Classification of Biological Process in Healing
Or.
Phases of Healing

Wound healing is a complex process that involves the organization of cells, chemical signs and extracellular matrix to repair the tissue. The overlapping segments of the repair process are conceptually defined as Inflammation, Inflammatory Phase, Hemostasis and an acute inflammatory infiltrate ensues. Following this is Proliferative phase that is characterized by Fibroplasia, Granulation, Contraction and Epithelialization.

I Inflammation :-

Its the 1st stage of Healing. After tissue injury, the damaged vessels immediately Constrict and thromboplastic tissue products are exposed. Process of blood extravassation fills the damaged area with ~~blood~~ plasma & cell elements, especially Platelets.

Platelet aggregation & Blood coagulation generate a buffer, rich in Fibrin which restores Hemostasis and forms a barrier against the invasion of microorganisms, organizes a temporary matrix required for Cell Migration.

The aggregated platelets DEGRANULATE, releasing potent Chemoattractants for inflammatory cells, Activation factors for local fibroblasts and Endothelial cells and Vasoconstrictors.

After transient vasoconstriction due to platelet factors, vessels dilate due to effects of coagulation & complement cascades and permeability is also increased. The Neutrophils infiltrate and scavange on Cellular debris, foreign bodies and bacteria etc to eventually Sterilize the wound. Within 2-3 days inflammatory cells turn from Neutrophil over to Monocyte predominance. Cytokines & growth factors released from Monocyte / Macrophages, regulate

the process of repair. The activated Macrophages is the main effector cell in process of tissue repair, degrading & removing components of damaged Connec. Tissue, such as Collagen, Elastin and Proteoglycans.

(II) **PROLIFERATIVE PHASE :-**

This phase actually responsible for CLOSING the Lesion.

(A) Fibroplasia :- Prolif phase begins with deposition of FIBRIN & FIBRINOGEN matrix and activation & turnover of fibroblasts.

Initial fibrin-fibrinogen matrix is populated with Platelets & Macrophages. These Macrophages & local Extracellular Matrix (ECM) release Growth factors that initiate fibroblast activation.

Fibroblasts migrate into the coound using the newly deposited FIBRIN & FIBRINOGEN Matrix as Scaffold.

Local fibroblasts become activated & increase PROTEIN SYNTHESIS in preparation for Cell Division.

As Fibroblasts enter & populate the coound, they utilize Hyaluronidase to digest the provisional hyaluronidase acid-rich matrix & subsequently gets Deposited.

At the same time, COLLAGEN Types I & III are deposited by Fibroblasts onto FIBRONECTIN & Glycosaminoglycan (GAG) Scaffold in disorganised way.

(B) Angiogenesis :- in this phase, new blood vessels are formed from pre-existing vessels. New vessels participate in the formation of temporary granulation tissue & supply nutrients & oxygen to growing tissue. Angiogenesis occurs in the Extracellular Matrix of Wound Bed with the migration and the mitogenic stimulation of Endothelial Cells.

(C) Granulation :- its usually prominent in wounds healing by Secondary Intention. This tissue is characterized by Beefy-Red Appearence (i.e. Proud Flesh), which is a

consequence of Rich bed of New Capillary Networks formed by endothelial cell division & migration.

Directed growth of Vascular Endothelial Cells is stimulated by Platelets & Activated Macrophages & Fibroblast products.

Granulation Tissue is a dense population of Blood vessels, macrophages, and fibroblasts EMBEDDED within a loose provisional matrix of Fibronectin, Hyaluronic acid and Collagen.

(d) Contraction :- seen in Open Wounds. It is process in which surrounding skin is pulled circumferentially towards the wound. It decreases the size of wound dramatically without new tissue formation. Amount of contraction is related to size of wound & mobility of the skin. Contraction is due to presence of MYOFIBROBLASTS that are modified Fibroblasts having functional features of Contractile Smooth Muscle Cells.

(e) EPITHELIALIZATION :-

After injury, mosphological changes in Keratinocytes at the wound margins take place.

The epidermis thickens → marginal basal cells enlarge and migrate over the wound defect. Once Epithelial cells begin migrating, they do not divide until epidermal continuity is restored.

New Epithelial Cells for wound closure are provided by Fixed Basal Cells in a zone near the edge of wound.

Their daughter cells flatten & migrate over the wound matrix as a sheet (Epiboly). Following the re-establishing of Epithelial Layer, → the Keratinocytes & Fibroblasts secrete Laminin & Type-IV Collagen to form the basement membrane.

Keratinocytes then become Columnar & divide as the layering of Epidermis is established.

EPIBOLY

III) REMODELLING PHASE :-

It is a phase marked by Maturation of Elements & Affections to extracellular matrix, leading to proteoglycan & Collagen deposits. Collagen cross-linking improves wound tensile strength.

Fibroblasts of granulation tissue are transformed to MYOFIBROBLASTS and behave as Contractile tissue.

At same time, there is Extra cellular Matrix Reorganisation which transform transient matrix into Definitive One.

Ultimately, wound heals by SCAR FORMATION.

[SCAR - is defined morphologically as Lack of Tissue organization compared to surrounding normal tissue architecture & is Charac. by disorganized Collagen deposits.

As Collagenous matrix forms, densely packed fibers fill the wound site & wound become gradually stronger with time.

As a result of Maturation & remodelling, most vessels, fibroblasts & inflamm cells disappear from wound site through process of Migration, Apoptosis & related mechanisms, resulting scar with fewer Cells.

Final result of Tissue Repair is SCAR, which is brittle, less elastic & do not contain any Appendages viz sweat glands or hair follicles.

[Scar (Cicatrix)]

[Exuberant Granulation / Proud flesh]: Accumulation of Excessive amount of Granulation tissue that may protrude above level of surrounding Skin & block re-epithelialization.

[KELOID]:- Excessive amount of Collagen may give rise to raised tumourous scar k a keloid. They are not true tumours.

[Contracture]: excess contraction resulted in deformation of wound & surrounding tissues