# **Wound Healing**

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- PHASES OF WOUND HEALING
- (1) hemostasis and inflammation
- (2) proliferation
- (3) maturation and remodeling

#### Hemostasis and Inflammation

- subendothelial collagen to platelets
- fibrin clot
- Platelet α granules :
- (PDGF)
- transforming growth factor-β (TGF-β)
- platelet-activating factor (PAF)
- fibronectin
- serotonin
- fibrin clot serves as scaffolding for the migration into the wound of inflammatory cells such as polymorphonuclear leukocytes (PMNs, neutrophils) and monocytes

### • PMNs

- peaking at 24–48 h
- Increased vascular permeability, local prostaglandin release, and the presence of chemotactic substances such as
- (IL-1)
- (TNF-α) TNF-β
- platelet factor 4, or bacterial products all stimulate neutrophil migration.

## Macrophage

- pivotal function is activation and recruitment of other cells via mediators such as cytokines and growth factors
- TGF-β, vascular endothelial growth factor (VEGF), (IGF), epithelial growth factor (EGF), and lactate

- T lymphocytes
- peak at about 1 week

- Proliferation
- days 4 through 12
- Fibroblasts and endothelial cells
- PDGF
- matrix synthesis and remodeling
- mediated mainly by the cytokines and growth factors released from wound macrophages
- Endothelial cells angiogenesis
- Endothelial cells migrate from intact venules close to the wound.
  Their migration, replication, and new capillary tubule formation are under the influence of such cytokines and growth factors as TNF-a, TGF-β, and VEGF.

- Matrix Synthesis & Collagen
- Vit C
- Cross linking

- Proteoglycan Synthesis
- GAG granulation tissue
- Fibroplast 1<sup>st</sup> 3 weeks

#### Maturation and Remodeling

- MMPs
- : fibronectin and collagen type III
- glycosaminoglycans and proteoglycans represent the next significant matrix components
- collagen type I is the final matrix
- By several weeks postinjury the amount of collagen in the wound reaches a plateau, but the tensile strength continues to increase for several more months.
- Fibril formation and fibril cross-linking result in decreased collagen solubility, increased strength, and increased resistance to enzymatic degradation of the collagen matrix
- Scar remodeling continues for many (6–12) months postinjury, gradually resulting in a mature, avascular, and acellular scar. The mechanical strength of the scar never achieves that of the uninjured tissue.

# Epithelialization

- Migration of epithelial cells
- Re-epithelialization is complete in less than 48
- mediated by a combination of a loss of contact inhibition;
  exposure to fibronectin; and cytokines produced by immune mononuclear cells
- EGF, TGF-β, basic fibroblast growth factor (bFGF), PDGF, and IGF-1

- Wound Contraction
- myofibroblast
- α-smooth muscle actin is undetectable until day 6, and then is increasingly expressed for the next 15 days of wound healing

# CLASSIFICATION OF WOUNDS

- primary intention
- secondary intention
- Delayed primary closure, or healing by tertiary intention

# Systemic

- Age
- Nutrition
- Trauma
- Metabolic diseases
- Immunosuppression
- Connective tissue disorders
- Smoking

- Local
- Mechanical injury
- Infection
- Edema
- Ischemia/necrotic tissue
- Topical agents lonizing radiation
- Low oxygen tension fibroplasia
- Foreign bodies

#### Steroids and Chemotherapeutic Drugs

- reduce collagen synthesis
- inhibit the inflammatory phase of wound healing and the release of lysosomal enzymes
- Steroids used after the first 3–4 days postinjury do not affect wound healing as severely as when they are used in the immediate postoperative period
- inhibit epithelialization and contraction and contribute to increased rates of wound infection,
- topical application of vitamin A. Collagen synthesis of steroidtreated wounds also can be stimulated by vitamin A
- All chemotherapeutic antimetabolite drugs adversely affect wound healing by inhibiting early cell proliferation and wound deoxyribonucleic acid (DNA) and protein synthesis.

- Metabolic Disorders
- granulocyte function, capillary ingrowth, and fibroblast proliferation
- type I diabetes mellitus was noted to decrease wound collagen accumulation in the wound, independent of the degree of glycemic control. Type II diabetic patients showed no effect
- Uremia

- Nutrition
- impaired healing response and reduced cell-mediated immunity
- Arginine
- vitamin C
- r extensively burned patients this requirement may increase to as high as 2 g
- vitamin A
- n increased influx of macrophages, with an increase in their activation and increased collagen synthesis

- Zinc
- decreased fibroblast proliferation, decreased collagen synthesis, impaired overall wound strength

### Infections

- Antibiotic prophylaxis is most effective when adequate concentrations
- repeat dosing of antibiotics has been shown to be essential in decreasing postoperative wound infections in operations with durations exceeding the biochemical half-life (T1/2) of the antibiotic, or in which there is large-volume blood loss and fluid replacement
- e source of pathogens for the infection is usually the endogenous flora of the patient's skin, mucous membranes, or from hollow organs

- clean—class I
- clean contaminated— class II
- contaminated—class III
- and dirty—class IV

# Chronic Wounds

 failed to proceed through the orderly process that produces satisfactory anatomic and functional integrity or that have proceeded through the repair process without producing an adequate anatomic and functional result

### Ischemic Arterial Ulcers

- Venous Stasis Ulcers
- distention of the dermal capillaries with leakage of fibrinogen into the tissues
- Venous hypertension and capillary damage lead to extravasation of hemoglobin
- Lipodermatosclerosis

- Diabetic Wounds
- Neuropathy, foot deformity, and ischemia
- Osteomyelitis
- Debridement
- Off-loading

### Decubitus or Pressure Ulcers

- Pressure ulcer formation is accelerated in the presence of friction, shear forces, and moisture
- stage I, nonblanchable erythema of intact skin
- stage II, partial-thickness skin loss involving epidermis or dermis or both
- stage III, full-thickness skin loss, but not through the fascia
- stage IV, full-thickness skin loss with extensive involvement of muscle and bone

#### EXCESS HEALING Excess Dermal Scarring

- Keloid
- autosomal dominant with incomplete penetration and variable expression
- t synthesize collagen at a rate 20 times greater than that observed in normal dermal fibroblasts, and 3 times higher than fibroblasts derived from HTSs
- n. TGF-β expression is higher in HTSs, and both HTS- and keloidderived fibroblasts respond to lower concentrations of TGF-β than do normal dermal fibroblasts. HTSs also express increased levels of insulin-like growth factor-1, which reduces collagenase messenger ribonucleoprotein acid (mRNA) activity and increases mRNA for types I and II procollagen



- . Silicone
- increased hydration of the skin, which decreases capillary activity, inflammation, hyperemia, and collagen deposition