Overview of Tissue healing and repair, tissue regeneration

By
Dr.Huma Riaz
Assistant professor Haematology
HMC/KGMC Peshawar

DEFINITIONS

- **REPAIR;** Regeneration of vascular, fibrous connective tissue. It can involve;
- 1. least inflammation
- 2. marked inflammation

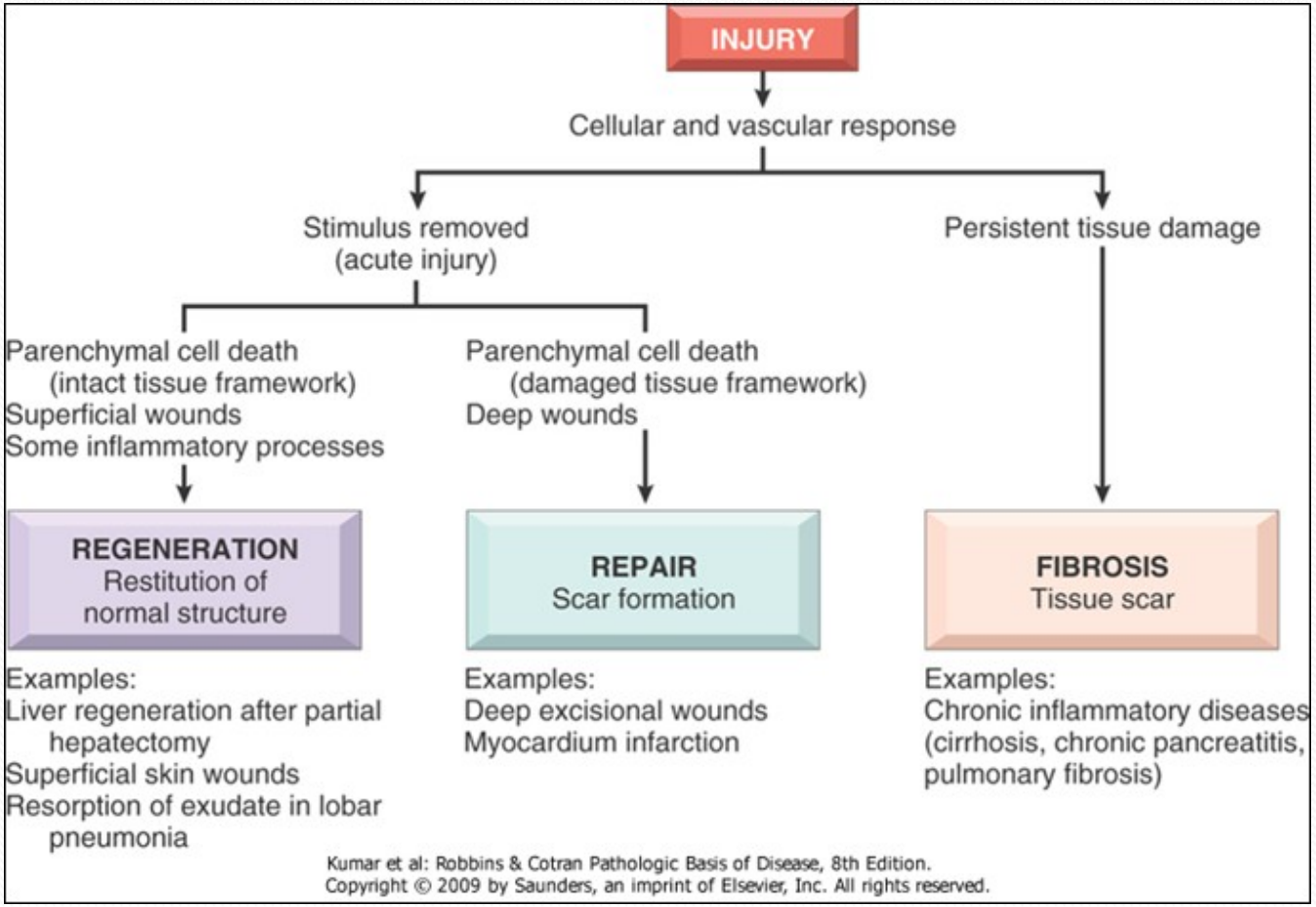
- • **REGENERATION:** Growth of cells to replace lost tissues
- • **HEALING:** A reparative tissue response to a wound, inflammation or necrosis, often leads to fibrosis
- • GRANULATION TISSUE
- • “ORGANIZING” INFLAMATION

REGENERATION

- • Replacement of lost structures
- • Is dependent on the type of normal turnover of the original tissue
- • [Can be differentiated from “compensatory” growth]

HEALING (repair)

- • Needs a wound, inflammatory process, or necrosis
- • Many disease appearances anatomically are the result of “healing” such as atherosclerosis
- • Often ends with a scar
- • Fibrosis
- • Requires a connective tissue “scaffold”
- • Fibrosis occurs in proportion to the damage of the ECM



CELL TYPES

- Labile: e.g., marrow, GI ,epidermis of skin
- Quiescent: liver, kidney
- NON-mitotic: neuron, striated muscle

- **Growth Factors (GFs)**
- • Polypeptides • Cytokines
- **Growth Factors (GFs)** • Epidermal • Transforming (alpha, beta) • Hepatocyte • Vascular Endothelial • Platelet Derived • Fibroblast • Keratinocyte • Cytokines (TNF, IL-1, Interferons)

- **CELL PLAYERS (source AND targets)** • Lymphocytes, especially T-cells • Macrophages • Platelets • Endothelial cells • Fibroblasts • Keratinocytes • “Mesenchymal” cells • Smooth muscle cells
- **E (Epidermal) GF** • Made in platelets, macrophages • Present in saliva, milk, urine, plasma • Acts on keratinocytes to migrate, divide • Acts on fibroblasts to produce “granulation” tissue
- **T (Transforming) GF-alpha** • Made in macrophages, T-cells, keratinocytes • Similar to EGF, also effect on hepatocytes
- **H (Hepatocyte) GF** • Made in “mesenchymal” cells • Proliferation of epithelium, endothelium, hepatocytes • Effect on cell “motility”
- **VE (Vascular Endothelial) GF** • Made in mesenchymal cells • Triggered by HYPOXIA • Increases vascular permeability • Mitogenic for endothelial cells • KEY substance in promoting “granulation” tissue

- **PD (Platelet Derived) GF** • Made in platelets, but also MANY other cell types • Chemotactic for MANY cells • Mitogen for fibroblasts • Angiogenesis • Another KEY player in granulation tissue
- **F (Fibroblast) GF** • Made in MANY cells • Chemotactic and mitogenic, for fibroblasts and keratinocytes • Re-epithelialization • Angiogenesis, wound contraction • Hematopoesis • Cardiac/Skeletal (striated) muscle
- **T (Transforming) GF-beta** • Made in MANY CELLS • Chemotactic for PMNs and MANY other types of cells • Inhibits epithelial cells • Fibrogenic • Anti-Inflammatory
- **K (Keratinocyte) GF** • Made in fibroblasts • Stimulates keratinocytes: • Migration • Proliferation • Differentiation
- **I (Insulin-like) GF-1** • Made in macrophages, fibroblasts • Stimulates: • Sulfated proteoglycans • Collagen • Keratinocyte migration • Fibroblast proliferation • Action similar to GH (Pituitary Growth Hormone)
- **TNF (Tumor Necrosis Factor)** • Made in macrophages, mast cells, T-cells • Activates macrophages (cachexin) • KEY influence on other cytokines • The MAJOR TNF is TNF-alpha
- **Interleukins** • Made in macrophages, mast cells, T-cells, but also MANY other cells • MANY functions: • Chemotaxis • Angiogenesis • REGULATION of other cytokines
- **INTERFERONS** • Made by lymphocytes, fibroblasts • Activates MACROPHAGES • Inhibits FIBROBLASTS • REGULATES other cytokines

REPAIR BY CONNECTIVE TISSUE

- **ANGIOGENESIS(NEOVASCULARIZATION)**

- • From endothelial precursor cells
- • From PRE-existing vessels
- • Stimulated/Regulated by GF's, especially VEGF
- • Also regulated by ECM proteins

"GRANULATION", "GRANULATION TISSUE", "ORGANIZATION", "ORGANIZING INFLAMMATION"

STEPS OF ANGIOGENESIS (from pre existing blood vessels)

- Vasodilation in response to NO and increased permeability of preexisting blood vessels induced by VEGF
- Migration of endothelial cells towards the area of injury
- Proliferation of endothelial cells just behind the leading point of migrating cells
- Inhibition of endothelial cells proliferation and remodeling into capillary tubes
- Recruitment of peri endothelial cells to form the mature vessels

- All these growth factors are the triggering mechanism of tissue regeneration process
- Extensive regeneration and compensatory hyperplasia only can occur if the residual tissue is intact both; structurally and functionally
- If tissue is damaged , regeneration is incomplete and accompanied with scarring

WOUND HEALING

- Occurs by either of the following
- 1) primary intention

  Edges lined up .as occurs in a surgical wound
- 2) 2nd INTENTION Edges NOT lined up
- More granulation More epithelialization MORE FIBROSIS

- **<u>FIBROSIS/SCARRING</u>** • DEPOSITION OF COLLAGEN by FIBROBLASTS • With time (weeks, months, years?) the collagen becomes more dense, ergo, the tissue becomes “STRONGER”

Factors retarding wound healing

- **<u>Wound RETARDING factors(LOCAL)</u>**
  - DECREASED Blood supply
  - Denervation
  - Local Infection
  - Hematoma
  - Mechanical stress
  - Necrotic tissue

- **Wound RETARDING factors(SYSTEMIC)**
- • DECREASED Blood supply
- • Age
- • Anemia
- • Malignancy
- • Malnutrition
- • Obesity
- • Infection
- • Organ failure

Thank you