**LECTURE 10**

***-boice-***

**HEALING, REPAIR & COMPLICATIONS**

Tissue repair refers to restoration of tissue architecture and function after an injury it occurs in two ways: Regeneration of injured tissue and replacement by connective tissue (scarring). Usually, tissue repair involves both processes.It involves cell proliferation, and interaction between cells and extracellular matrix. Lots of cells proliferate during tissue repair including; injured tissue remnants, vascular endothelial cells and fibroblasts.Growth factors play an important role.



HEALING OF A CUTANEOUS WOUND

Cutaneous wounds heal by any of two methods:

* Healing by first intention
* Healing by second intention

**Healing by first intention**

* refers to healing that occurs when wound margins are in close apposition (e.g., surgical Incision). The edges are sealed together by-a blood clot, which dries to protect and seal the wound.
* Minimal tissue loss no Foreign body and minimal contamination
* First 24 hours. An acute inflammatory reaction occurs, with neutrophils infiltrating the injured area.
* Third day. Macrophages arrive to clean up cellular debris. Fibroblasts begin to synthesize collagen on the margins of the incision.
* Fifth day. Vascularizaiton occurs and collagen fibrils bridge the wound gap, creating a red, fibrous scar.
* Collagen continues to form a firm scar, increasing in strength by the end of the first month.
* Epithelialization across superficial layers restores a smooth contour. As vascularity decreases, a thin white line remains.

**Healing by second intention**

* Healing by second intention is associated with the destruction of larger areas of viable tissue or wounds complicated by infection. The inflammatory reaction is more intense, and healing occurs over a longer period of time.
* Large amounts of granulation tissue must be formed. The wound must granulate from the margins and base, with collagen gradually filling in the defect.
* Fibroblasts contract and pull the wound edges into closer proximity. Epithelialization across the granulation tissue occurs to provide a smooth surface.
* A large, often deforming scar results.
* Sweat glands, hair follicles, and melanin-producing cells are lost, accounting for the hairless, white appearance of the scar.

**Complications of wound healing**:

 Abnormal healing results when the healing process deviates from normal and causes complications, deformity, and decrease in function of the injured tissue. Examples include:

1. **Excess scar tissue:** Exuberant granulations, or “proud flesh,” are very large protrusions of scar tissue that block the epithelialization of the wound. They do not return when removed.

Keloids are bulging, non-cancerous scars that result from abnormalities in collagen synthesis and degradation. Fibroblasts continue to be multiply even after wound is healed/closed.

Keloid is excess production of scar tissue that is out of proportion to the wound

1. Characterized by excess type III collagen

2. Genetic predisposition (more common in African Americans)

3. Classically affects earlobes, face, and upper extremities

They tend to recur even after removal.

Hypertrophic scars is different from keloids

1. **Contracture:** A disfiguring scar or disability occurs as wounds continue to contract over areas of skin that are flexible.
2. **Dehiscence:** A disruption of primary or secondary healing may cause the bursting open of a previously closed wound. The collagen framework was not strong enough to hold against the forces imposed on the wound. Wound dehiscence is often related to poor circulation.

Dehiscence wound is most commonly seen after abdominal surgery

1. **Evisceration** is the protrusion of abdominal organs through a dehiscence.
2. **Stenosis** is the narrowing or obstruction of an opening and may be caused by the formation of scar tissue around a tubular area eg ureter.
3. **Adhesions:** Inflamed serous or mucous membranes may produce exudate that causes scar tissue to bind or adhere to adjacent surfaces e.g loops of bowel or abdominal viscera. Partial or complete obstruction may occur.

**FACTORS THAT INFLUENCE WOUND HEALING**

**Local**

1. Blood supply
2. Infection
3. Foreign bodies
4. Tissue destroyed
5. Type of tissues
6. Type of stimulus
7. Wound care eg surgical debridement

**Systemic**

1. Nutrition
2. Co-morbidities
3. Immune status
4. Medication

**REGENERATION**

This is replacement of damaged tissue with native tissue; dependent on regenerative capacity of tissue

Tissues are divided into three types based on regenerative capacity:-

* *labile,*
* *stable*
* *permanent.*

(a). ***Labile tissues*** possess stem cells that continuously cycle to regenerate the tissue.

1. Small and large bowel

2. Skin

3. Bone marrow (hematopoietic stem cells)

(b). ***Stable tissues*** are comprised of cells that are quiescent (G0**),** but can reenter the cell

cycle to regenerate tissue when need arises.

example is regeneration of liver by compensatory hyperplasia after partial

resection. Each hepatocyte produces additional cells and then reenters quiescence.

(c). ***Permanent tissues*** lack significant regenerative potential (e.g., myocardium, skeletal

muscle, and neurons).

**REPAIR**

This is replacement of damaged tissue with fibrous scar

Occurs when regenerative stem cells are lost (e.g., deep skin cut) or when a tissue lacks regenerative capacity (e.g., healing after a myocardial infarction)

Granulation tissue formation is the initial phase of repair

**1.** Consists of fibroblasts (deposit type III collagen), capillaries (provide nutrients),

and myofibroblasts (contract wound)

 Eventually results in scar formation, in which type III collagen is replaced with typeI collagen

* + Type III collagen is pliable and present in granulation tissue, embryonic tissue,uterus, and keloids.
	+ Type I collagen has high tensile strength and is present in skin, bone, tendons,and most organs.
	+ Collagenase removes type III collagen and requires zinc as a cofactor.

**MECHANISMS OF TISSUE REGENERATION AND REPAIR**

Mediated by paracrine signaling via growth factors (e.g., macrophages secrete

growth factors that target fibroblasts)

Interaction of growth factors with receptors (e.g., epidermal growth factor with

growth factor receptor) results in gene expression and cellular growth.

 Examples of mediators include

1. TGF-α - epithelial and fibroblast growth factor

2. TGF-β - important fibroblast growth factor; also inhibits inflammation

3. Platelet-derived growth factor - growth factor for endothelium, smooth muscle,

and fibroblasts

4. Fibroblast growth factor - important for angiogenesis; also mediates skeletal

development

5. Vascular endothelial growth factor (VEGF) - important for angiogenesis

**NORMAL AND ABERRANT WOUND HEALING**

Cutaneous healing occurs via primary or secondary intention.

1. *Primary intention*-Wound edges are brought together (e.g., suturing of a surgical incision) leads to minimal scar formation

2. *Secondary intention*-Edges are not approximated. Granulation tissue fills the

defect; myofibroblasts then contract the wound, forming a scar.

Delayed wound healing occurs due to several factors such as:-

1**.** Infection (most common cause; ***S aureus*** is the most common offender)

2. Vitamin C, copper, or zinc deficiency

* Vitamin C is an important cofactor in the hydroxylation of proline and lysine procollagen residues; hydroxylation is necessary for eventual collagen cross-linking.
* Copper is a cofactor for lysyl oxidase, which cross-links lysine and hydroxylysine to form stable collagen.
* Zinc is a cofactor for collagenase, which replaces the type III collagen of granulation tissue with stronger type I collagen.

3. Other causes include foreign body, ischemia, diabetes, and malnutrition.