**Wound Healing**

Wound repair is the effort of injured tissues to restore normal function and structural integrity after injury

The wound healing continuum is divided into three phases: inflammation, proliferation, and maturation

**Briefly stage of wound healing**

During the inflammatory phase, inflammation is initiated within the wounded tissue, and this event is followed closely by removal of wound contaminants and damaged or dead tissue.

The proliferative phase represents the phase of repair of wounded tissue during which blood flow, components of the extracellular matrix, and the epithelial covering of the wound are all restored

Maturation, sometimes termed the remodeling phase, is dominated by reorganization of collagen and return of some level of pre-wound tissue strength.

Although most wounds undergo the same basic steps of wound repair, acute wounds proceed in accordance with a more predictable fashion and timeline than chronic wounds.

على الرغم من أن معظم الجروح تخضع لنفس الخطوات الأساسية لإصلاح الجروح ، إلا أن الجروح الحادة تسير وفقًا لطريقة وإطار زمني يمكن التنبؤ بهما أكثر من الجروح المزمنة.

Chronic wounds are defined as those that do not progress through the normal phases of wound healing. Chronic wounds most frequently do not progress beyond the inflammatory phase of wound healing and therefore fail to achieve return of functional integrity.

تعرف الجروح المزمنة بأنها تلك التي لا تتطور خلال المراحل الطبيعية لالتئام الجروح. في أغلب الأحيان لا تتطور الجروح المزمنة إلى ما بعد المرحلة الالتهابية من التئام الجروح ، وبالتالي تفشل في تحقيق عودة السلامة الوظيفية.

**Inflammation and Debridement**

Tissue disruption initiates hemostasis and inflammation.

1. As the vascular endothelium in the wound is disrupted, it produces endothelin, which, in combination with other mediators such as epinephrine, norepinephrine, and prostaglandins, initiates contraction of smooth muscle within the vessel walls, resulting in *vasoconstriction.*
2. *The coagulation cascade is initiated,* and thrombin is formed. Thrombin serves as a catalyst for *fibrinogen conversion to fibrin and contributes to platelet activation.*

*Release of platelet alpha granules and their contents*

1. *vasodilation and increased vascular permeability*

Vasodilation results in *increased blood flow to the wound bed and extravasation of fluid, creating the classic signs of inflammation—heat, redness and swelling.*

1. *Leukocyte migration from dilated vessels into the wound bed occurs in two phases: neutrophil migration and monocyte migration.*

*Neutrophils have many functions within the wound, including the killing of bacteria through release of reactive oxygen species, breakdown of extracellular matrix via release of proteolytic enzymes, phagocytosis of degraded bacteria and matrix debris, and release of additional cytokines that prolong the inflammatory phase*.

*Activated inflammatory cells consume oxygen at high rates, and when this process is combined with an impaired blood supply to the wound, local hypoxia develops*

1. *Lactate, produced within the wound secondary to hypoxia, stimulates collagen secretion and angiogenesis.*
2. Monocytes migrate through the vessel walls and, with the influence of TGF-β, mature to macrophages. *Although neutrophils and monocytes both work to aid in debridement of the wound, the macrophage is essential for further secretion of signaling molecules(*cytokines and growth factors*), which, in turn, facilitate recruitment of the other cell types necessary for wound repair.*

*Approximately 48 to 96 hours after wounding, the macrophage has become the primary leukocyte in the wound.*

*most neutrophils have been phagocytized by macrophages or have undergone apoptosis*

*Macrophages continue phagocytosis of debris, as well as secretion of proteases and removal of bacteria. The Macrophages within the wound also release matrix metalloproteinases* *that degrade the extracellular matrix.*

The degradation of extracellular matrix facilitates movement of cells through the tissues.

*This phase of wound healing is characterized clinically by erythema and edema of the wound edges. Following debridement by macrophages, the wound enters a repair or proliferation phase.*

Proliferation

*Following wound debridement, wound healing enters a constructive or repair phase that occurs from approximately day 4 through day 12.*

*The goals of this phase include achieving permanent closure of the wound and replacing lost tissue*

*Predominant cell types of the repair or proliferative phase of wound healing include fibroblasts, endothelial cells, and epithelial cells*

*During this period, capillary ingrowth, collagen production, wound contraction, and wound coverage take place*

1. development of a *microvascular network* within the wound that *provides oxygen and nutrients to the cells and becomes an integral part of the developing granulation tissue bed*
2. *Fibroblasts migrate into the wound from surrounding tissue and proliferate, fibroblasts begin to synthesize type III collagen, glycosaminoglycans, and fibronectin.*
3. *Fibroblasts that are anchored within the wound are transformed into myofibroblasts in response to TGF-β1. Myofibroblasts form focal adhesions that provide adequate mechanical force to cause wound contraction*

*Grossly, this phase of wound healing is characterized by the development of a granulation bed (Figure 9-5, A), which is composed of a capillary bed, fibroblasts, macrophages, and a ground substance of collagen, fibronectin, and hyaluronic acid (Figure 9-5, B).*

1. *epithelial cells begin to proliferate (Figure 9-6, A) and move into the wound to minimize fluid loss and bacterial invasion. Migration is stop, although cellular proliferation continues in an attempt to re-create normal epidermal thickness*

**Remodeling and Maturation**

*The final phase of wound repair is dedicated to remodeling and strengthening of collagen and is clinically the most important phase of wound healing*.

1. *Thirty percent of the collagen in granulation tissue is type III collagen, but it is progressively remodeled and replaced so that the final scar contains only 10% type III collagen*

*As the collagen composition changes, eventually approximating the ratio of type I to type III collagen in intact tissues, stiffness increases, and the matrix becomes more rigid (*

1. *tension on the wound edges decreases secondary to collagen deposition, myofibroblasts regress, and collagen synthesis by other fibroblasts is progressively decreased*

*HEALING OF SPECIFIC TISSUES*

Gastrointestinal Healing

*the gastrointestinal tract, it is important to consider the nature of the 1. injury. Disruptions of the mucosa alone heal via epithelial cell migration and proliferation.*

*An epithelial seal of the defect and the creation of a barrier to luminal contents may be achieved within 3 days if direct mucosal apposition is accomplished*. *In contrast, longer periods of time are required to gain a seal with inversion or eversion of the mucosa.*

1. *Unlike in the skin, where collagen is synthesized exclusively by fibroblasts, in the gastrointestinal tract, fibroblasts and smooth muscle cells synthesize collagen, with smooth muscle cells contributing more to absolute collagen formation than fibroblasts (*
2. *Collagen composition in the gastrointestinal tract differs from that in skin; three types of collagen (I, III, and V) are present in the gastrointestinal tract, whereas only two types of collagen (I and III) are present in the skin*
3. *Gastrointestinal wound healing differs from healing of the skin in other ways as well.* ***Shear stress****, which is typically absent in healing skin, is high in the gastrointestinal tract secondary to increased intraluminal pressure placed on the healing wound during peristalsis and transport of ingesta*
4. *In addition, the bacterial flora of the two areas is different, in that the gastrointestinal tract contains both aerobic and anaerobic bacteria that may significantly influence anastomotic healing, but the skin flora is largely aerobic and does not affect healing*.
5. *During states of hypovolemic shock, vascular perfusion to the gastrointestinal tract is downregulated, and this may have an impact on anastomotic healing; however, vascular perfusion to the skin is typically constant.*

***Fascial Healing***

*In contrast to the relatively rapid gain in wound strength associated with the skin and gastrointestinal tract, restoration of fascial integrity is prolonged.*

*It is hypothesized that inflammatory cells and fibroblasts must migrate longer distances through normal tissues to reach the relatively avascular and acellular fascial wound, resulting in a prolonged inflammatory phase of wound healing*.

**Urinary Bladder Healing**

*when injured, the bladder reepithelializes in 2 to 4 days*. *is due primarily to an increase in mitotic activity in the basal layer adjacent to the wound site*,

*Collagen synthesis reaches a peak level 5 days following injury, and although urinary bladder regains 100% of its unwounded strength within 21 days, collagen synthesis does not return to normal until 70 days post injury*

Bone Healing

*The process of bone healing begins similarly to that of other tissue types, but as the process progresses*

*A combination of fibrous tissue, cartilage, and loosely woven bone is produced that forms the initial callus.*

*The maturation phase of bone may last longer than 1 year*