

Healing: is the body response to injury in an attempt to restore normal structure and function. Healing involves 2 distinct processes:

- 1- **Regeneration:** when healing takes place by proliferation of parenchymal cells and usually results in complete restoration of the original tissues.
- 2- **Repair:** when healing takes place by proliferation of connective tissue elements resulting in fibrosis and scarring.

At times, both the processes take place simultaneously.

REGENERATION

Some parenchymal cells are short-lived while others have a longer lifespan. In order to maintain proper structure of tissues, these cells are under the constant regulatory control of their cell cycle. The regulatory control includes growth factors such as: epidermal growth factor, fibroblast growth factor, platelet-derived growth factor, endothelial growth factor, transforming growth factor- β .

Depending upon their capacity to divide, the cells of the body can be divided into 3 groups: labile cells, stable cells, and permanent cells.

1. Labile cells. These cells continue to multiply throughout life under normal physiologic conditions. These include: surface epithelial cells of the epidermis, alimentary tract, respiratory tract, urinary tract, vagina, cervix, uterine endometrium, haematopoietic cells of bone marrow and cells of lymph nodes and spleen.

2. Stable cells. These cells decrease or lose their ability to proliferate after adolescence but retain the capacity to multiply in response to stimuli throughout adult life. These include: parenchymal cells of organs like liver, pancreas, kidneys, adrenal and thyroid; mesenchymal cells like smooth muscle cells, fibroblasts, vascular endothelium, bone and cartilage cells.

3. Permanent cells. These cells lose their ability to proliferate around the time of birth. These include: neurons of nervous system, skeletal muscle and cardiac muscle cells.

Regeneration of any type of parenchymal cells involves the following 2 processes:

- i) Proliferation of original cells from the margin of injury with migration so as to cover the gap.
- ii) Proliferation of migrated cells with subsequent differentiation and maturation so as to reconstitute the original tissue.

REPAIR

Repair is the replacement of injured tissue by fibrous tissue. Two processes are involved in repair:

1. Granulation tissue formation
2. Contraction of wounds.

Repair response takes place by participation of mesenchymal cells (consisting of connective tissue stem cells, fibrocytes and histiocytes), endothelial cells, macrophages, platelets, and the parenchymal cells of the injured organ.

Granulation Tissue Formation

The term granulation tissue derives its name from slightly granular and pink appearance of the tissue. Each granule corresponds histologically to proliferation of new small blood vessels which are slightly lifted on the surface by thin covering of fibroblasts and young collagen. The following 3 phases are observed in the formation of granulation tissue:

1. PHASE OF INFLAMMATION. Following trauma, blood clots at the site of injury. There is acute inflammatory response with exudation of plasma, neutrophils and some monocytes within 24 hours.

2. PHASE OF CLEARANCE. Combination of proteolytic enzymes liberated from neutrophils, autolytic enzymes from dead tissues cells, and phagocytic activity of macrophages clear off the necrotic tissue, debris and red blood cells.

3. PHASE OF INGROWTH OF GRANULATION TISSUE. This phase consists of 2 main processes: angiogenesis or neovascularisation, and fibrogenesis.

i) Angiogenesis (neovascularisation). Formation of new blood vessels at the site of injury takes place by proliferation of endothelial cells from the margins of severed blood vessels.

ii) Fibrogenesis. The new fibroblasts originate from fibrocytes as well as by mitotic division of fibroblasts. Some of these fibroblasts have combination of morphologic and functional characteristics of smooth muscle cells (*myofibroblasts*). Collagen fibrils begin to appear by about 6th day. As maturation proceeds, more and more of collagen is formed while the number of active fibroblasts and new blood vessels decreases. This results in formation of inactive looking scar known as *cicatrization*.

Contraction of Wounds

The wound starts contracting after 2-3 days and the process is completed by the 14th day. During this period, the wound is reduced by approximately 80% of its original size. Contracted wound results in rapid healing since lesser surface area of the injured tissue has to be replaced.

Wound Healing

Healing of skin wounds provides a classical example of combination of regeneration and repair described above. Wound healing can be accomplished in one of the following two ways:

Healing by First Intention (Primary Union)

This is defined as healing of a wound which has the following characteristics:

- i) clean and uninfected;
- ii) surgically incised;
- iii) without much loss of cells and tissue; and
- iv) edges of wound are approximated by surgical sutures.

The sequence of events in primary union are

1. Initial haemorrhage. Immediately after injury, the space between the approximated surfaces of incised wound is filled with blood which then clots and seals the wound against dehydration and infection.

2. Acute inflammatory response. This occurs within 24 hours with appearance of polymorphs from the margins of incision. By 3rd day, polymorphs are replaced by macrophages.

3. Epithelial changes. The wound is covered by a layer of epithelium in 48 hours..

4. Organisation. By 3rd day, fibroblasts also invade the wound area. By 5th day, new collagen fibrils start forming which dominate till healing is completed. In 4 weeks, the scar tissue with scanty cellular and vascular elements, a few inflammatory cells and epithelialised surface is formed.

5. Suture tracks. Each suture track is a separate wound and incites the same phenomena as in healing of the primary wound

Healing by Second Intention (Secondary Union)

This is defined as healing of a wound having the following characteristics:

- i) open with a large tissue defect, at times infected;
- ii) having extensive loss of cells and tissues; and
- iii) the wound is not approximated by surgical sutures but is left open.

The basic events in secondary union are similar to primary union but differ in having a larger tissue defect which has to be bridged. Hence healing takes place from the base upwards as well as from the margins inwards. The healing by second intention is slow and results in a **large**, at times **ugly**, **scar** as compared to rapid healing and neat scar of primary union.