PATHOLOGY

MD3

PATHOLOGY

TISSUE REPAIR

Tissue Repair

Learning Objectives

- ❑ Demonstrate understanding of regeneration and healing
- ❑ Answer questions about aberrations in wound healing

Tissue Repair

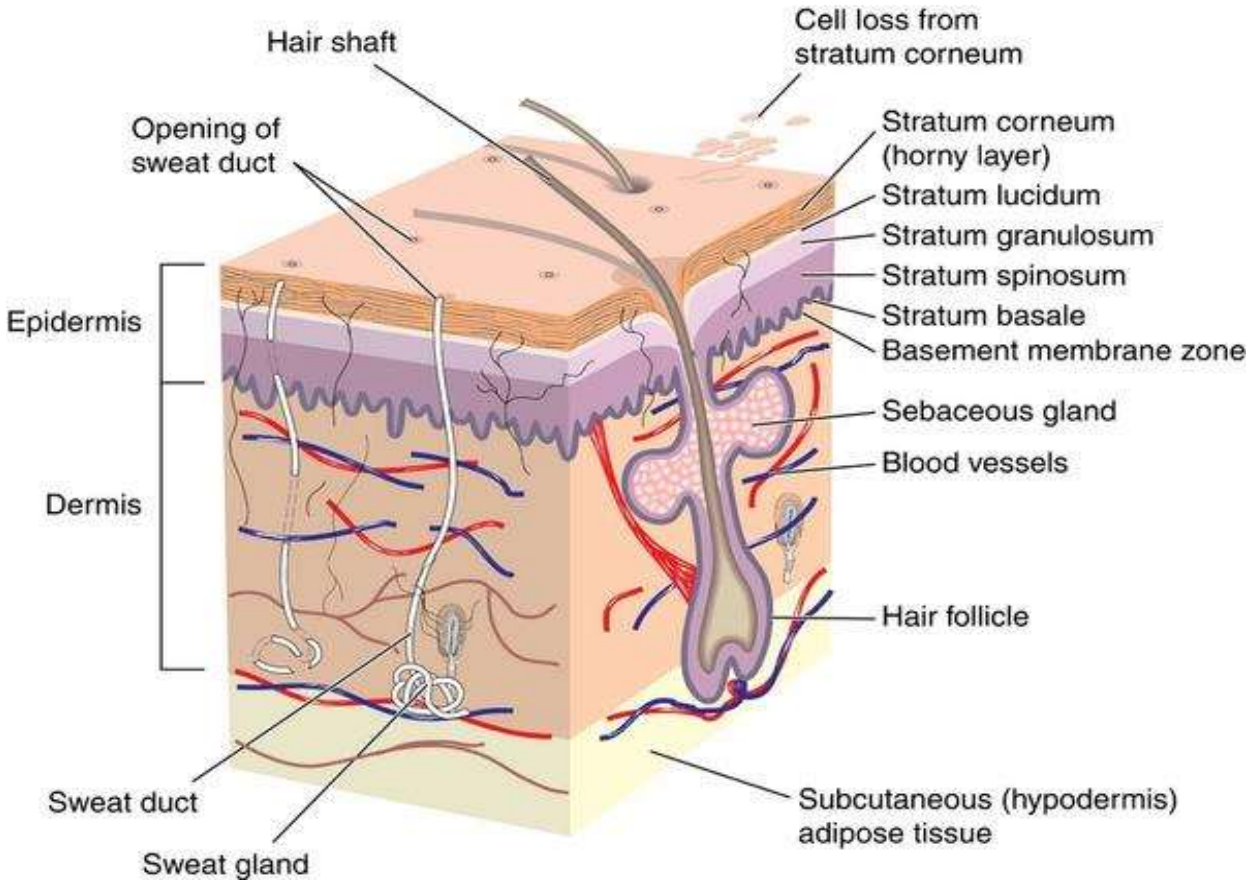
REGENERATION AND HEALING

Regeneration and healing of damaged cells and tissues start almost as soon as the inflammatory process begins. Tissue repair involves 5 overlapping processes:

- Hemostasis (coagulation, platelets)
- Inflammation (neutrophils, macrophages, lymphocytes, mast cells)
- Regeneration (stem cells and differentiated cells)
- Fibrosis (macrophages, granulation tissue [fibroblasts, angiogenesis], type III collagen)
- Remodelling (macrophages, fibroblasts, converting collagen III to I)

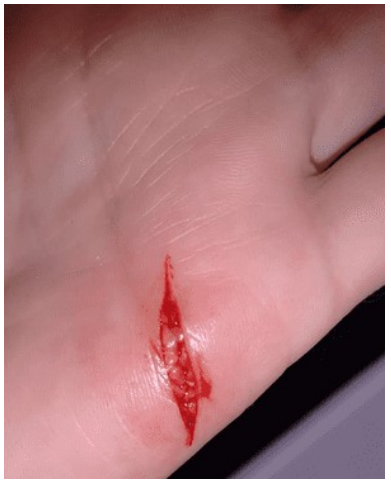
Tissue Repair

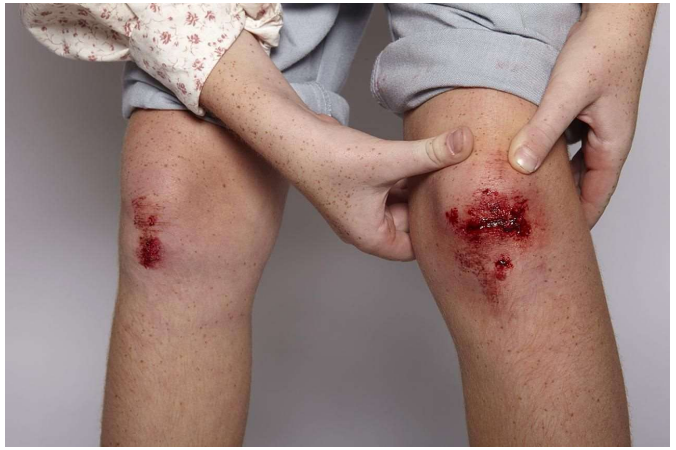
Skin

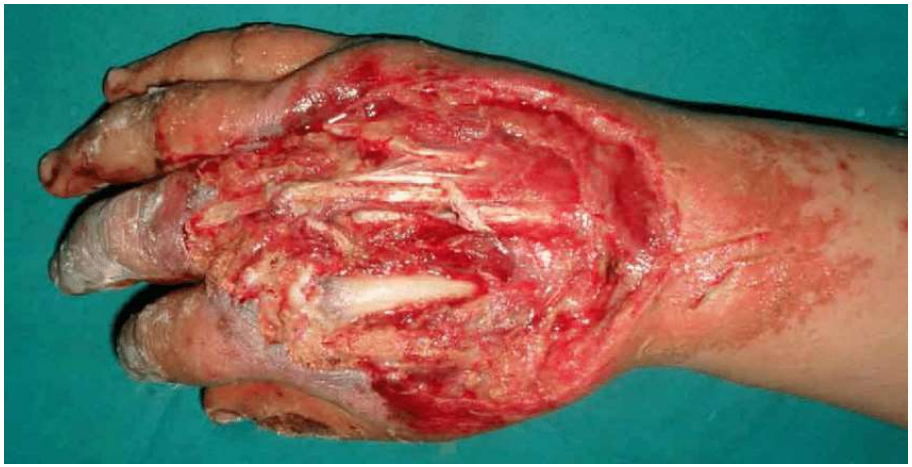


TISSUE REPAIR

Skin Injury





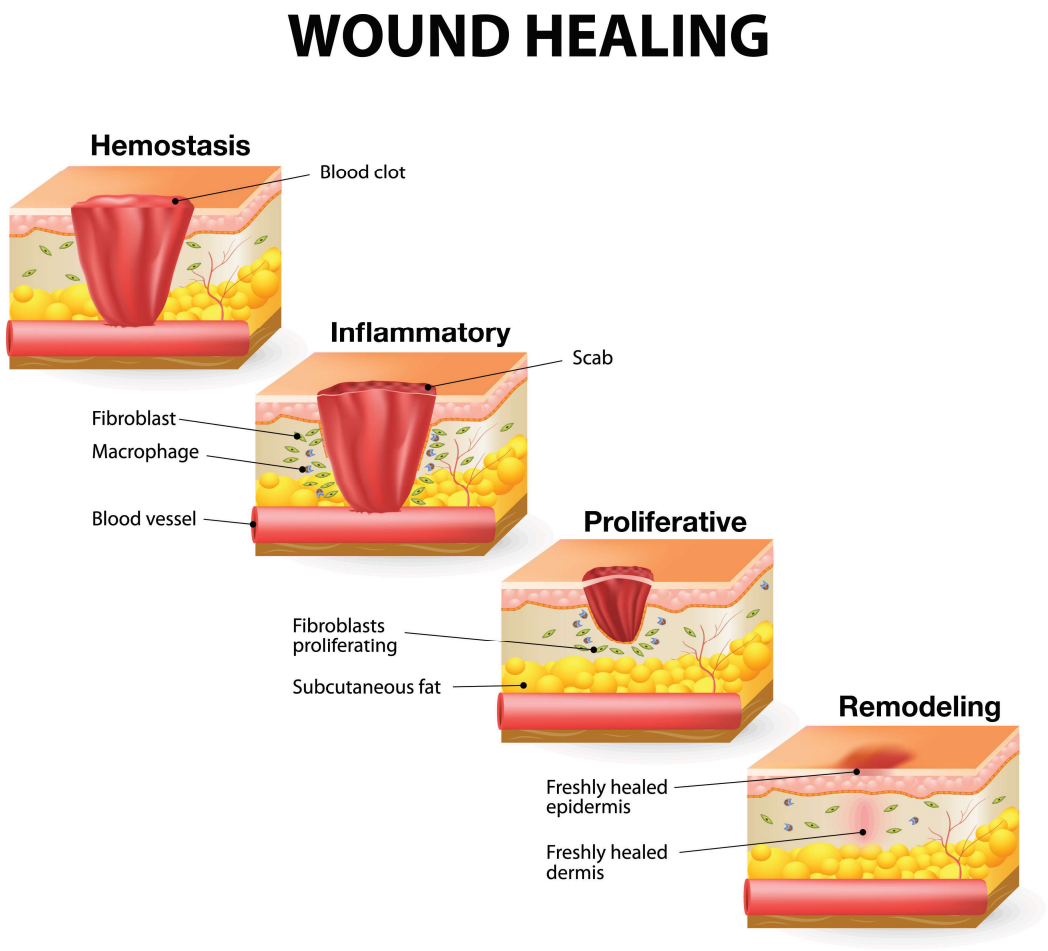


TISSUE REPAIR

Tissue injury

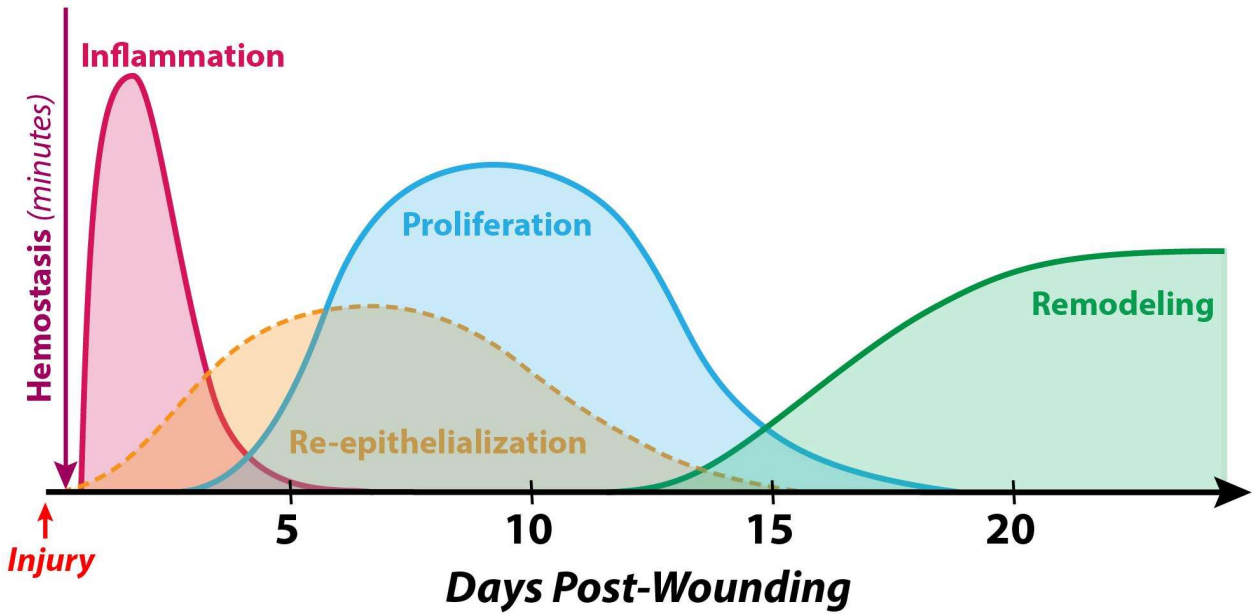
Tissue repair

Wound Healing



TISSUE REPAIR

Wound healing



Tissue Repair

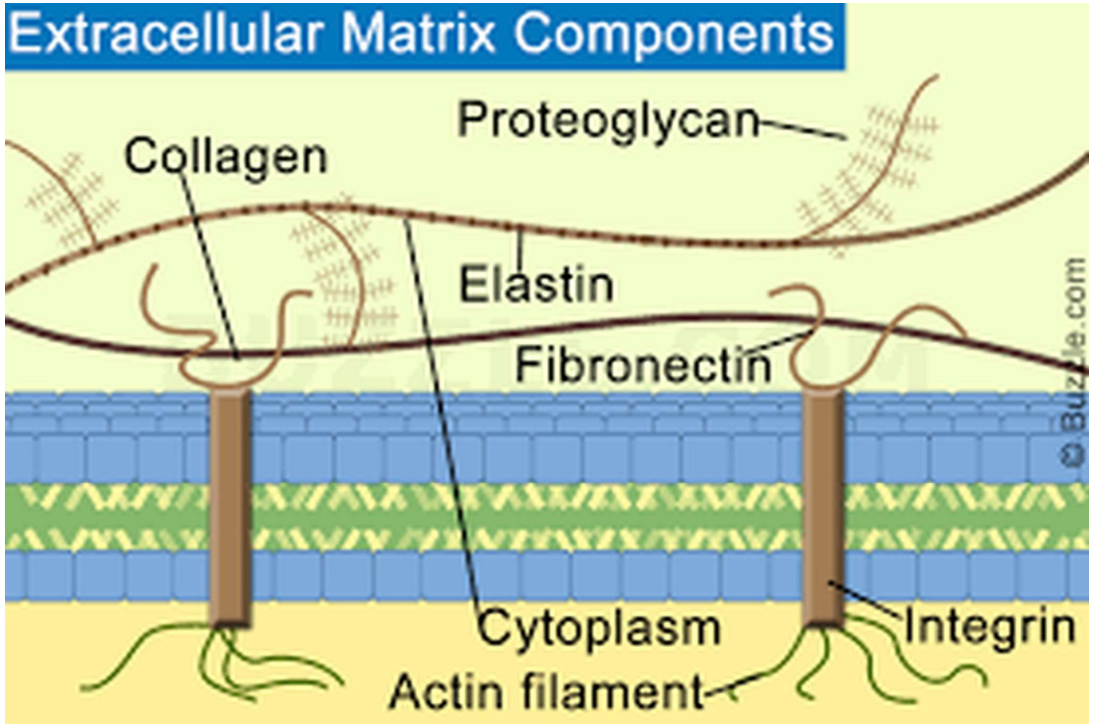
The extracellular matrix (ECM) is an important tissue scaffold with 2 forms, the interstitial matrix and the basement membrane (type IV collagen and laminin).

There are 3 ECM components:

- Collagens and elastins
- Gels (proteoglycans and hyaluronan)
- Glycoproteins and cell adhesion molecules

Tissue Repair

Extra cellular Matrix



Tissue Repair

Different tissues have different **regenerative** capacities.

- **Labile cells** (primarily stem cells) regenerate throughout life. Examples include surface epithelial cells (skin and mucosal lining cells), hematopoietic cells, stem cells, etc.
- **Stable cells** (stem cells and differentiated cells) replicate at a low level throughout life and have the capacity to divide if stimulated by some initiating event. Examples include hepatocytes, proximal tubule cells, endothelium, etc.
- **Permanent cells** (few stem cells and/or differentiated cells with the capacity to replicate) have a very low level of replicative capacity. Examples include neurons and cardiac muscle.

Tissue Repair

Scar formation occurs in a series of steps when repair cannot be brought aboutby regeneration.

- First, angiogenesis is promoted by vascular endothelial growth factor (VEGF) and the fibroblast growth factor (FGF) family of growth factors.
- Next, platelet-derived growth factor (PDGF), fibroblast growth factor 2 (FGF-2), and transforming growth factor β (TGF-β) drive fibroblast activation for the formation of granulation tissue.
- Then, TGF-β, PDGF, and FGF drive ECM deposition. Cytokines IL-1 and IL-13 stimulate collagen production for scar formation.

Tissue Repair

Types of Wound Healing

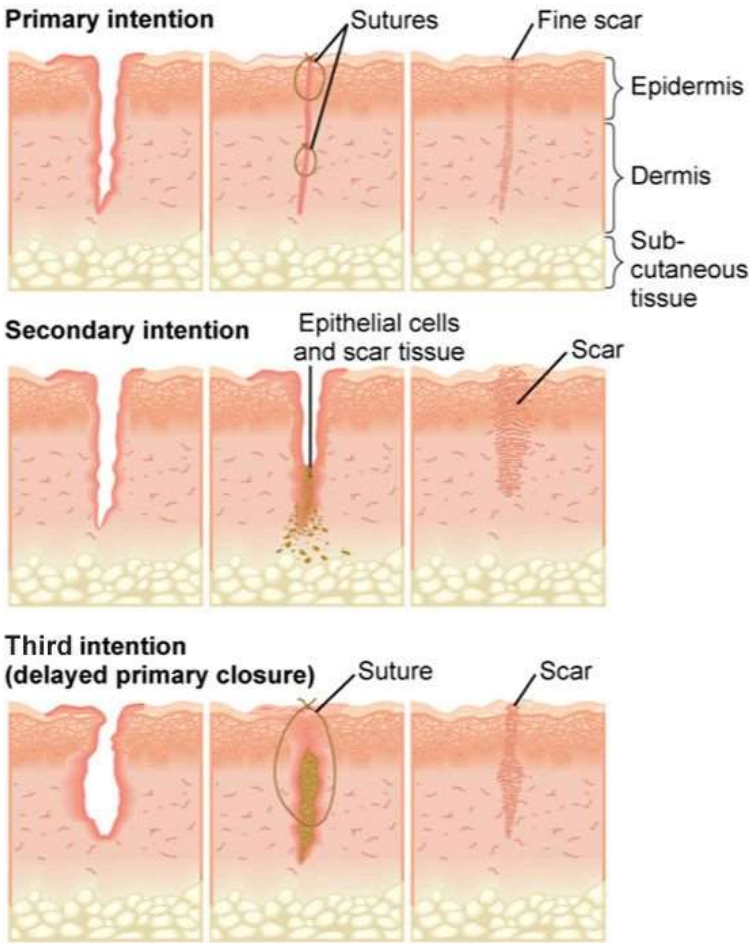
Primary union (healing by first intention) occurs when wounds are closed physically with sutures, metal staples, dermal adhesive, etc.

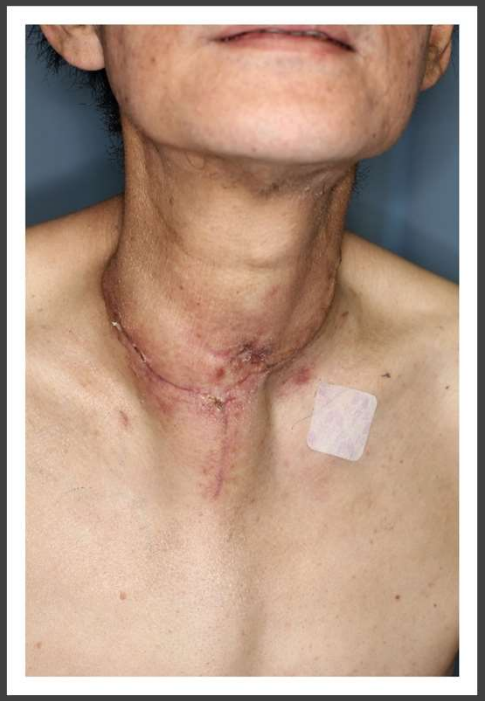
Secondary union (healing by secondary intention) occurs when wounds can heal by wound contraction and is mediated by myofibroblasts at the edge of the wound.

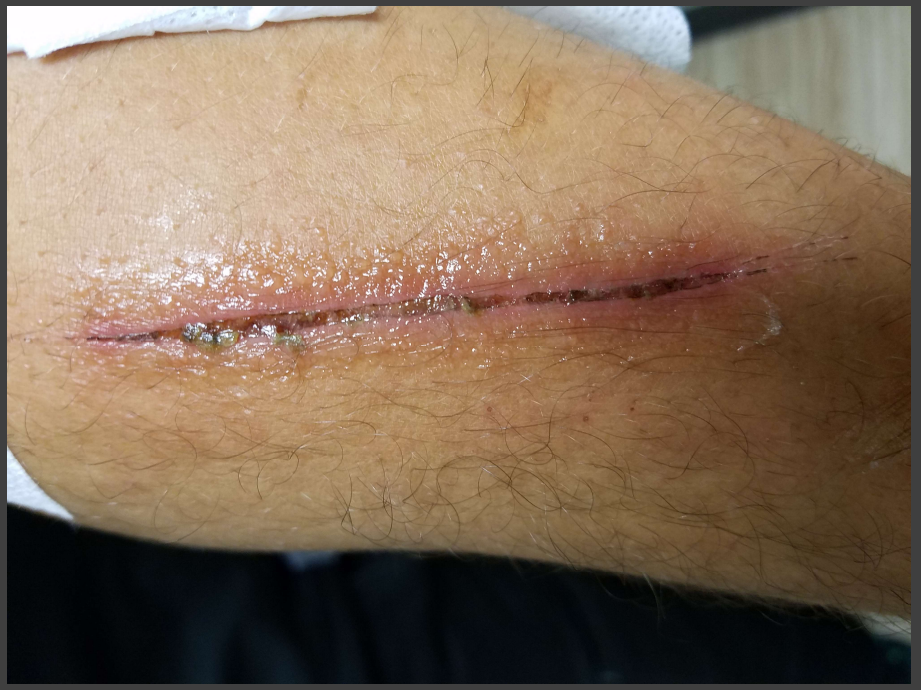
Healing by tertiary intention

Tissue Repair

Wound healing





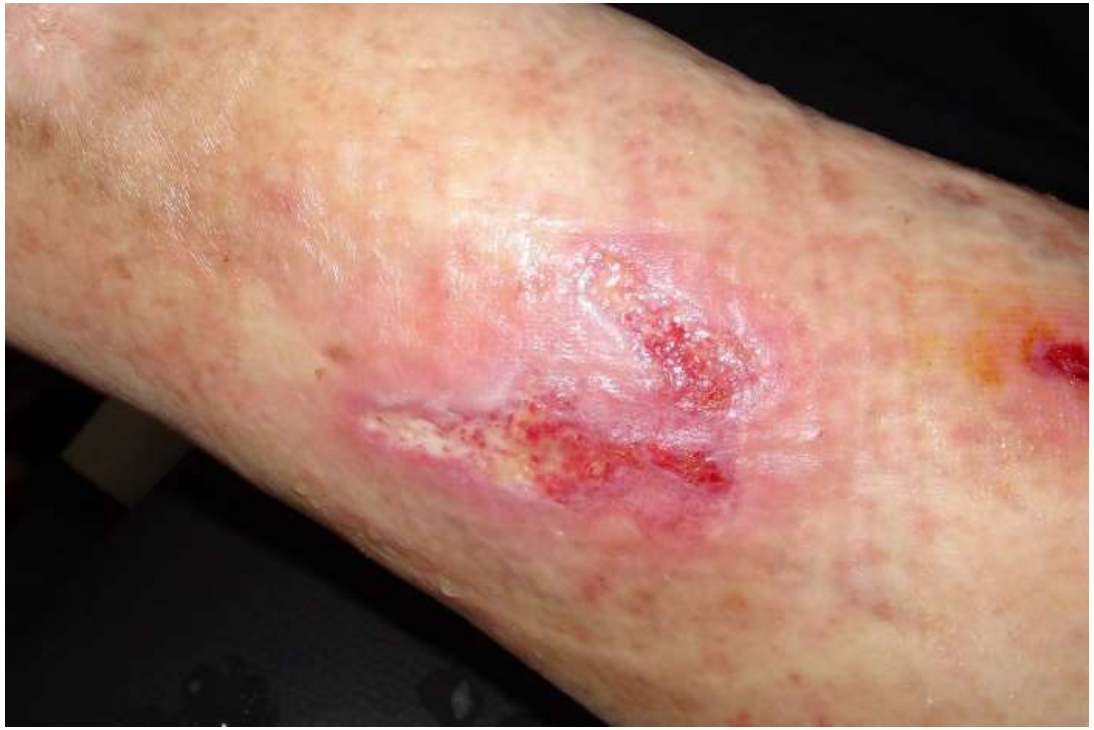


Tissue repair

Wound after surgery

Tissue repair

Wound healing by secondary intention



Tissue Repair

Repair in specific organs occurs as follows:

• **Liver:** Mild injury is repaired by regeneration of hepatocytes, sometimes with restoration to normal pathology. Severe or persistent injury causes formation of regenerative nodules that may be surrounded by fibrosis, leading to hepatic cirrhosis.

• In the **brain**, neurons do not regenerate, but microglia remove debris and astrocytes proliferate, causing gliosis.

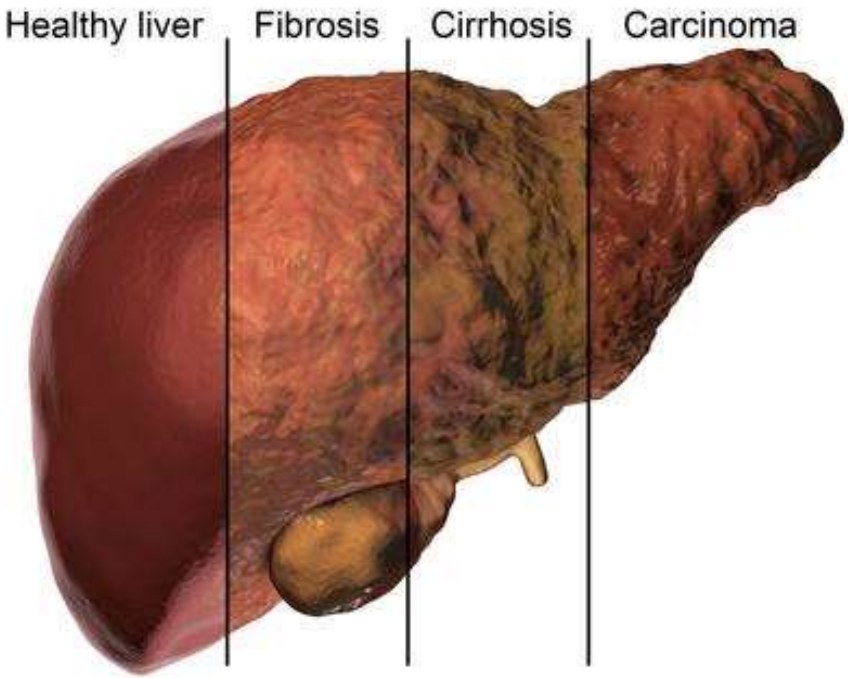
• Damaged **heart muscle** cannot regenerate, so the heart heals by fibrosis.

• In the **lung**, type II pneumocytes replace type I pneumocytes after injury.

• In **peripheral nerves**, the distal part of the axon degenerates while the proximal part regrows slowly, using axonal sprouts to follow Schwann cells to the muscle.

Tissue Repair

Repair in Liver



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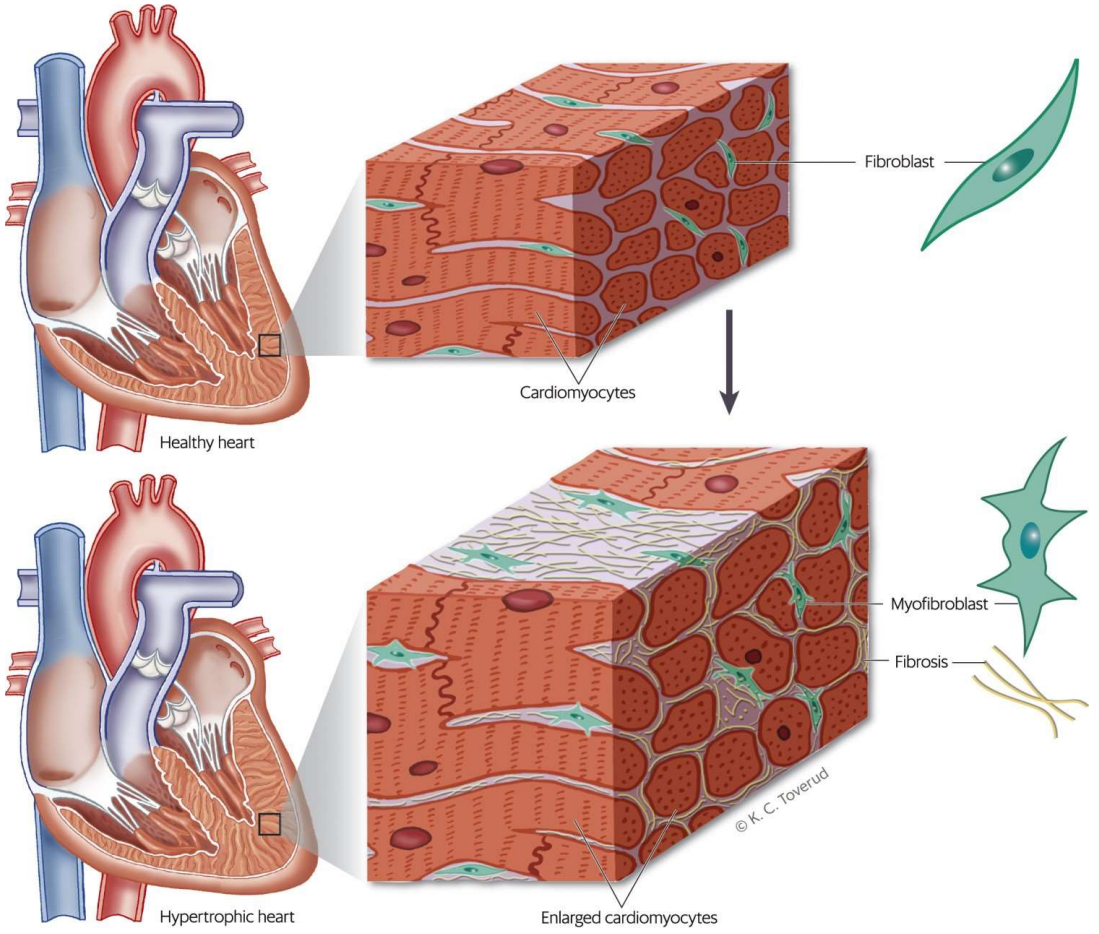
Heart muscle Healing



Tissue Repair

ABERRATIONS IN WOUND HEALING

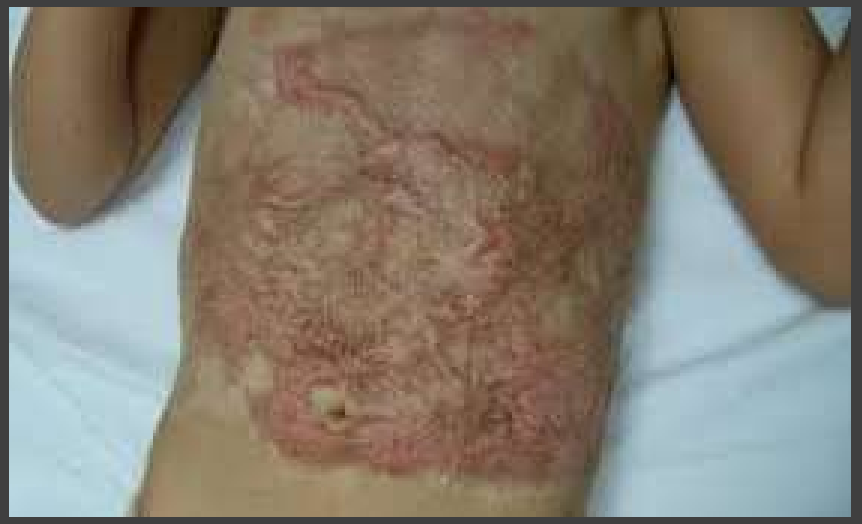
- **Delayed wound healing**
- **Hypertrophic scar**
- **Keloid formation**

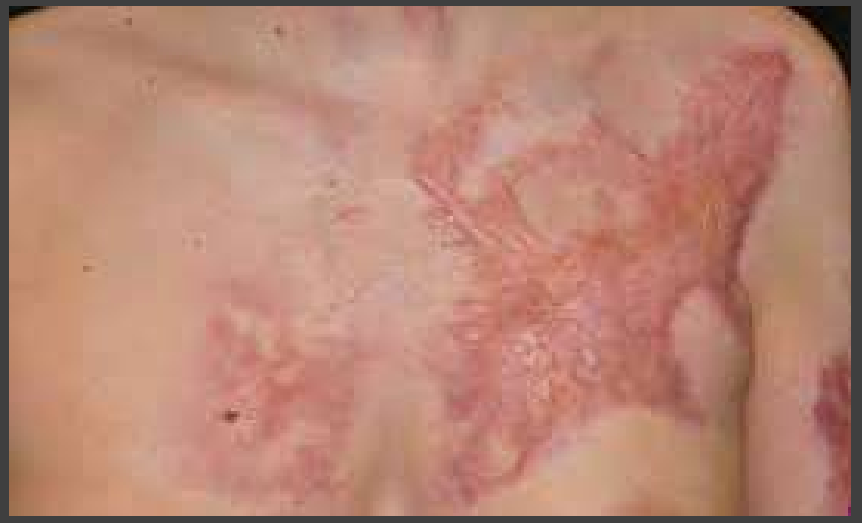
Tissue Repair

Delayed wound healing may be seen in wounds complicated by foreign bodies, infection, ischemia, diabetes, malnutrition, scurvy, etc.

Tissue Repair

Hypertrophic scar results in a prominent scar that is localized to the wound, due to excess production of granulation tissue and collagen. It is common in burn patients.





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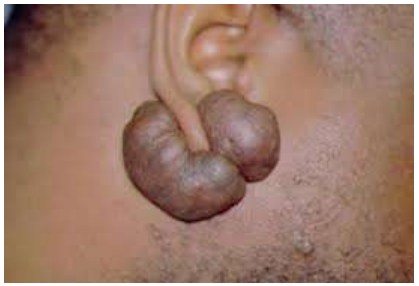
Keloid formation is a genetic predisposition that is common in African

Americans. It tends to affect the earlobes, face, neck, sternum, and forearms, and it may produce large tumor-like scars extending beyond the injury site. There is excess production of collagen that is predominantly type III.



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