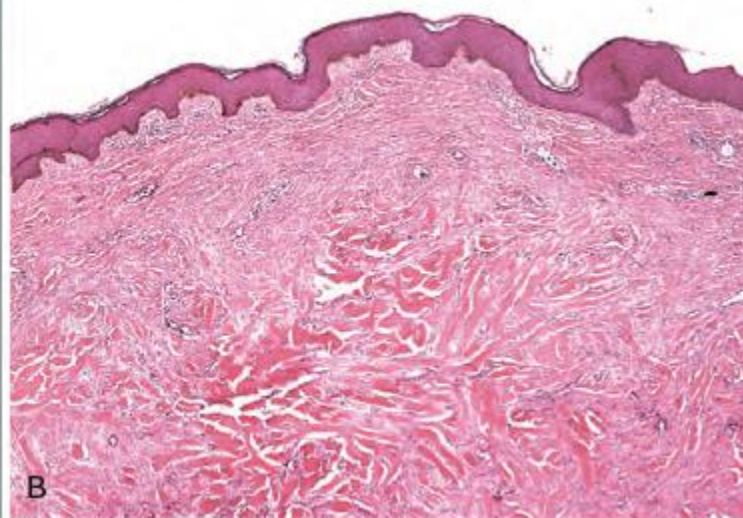


Healing by secondary intention

- **When cell or tissue loss is more extensive, such as in large wounds, abscesses, ulceration, and ischemic necrosis (infarction) in parenchymal organs, the repair process involves a combination of regeneration and scarring**

Abnormalities in tissue repair

- Inadequate formation of granulation tissue or formation of a scar: wound dehiscence and ulceration
- Excessive formation of the components of the repair process: hypertrophic scars and keloids
- Exuberant granulation: Proud flesh
- Desmoids/ fibromatoses
- *Contraction: Contractures*



- End