3RD LECTURE: WOUND, WOUND HEALING AND SCARS

Dr.Ammar Karim Alaraji

Definition:

Wound is a break in the integrity of the skin or tissues often which may be associated with disruption of the structure and function.

Wound is a cut or break in the continuity of any tissue, caused by injury or operation.

Wound healing is a complex cellular and biochemical cascade that leads to restitution of integrity and function.

All tissues heal by similar mechanisms, and the process undergoes phases of inflammation, cellular migration, proliferation, matrix deposition, and remodeling.

PHASES OF WOUND HEALING

Normal wound healing is divided into phases defined by characteristic cellular populations and biochemical activities:

- hemostasis and inflammation:
    1. wound >>>>Exposure of subendothelial collagen to platelets >>> platelet aggregation, degranulation, and activation of the coagulation cascade.
    2. Platelet granules release a number of wound-active substances, such as
        A. platelet-derived growth factor (PDGF).
        B. transforming growth factor-β (TGF-β).
        C. platelet activating factor (PAF).
        D. Fibronectin.
        E. serotonin.
    3. Platelet plaque formation: achieving hemostasis and this fibrin clot serves as scaffolding for the migration of inflammatory cells such as polymorphonuclear leukocytes (PMNs, neutrophils) and monocytes into the wound.

4. PMNs infiltration: the first infiltrating cells to enter the wound site peaking at 24 to 48 hours.
5. Increased vascular permeability: local prostaglandin release >>> chemotactic substances such as
    A. complement factors.
    B. interleukin-1 (IL-1).
    C. tumor necrosis factor-α (TNF-α).
    D. TGF-β.
    E. Platelet factor 4.
6. Roles of neutrophil:
    A. Phagocytosis of bacteria and tissue debris.
    B. Cytokines release during early inflammation, especially TNF-α (subsequent angiogenesis, collagen formation).
    C. Release proteases such as collagenases (matrix and ground substance degradation).
7. The second population of inflammatory cells that invades the wound consists of macrophages, essential to successful healing.
8. Derived from circulating monocytes, macrophages achieve significant numbers in the wound by 48 to 96 hours post injury and remain present until wound healing is complete.
9. Roles of Macrophages
    A. wound debridement via phagocytosis.
    B. activation and recruitment of other cells via mediators such as cytokines and growth factors.
    C. Releasing mediators as
        - TGF-β.
        - vascular endothelial growth factor (VEGF).
        - insulin-like growth factor (IGF).
        - epithelial growth factor (EGF).
        - regulate cell proliferation, matrix synthesis, and angiogenesis.
        - matrix deposition and remodeling.
10. T lymphocytes peak at about 1 week post injury and truly bridge the transition from the inflammatory to the proliferative

phase of healing. The role of lymphocytes in wound healing is not fully defined.

A. in the modulation of the wound environment.
B. Depletion of most wound T lymphocytes decreases wound strength and collagen content.
C. exert a downregulating effect on fibroblast collagen synthesis by cell-associated interferon IFN-γ, TNF-α, and IL-1.

- Proliferation

1. days 4 through 12 .
2. It is during this phase that tissue continuity is reestablished.
3. Fibroblasts and endothelial cells are the last cell populations to infiltrate the healing wound, and the strongest chemotactic factor for fibroblasts is PDGF. Upon entering the wound, recruited fibroblasts >>> proliferate, and activated, to carry out their primary function of matrix synthesis remodeling. This activation is mediated mainly by the cytokines and growth factors released from wound macrophages. Endothelial cells also proliferate and participate in the formation of new capillaries (angiogenesis), a process essential to successful wound healing. Endothelial cells migrate from intact venules close to the wound. Their migration, replication, and new capillary tubule formation is under the influence of such cytokines and growth factors as TNF-α, TGF-β, and VEGF. Although many cells produce VEGF, macrophages represent a major source in the healing wound, and VEGF receptors are located specifically on endothelial cells.

- maturation and remodeling:

1. begins during the fibroplastic phase.
2. a reorganization of previously synthesized collagen.
3. a balance between collagenolysis and collagen synthesis.
4. Wound scars are determined by both the quantity and quality of the newly deposited collagen.
5. The deposition of matrix at the wound site follows a characteristic pattern: fibronectin and collagen type III.

6. glycosaminoglycans and proteoglycans represent the next significant matrix components.
7. collagen type I is the final matrix.
8. Fibril formation and fibril cross-linking result in decreased collagen solubility.
9. increased strength, and increased resistance to enzymatic degradation of the collagen matrix.
10. Scar remodeling continues for many (6 to 12) months post injury.
11. Collagenolysis and collagen synthesis are strictly controlled by cytokines and growth factors.

- Epithelialization:
  1. proliferation and migration of epithelial cells adjacent to the wound.
  2. The migrating epithelial cells lose their flattened appearance, become more columnar in shape, and increase their mitotic activity.
  3. Reepithelialization is complete in less than 48 hours in the case of approximated incised wounds but may take substantially longer in the case of larger wounds, where there is a significant epidermal/dermal defect.
  4. In particular EGF, TGF-β, basic fibroblast growth factor (bFGF), PDGF, and IGF-1 have been shown to promote epithelialization
- Wound Contraction
  1. For wounds that do not have surgically approximated edges, the area of the wound will be decreased by this action (healing by secondary intention).
  2. The myofibroblast are the major cell responsible for contraction, and it differs from the normal fibroblast in that it possesses a cytoskeletal structure.
  3. Typically this cell contains α-smooth muscle actin in thick bundles called stress fibers, giving myofibroblasts contractile capability.

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CLASSIFICATION OF WOUNDS

1. Wounds are classified as either
    A. Acute < 4 wks
    B. Chronic > 4 wks
    C. Simple wound
    D. Compound wound
2. Classification of the accidental wounds
    A. Based on the origin:
        - I. Mechanical:
            - Abraded wound (vulnus abrasum).
            - Puncured wound (v. punctum).
            - Incised wound (v. scissum).
            - Cut wound (v. caesum).
            - Crush wound (v. contusum).
            - Torn wound (v. lacerum).
            - Bite wound (v. morsum).
            - Shot wound (v. sclopetarium).
        - II. Chemical:
            - Acid.
            - Base.
        - III. Wounds caused by radiation.
        - IV. Wounds caused by thermal forces:
            - 1. Burning.
            - 2. Freezing.
        - V. Special
    B. According to the bacterial contamination:
        - Clean wound.
        - Clean-contaminated wound.
        - Contaminated wound.
        - Dirty wound
    C. Depending on the depth of injury:
        - Superficial.
        - Partial thickness.
        - Full thickness
        - Deep wound

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D. According to healing pattern:
   - primary intention.
   - Secondary intention: because of bacterial contamination or tissue loss, a wound will be left open to heal by granulation tissue formation and contraction
   - Delayed primary closure, or healing by tertiary intention, represents a combination of the first two, consisting of the placement of sutures, allowing the wound to stay open for a few days, and the subsequent closure of the sutures.

- Factors Affecting Wound Healing
  1. Local:
     A. Ischemia.
     B. Infection
     C. Foreign body
     D. Edema, elevated tissue pressure.
  2. Systemic:
     A. Age and gender.
     B. Sex hormones.
     C. Stress.
     D. Ischemia.
     E. Diseases.
     F. Obesity.
     G. Medication.
     H. Alcoholism and smoking.
     I. Immunocompromised conditions.
     J. Nutrition.
- Complications of wound healing:
  1. Early complications.
     A. Seroma.
     B. Hematoma.
     C. Wound disruption.

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D. Superficial wound infection.
E. Deep wound infection.
F. Mixed wound infection

2. Late complications:
   A. Hypertrophic scar.
   B. Keloid formation.
   C. Necrosis.
   D. Inflammatory.
   E. Infiltration.
   F. Abscesses.
   G. Foreign body containing abscesses.

Scars:

☒ **Keloid scars:**

- are the result of an overly aggressive healing process. They extend beyond the original injury.
- Treatments include :
  - surgery to remove the scar.
  - steroid injections.
  - silicone sheets to flatten the scar.
  - cryotherapy (freezing therapy using liquid nitrogen).
- prevent keloid formation by using pressure treatment or gel pads with silicone when you are injured.
- Keloid scars are most common among people with dark skin.

☒ **Contracture scars.** If your skin has been burned, you may have a contracture scar. These scars tighten skin, which can impair your ability to move.

☒ **Hypertrophic scars.** These are raised, red scars that are similar to keloids but do not go beyond the boundary of the injury. Treatments include injections of steroids or silicone sheets, which flatten the scar.

☒ **Acne scars.** ranging from deep pits to scars that are angular or wavelike in appearance.