Histopathology

Lecture 5

Tissue Repair (Healing)

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Repair

Overview: The process of repair begins very early. Repair involves regeneration of the parenchyma or replacement of damaged tissue with a scar if regeneration is not possible.

Definitions: Healing versus regeneration

Regeneration is complete replacement of damaged cells, with no scar formation.

- Can occur in renewing tissues (e.g., gastrointestinal tract and skin).
- Can occur in stable tissues (e.g., compensatory growth in the liver).

Healing is regeneration of cells combined with scarring and fibrosis.

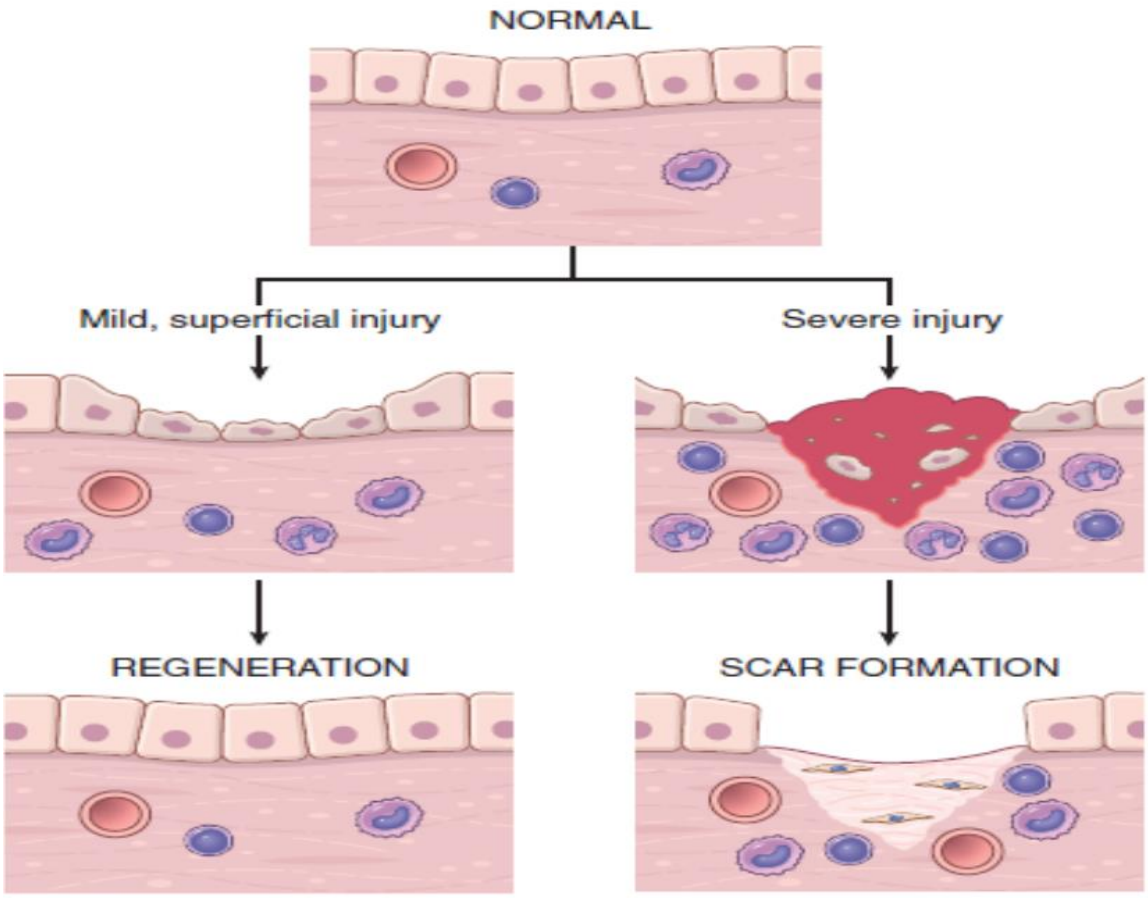

Figure 1. **Healing vs regeneration**

Important mediators in repair

■ **Epidermal growth factor (EGF):** Stimulates granulation tissue formation.

■ **Vascular endothelial growth factor (VEGF):** Induces blood vessel formation.

■ **Platelet-derived growth factor (PDGF):** Promotes migration and proliferation of fibroblasts, smooth muscle cells, and monocytes.

■ **Fibroblast growth factor (FGF):** Stimulates blood vessel formation and wound repair through macrophages, fibroblasts, and endothelial cell migration.

■ **Transforming growth factor beta (TGF-β):** Acts as growth inhibitor for epithelium.

Components of healing

■ Induction of inflammatory process to deal with the source of injury (cell injury is prequel to healing). The inflammatory process acts to contain damage, remove injuring substance, remove dead tissue, and start deposition of extracellular matrix.

■ Formation of new blood vessels.

■ Production of extracellular matrix.

■ Tissue remodeling.

■ Wound contracture.

Replacement by scar: The following four processes occur:

1. Formation of new blood vessels.

2. Migration and proliferation of fibroblasts.

3. Deposition of extracellular matrix.

4. Maturation and reorganization of fibrous tissue. Tissue remodeling is a balance between extracellular matrix synthesis and degradation.

Important point: Formation of the scar occurs via either first or second intention.

HEALING BY FIRST INTENTION

Basic description: Healing of a wound that has clean edges.

Example: Healing of surgical incision.

Result: Small to nonexistent scar.

HEALING BY SECOND INTENTION

Basic description: Healing of a wound that has unclean edges, extensive tissue disruption, and tissue necrosis.

Example: Healing of a cutaneous ulcer or a large laceration inflicted by a blow from a baseball bat.

Result: Larger, more prominent scar.

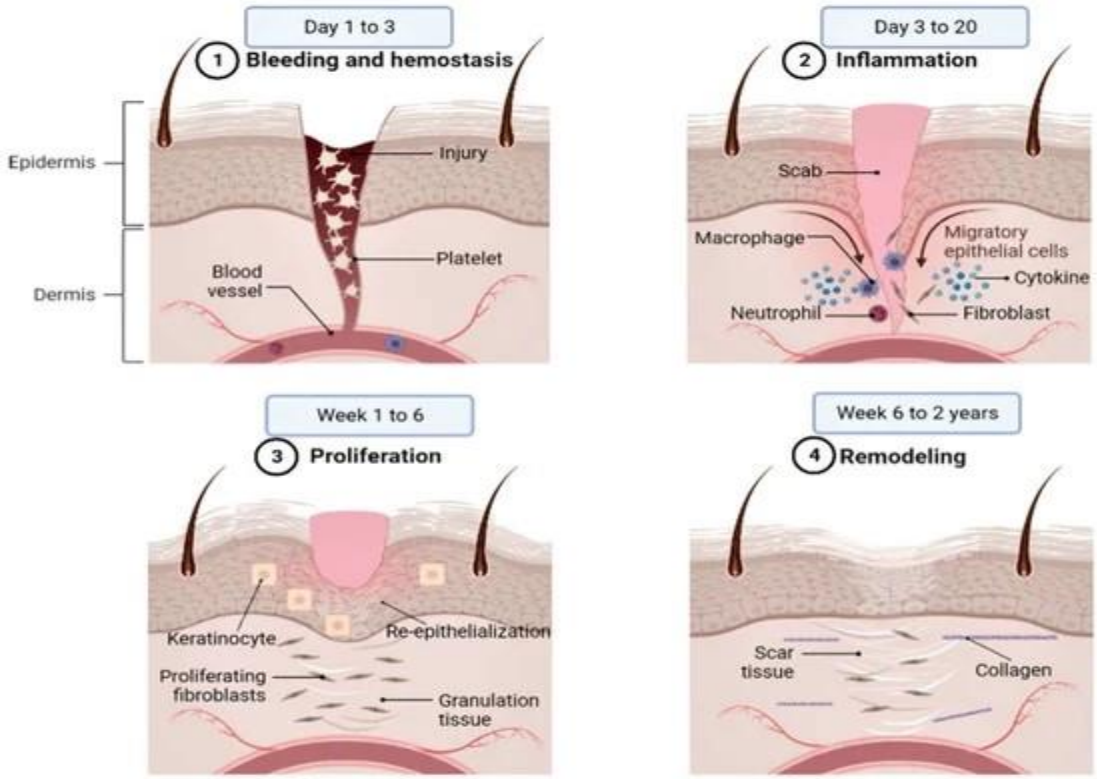

Figure 2. Physiological wound-healing phases. ① **Bleeding and hemostasis:** hemostasis occurs immediately after bleeding and reduces blood flow by constricting blood vessels to stop bleeding following vascular injury. ② **Inflammation:** the release of cytokines, growth factors, and the migration of leukocytes into the area cause hemostasis and acute inflammation in the area of a wound. ③ **Proliferation:** an increase in the keratinocyte, fibroblast, endothelial, and leukocyte migration and proliferation in the wound area. ④ **Remodeling:** the process in which stretching and pulling forces interact with the scar tissue.