SAWA UNIVERSITY

HISTOPATHOLOGY
1

TISSUE REPAIR (HEALING)

Sawa University — جامعـــــة ســـــــاوة الاهلية

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Third Stage — المرحلـــــــــــة الثالثة

الجانب النظري محاضرة رقم 5

Theoretical Lecture No. 5

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OBJECTIVE

- Define tissue repair and its importance.
- Distinguish between regeneration and scar formation.
- List factors affecting tissue repair.
- Identify the main phases of tissue repair.
- Describe key growth factors in wound healing.
- Explain first vs. second intention healing.

Tissue Repair (healing)

- **Restoration of tissue architecture and function after an injury.**
- **Replacement of destroyed or damaged tissue by newly produced tissue.**
- It occurs by two types of reactions: **regeneration** of the injured tissue and **scar formation** by the deposition of connective tissue

Regeneration: **Able the tissues to replace the damaged cells and essentially return to a normal state** ; occurs by proliferation of residual (uninjured) cells that retain the capacity to divide, and by replacement from tissue stem cells. It is the typical response to injury in the rapidly dividing epithelia of the skin and intestines, and some parenchymal organs, notably the liver.

Scar formation: **repair occurs by modulate of connective (fibrous) tissue, If the injured tissues are incapable of regeneration, or if the supporting structures of the tissue are severely damaged.**

* Fibrosis is most often used to describe the extensive deposition of collagen that occurs in the lungs, liver, kidney, and other organs as a consequence of chronic inflammation, or in the myocardium after extensive ischemic necrosis (infarction).

* **If fibrosis develops in a tissue space occupied by an inflammatory exudate, it is called organization (as in organizing pneumonia affecting the lung).**

Factors Influencing Tissue Repair

Many systemic and local factors affect the efficiency of tissue repair, including:

1. Nutrition (especially vitamin C, zinc, and protein)
2. Blood supply and oxygenation.
3. Age and general health
4. Presence of infection or foreign material.
5. Hormonal status (e.g., corticosteroids delay healing).
6. Mechanical stress on the wound.

Phases of Tissue Repair

Tissue repair follows three overlapping phases:

1. Inflammatory Phase: This phase begins immediately after injury and lasts for a few days. It is characterized by the formation of a blood clot, vasodilation, increased vascular permeability, and the recruitment of neutrophils and macrophages to the site of injury.

2. Proliferative Phase: This phase involves fibroblast proliferation, collagen deposition, angiogenesis (formation of new blood vessels), and re-epithelialization. Granulation tissue forms during this stage.

3. Remodeling (Maturation) Phase: In this final phase, collagen fibers are reorganized, and the wound gains tensile strength. The scar becomes less cellular and more fibrous over time.

Cells involved in Repair:

Several cell types proliferate during tissue repair. These include:

1. **The remnants of the injured tissue** (which attempt to restore normal structure).
2. **Vascular endothelial cells** (to create new vessels that provide the nutrients for the repair process).
3. **Fibroblasts** (the source of the fibrous tissue that fills defects).
4. The proliferation of the above cell types is driven by **growth factors.**
5. The normal size of cell populations in any given tissue is determined by a balance of cell proliferation, cell death by apoptosis, and emergence of new differentiated cells from stem cells .

Proliferative Capacities of Tissues:

1. Labile tissues(Continuously Dividing Tissues): Continuously being lost and replaced by maturation from stem cells and proliferation of mature cells**(Repair by regeneration)**

Example of labile tissues:

1- Hematopoietic cells in the bone marrow.

2- The majority of surface epithelium(skin, oral cavity, vagina, and cervix).

3- The cuboidal epithelia of the ducts draining exocrine organs (salivary glands, pancreas, biliary tract)

4- The columnar epithelium of the GIT, uterus, fallopian tubes & the transitional epithelium of the urinary tract.

2. Stable Tissues (Quiescent cells)

- Cells are quite

- Minimal proliferative activity in normal state.

- Capable of proliferating in response to injury.

Examples:

1. The parenchyma of most solid tissues (liver, kidney, and pancreas).
2. The endothelial cells.
3. The fibroblasts.
4. The smooth muscle cells.

3. Permanent Tissues (Non dividing cells)

- Terminally differentiated and non-proliferative in postnatal life.

Example: neurons and cardiac muscle cells.

↓

injury

↓

irreversible

↓

scar formation

Control of cell proliferation:

Cell proliferation can be triggered by:

1. **Chemical mediators:** stimulation or inhibition of cell growth

A. Growth factors: are produced by: **Leukocytes and Connective tissue cells**

B. Hormones.

C. Cytokines.

2. Signals from the extracellular matrix (ECM).

Growth factor:

- Epidermal growth factor (EGF).
- Vascular endothelial cell growth factor (VEGF).
- Transforming growth factor alpha (TGF-α).

Function of GR:

- Stimulate cell division.

- Promoting cell survival.

- Stimulate migration.

- Stimulate differentiation.

- Enhance the synthesis of collagen in fibroblasts.

Extracellular matrix (ECM).

Dynamic, constantly remodeling macromolecular complex synthesized locally as a network surrounding the cells.

Components of the Extracellular Matrix

1. Fibrous structural proteins (collagen and elastin).

2. Water-hydrated gels (proteoglycans and hyaluronan).

3. Adhesive glycoproteins (that include fibronectin and adhesive receptors (selectin, integrin and cadherin).

ECM occurs in two basic forms:-

1.Interstitial matrix:

- **Present in the spaces between mesenchymal (connective tissue) cells, and between epithelium and supportive vascular & smooth muscle structures.**
- **It is synthesized by the mesenchymal cells (e.g., fibroblasts).**
- **Its major constituents are:**
- **Collagens (fibrillar and nonfibrillar),**
- **Fibronectin, Elastin, Proteoglycans,**
- **Hyaluronate & Other elements.**

2. Basement membrane:

- Which lies beneath the epithelium and is synthesized by overlying epithelium and underlying mesenchymal cells
- Its major constituents are : amorphous nonfibrillar type IV collagen and laminin.

Wound healing:

Types:

1. Healing by First Intention (primary union).
2. Healing by Second Intention (secondary union).

Steps of primary union

- The incision space is filled with fibrin clotted blood

Then

- It is rapidly invaded by granulation tissue

Then

- Covered by new epithelium

Within 24 hours:

- **Neutrophils:** migrate toward the fibrin clot.
- **Basal cells:** increased mitotic activity at the cut edge of the epidermis.

After 24 up to 48 hours

- **Epithelial cell migrate from both edges & proliferate along the dermis with depositing basement membrane components.**
- **Cells meet in the midline beneath the surface cut Forming a thin but continuous epithelial layer.**

By the 3rd day

- Neutrophils replaced by macrophages.
- The granulation tissue progressively invades the incision space.
- Collagen fibers are now evident at the incision margins.
- Epithelial cell proliferation continues, forming a thick epidermal covering layer.

By 5th day

- Neovascularization reaches its peak.
- Collagen fibrils more abundant forming a bridge in the area of incision.
- The epidermis recovers its normal thickness with surface keratinization.

By 2nd week

- Collagen continue to accumulation

- Fibroblast continue to proliferation.

- ↓leukocyte infiltrate, edema, vascularity

- ↑collagen deposition ⟶ Regression of vascular channels ⟶ Blanching

By the end of the 1st month

Features of the scar:

1. Formed of cellular connective tissue

2. Devoid of inflammatory cells

3. Covered by normal epidermis.

2. Healing by Second Intention(secondary union):

Secondary union occurs in :

1. Extensive tissue loss (large wounds)
2. Chronic inflammation
3. Abscess formation
4. Ulceration.

Begins within 24 hours of injury

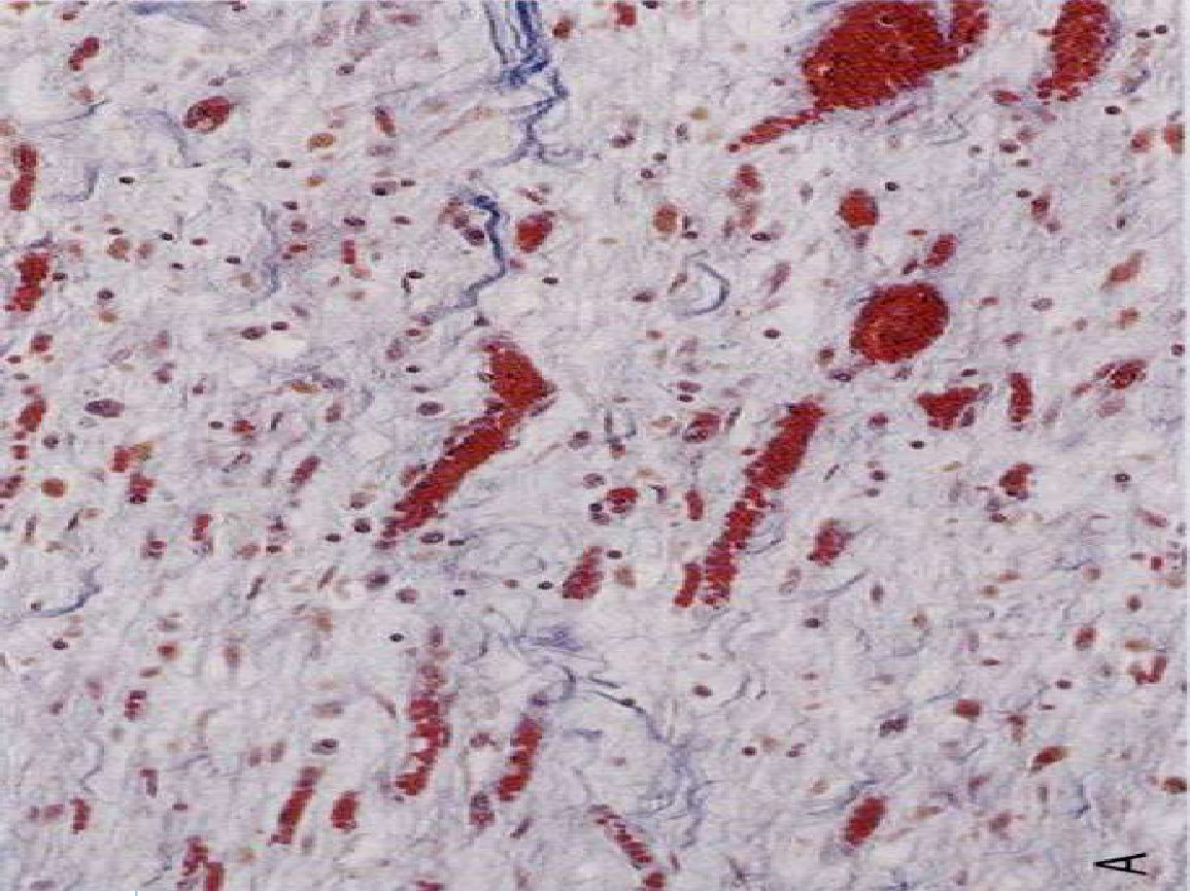
- Start by Emigration of fibroblasts
- Induction of fibroblast and endothelial cell proliferation.

By 3rd – 5th days:

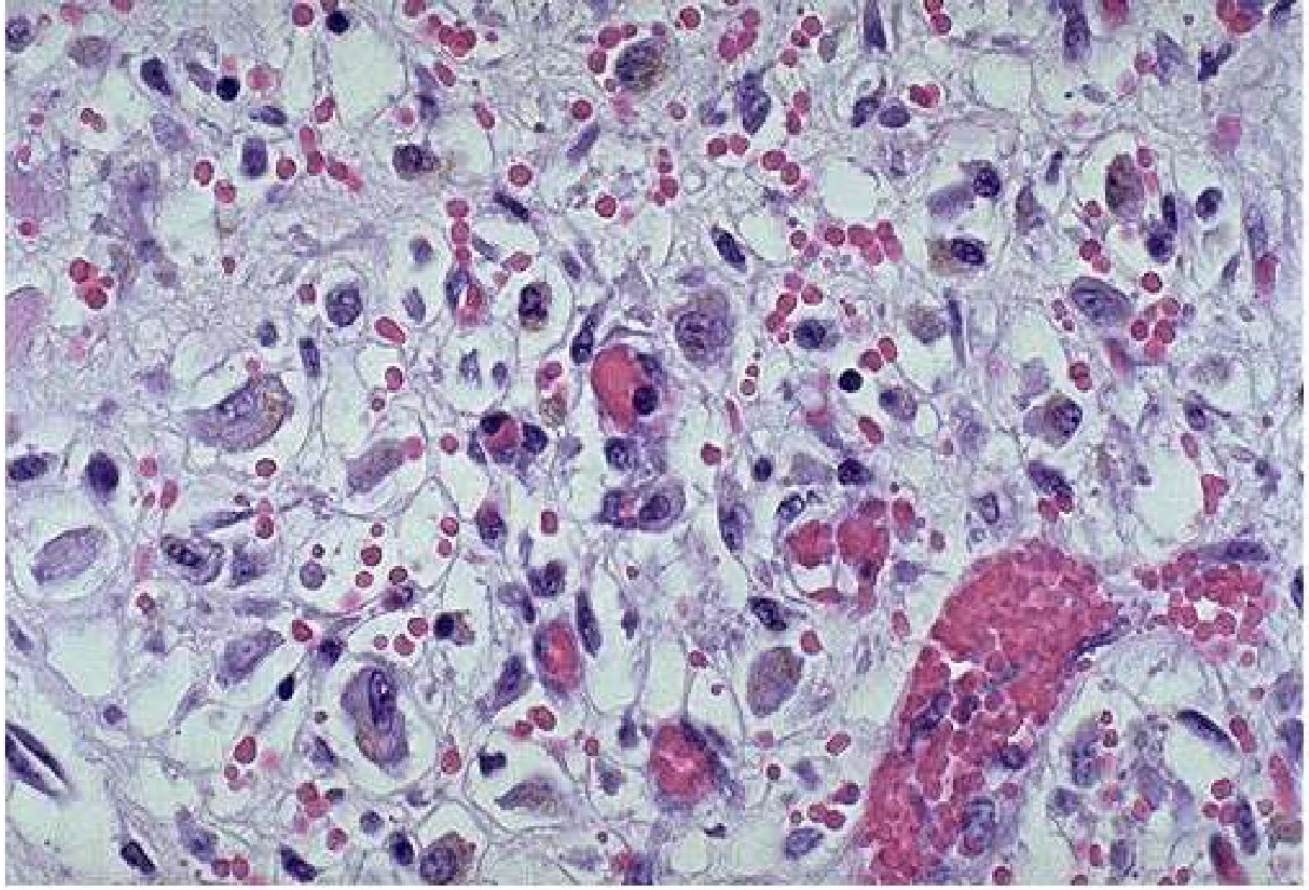
- **Granulation tissue formation:** Specialized type of tissue that is characteristic of healing. The term granulation tissue derives from the pink, soft, granular gross appearance.

Histologic appearance:

1. **Proliferation of fibroblasts**
2. **Formation of new thin-walled, delicate capillaries (angiogenesis)**
3. **Loose ECM**



At high magnification, granulation tissue has capillaries, fibroblasts, and a variable amount of inflammatory cells.



There are numerous blood vessels, edema, and a loose extracellular matrix containing occasional inflammatory cells.

References

1. Kumar, V., Abbas, A. K., & Aster, J. C. (2023). Robbins & Cotran Pathologic Basis of Disease (11th ed.). Elsevier.

2. Mitchell, R. N. (2023). Basic Pathology. Elsevier.

Any questions?