Wound Healing

451-SURG
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Objectives

- Types of wounds
- Wound healing and its types
- Phases of wound healing
- Factors affecting wound healing
- Abnormal scarring
  - Keloids
  - Hypertrophic scars
- Fetal wound healing

Definitions

- Wound: disruption of normal anatomical structure and function
- Acute wound: proceeds through an orderly and timely reparative process to restore function and anatomical integrity (3-4 wk)
- Chronic wound: proceeds through a reparative process without establishing a sustained anatomic and functional result (beyond 6 wk)

- Healing: Response of an organism to a physical disruption in an organ or a tissue to repair the defect

Abnormal Healing

- Overgrowth → keloid or hypertrophic scar
- Undergrowth → wide or thin or chronic unstable
- Abnormal pigmentation → hypo/hyper

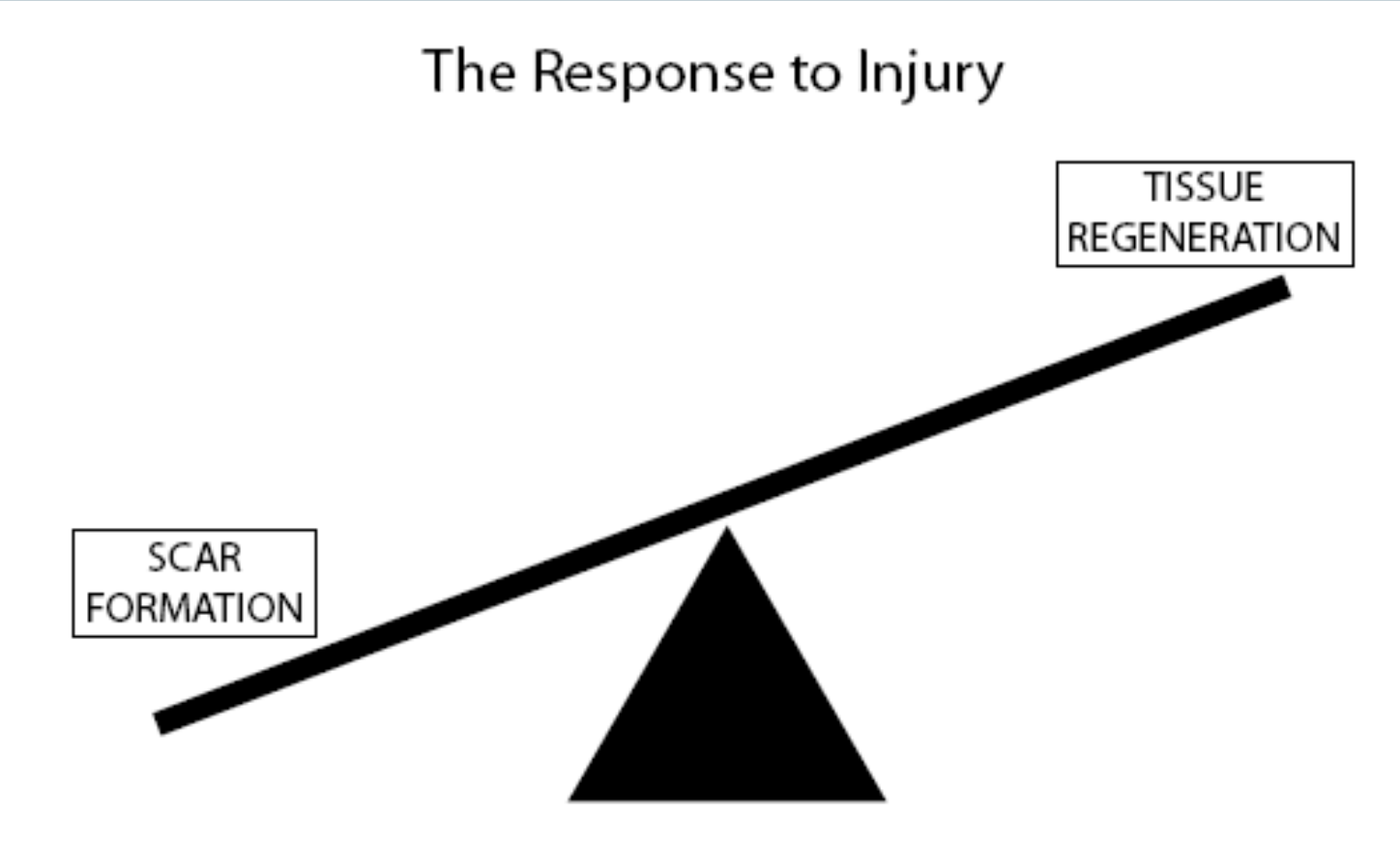
Scar formation

- Substitution of a different cellular matrix as a patch to immediately re-establish both a physical and a physiological continuity of the injured organ

Regeneration

- Recreating the original organ by the developmental process which created it

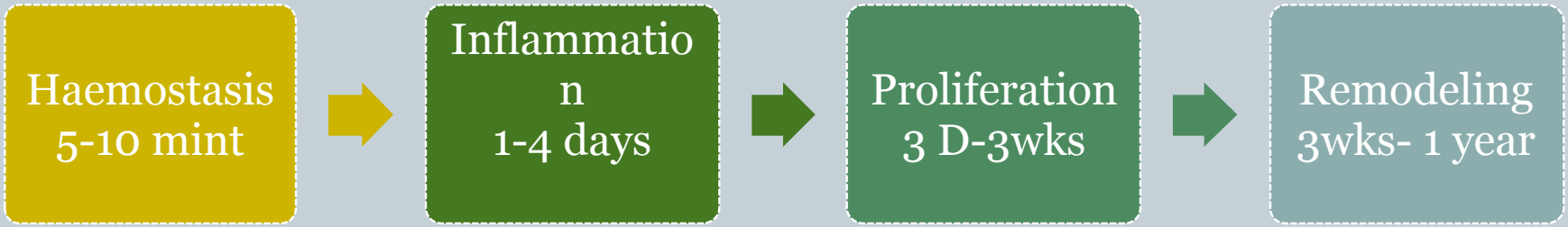
Scar formation vs. Regeneration ??



Phases of Normal Wound Healing

1. Hemostasis
2. Inflammatory phase
3. Proliferative phase
4. Remodeling phase

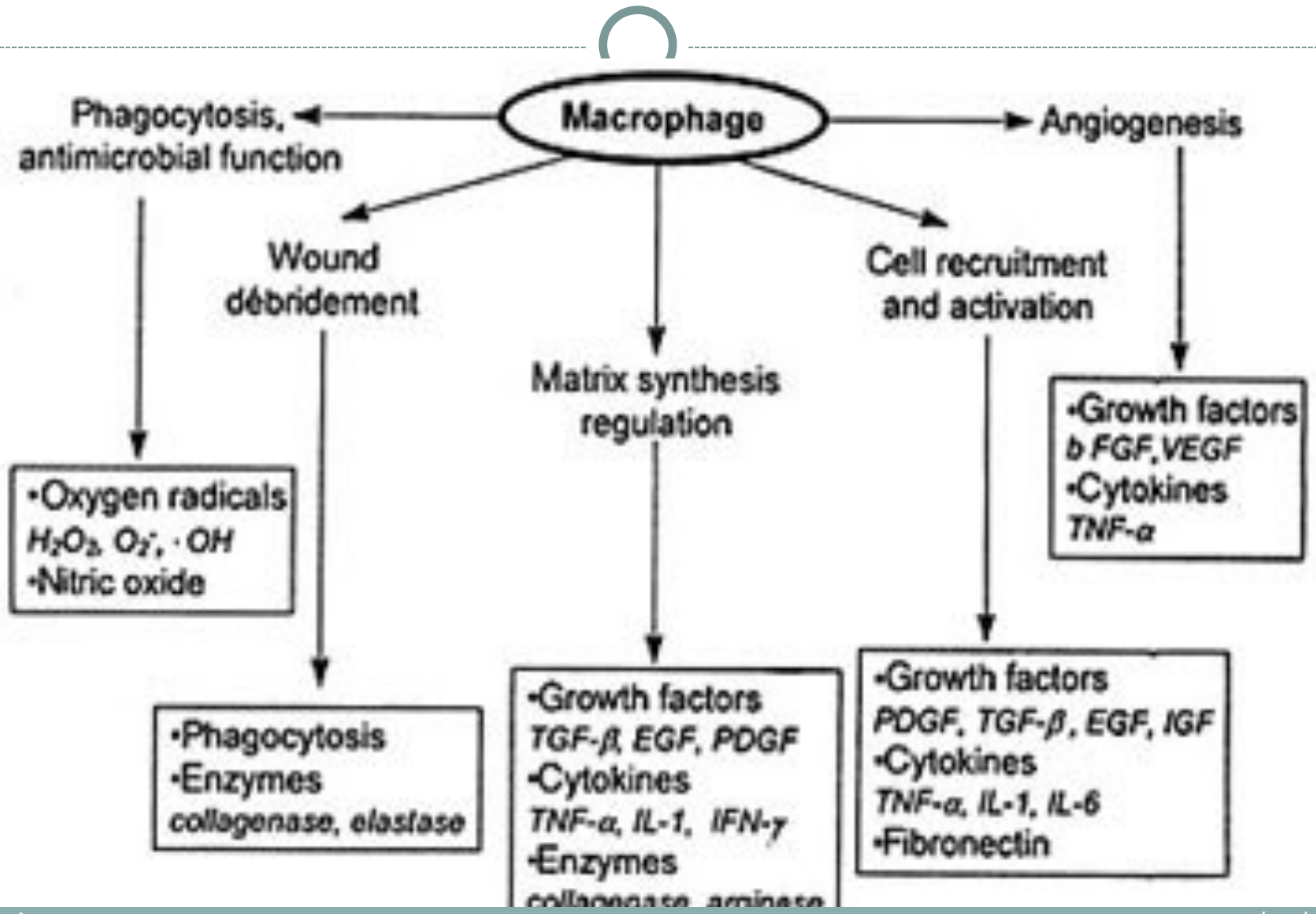
- Wound contracture is a process that occurs throughout the healing process starting from the proliferative phase


Haemostasis
5-10 mint
Inflammation
1-4 days
Proliferation
3 D-3wks
Remodeling
3wks- 1 year

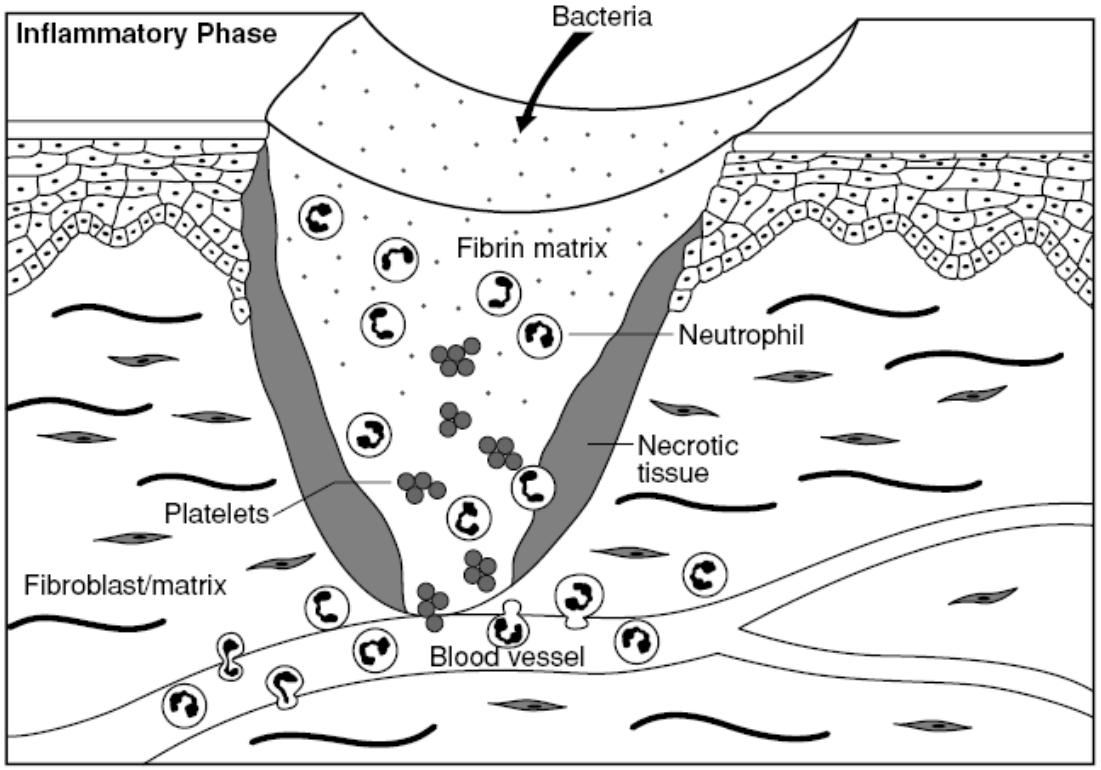
Hemostasis

- Initial response to injury ⚿ vasoconstriction ⚿ **platelet plug** ⚿ activation of intrinsic and extrinsic pathways

- Platelet stimulate release of factors
  - PDGF
  - TGFBeta
  - FGF
    - All promote chemotaxis, fibrogenesis and angiogenesis


Macrophage
Phagocytosis, antimicrobial function
Wound débridement
Matrix synthesis regulation
Cell recruitment and activation
Angiogenesis
•Oxygen radicals
H_2O_2, O_2^-, ·OH
•Nitric oxide
•Phagocytosis
•Enzymes
collagenase, elastase
•Growth factors
TGF-β, EGF, PDGF
•Cytokines
TNF-α, IL-1, IFN-γ
•Enzymes
•Growth factors
PDGF, TGF-β, EGF, IGF
•Cytokines
TNF-α, IL-1, IL-6
•Fibronectin
•Growth factors
b FGF, VEGF
•Cytokines
TNF-α

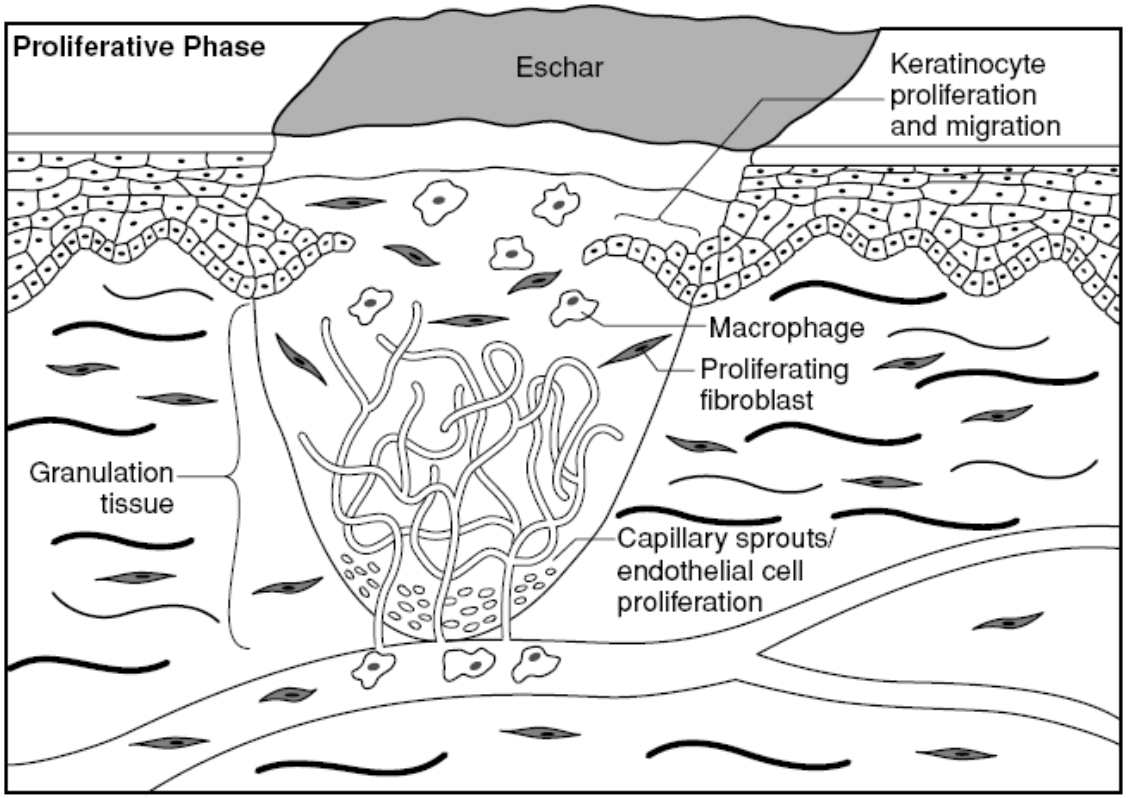
Inflammatory/Migratory phase



- Rubor, tumor, calor & dolor
- PMN within 6-8 hr for 48-72 hr
- Monocytes ⓜ max in 24-36 hr ⓜ mature into macrophages

FIGURE 2.3. The inflammatory phase of wound healing begins immediately following tissue injury and serves to obtain hemostasis, remove devitalized tissues, and prevent invasive infection by microbial pathogens.

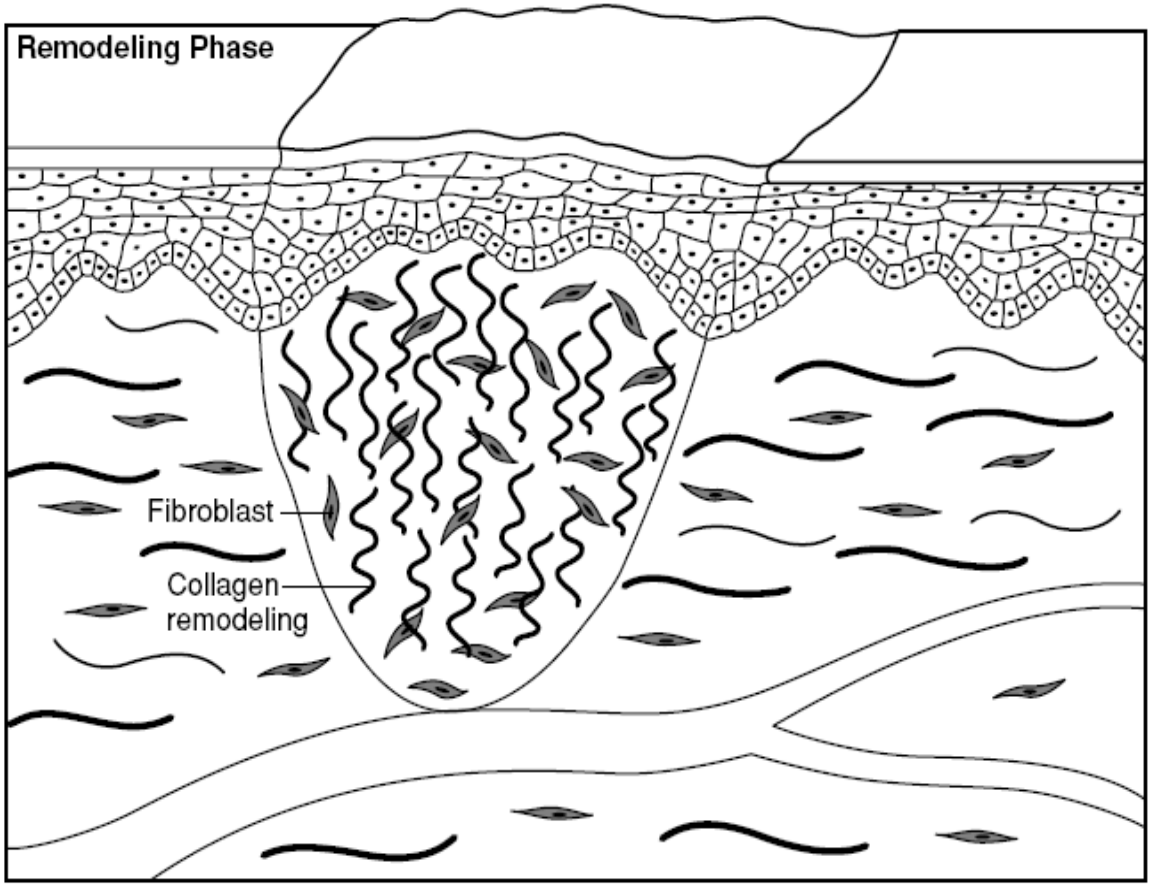
Proliferative (fibroplasia) Phase



- Starts at day 2-3
- Fibroblasts peaking at 7-14 days
- Collagen synthesis (for 3-6 weeks)
- Lasts for 2-4 weeks

FIGURE 2.4. The proliferative phase of wound healing occurs from days 4 to 21 after wounding. During this phase, granulation tissue fills the wound and keratinocytes migrate to restore epithelial continuity.

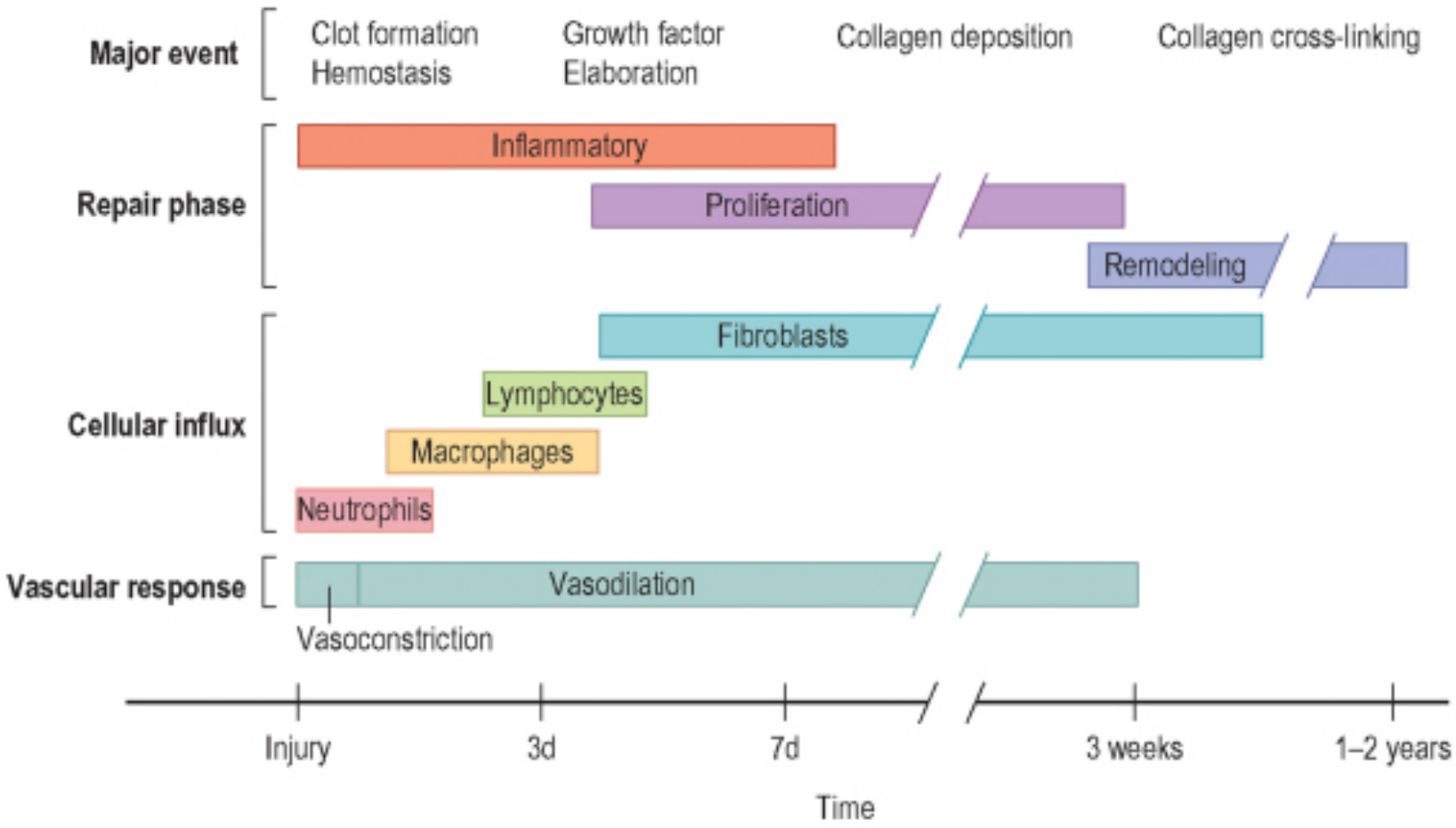
Remodeling Phase



- Starts at 3 weeks
- Collagen synthesis peaks at 3 weeks then synthesis/ degradation is at equilibrium - Collagen fibers become reorganized
- Collagen III is replaced by I to restore normal 4:1 ratio of type I:III
- May take up to 1- years
- Tensile strength 80% of preinjured state at 60 days

FIGURE 2.5. The remodeling phase of wound healing is the longest phase and lasts from 21 days to 1 year. Remodeling, although poorly understood, is characterized by the processes of wound.

Timeline of wound repair events



Collagen

- 90% type I
- Normal ration I:III is 4:I
- Hypertrophic scars 2:1
- Formation inhibited by:
  - Colchicine
  - Penicillamide
  - Steroids
  - Vit. C deficiency
  - Fe deficiency

Epithelial Repair

- Epithelial continuity is reestablished across a wound
- Mobilization
- Migration
- Mitosis
- Cellular differentiation

Wound Contraction

- Active, normal & essential part of healing
- Rate depends on the number of myofibroblasts
  - Resemble fibroblast but contain smooth muscle **actin**
  - Responsible for wound contraction
- From end to end
- Contracture:
  - Undesirable result of healing due to excessive contraction and fibrosis

Factors Affecting Healing

- Local factors
- Systemic factors
  - Congenital
  - Acquired

Local factors

- Infection
- Radiation
- Blood supply
- Nerve supply
- Trauma
- Hydration
- Temperature

Systemic factors : congenital

- Pseudoxanthoma elasticum
- Ehler-Danlos syndrome
  - AD, defect in synthesis, structure and cross linkage of collagen
- Cutis laxa
- Progeria
- Werner syndrome
- Epidermolysis bullosa

Systemic factors : Acquired

- Nutrition
- Pharmacological
- Endocrine abnormalities
- Age
- Smoking

Nutrition

Vitamin A

- Deficiency delays wound healing
- 25,00 0 IU po OD increases tensile strength
- 200,000 IU topical Q8 increases epitheliazation

Vitamin C

- Collagen synthesis

- Scurvy :
  - Immature fibroblasts
  - Deficient collagen synthesis
  - Capillary hemorrhage
  - Decreased tensile strength

Vitamin E

- Antioxidant
- Membrane stabilizer
- Large doses may inhibit healing but unproven to reduce scarring

Zinc

- Cofactor for many enzymes
- Deficiency causes impaired epithelial and fibroblast proliferation

Pharmacological

- Steroids decrease inflammation and subsequent wound healing
- NSAIDS decrease collagen synthesis and inhibit platelet aggregation
- Antineoplastic agents decrease fibroblasts proliferation and wound contraction
  - Few or no adverse reaction if administered 10-14 days after wound closure

Endocrine abnormalities

- Diabetics often have delayed wound healing
- Neuropathy rather than small vessel occlusive disease may be responsible for delayed healing

Age

- Rate of cell multiplication decreases with age
- All stages of healing are protracted in elderly
- Healed wounds have less tensile strength in elderly

Smoking

- Nicotine causes vasoconstriction decreasing perfusion
- CO shifts oxygen dissociation curve and reduces tissue oxygenation

Infection

- Wounds with over 10^5 organisms per gram of tissue are considered infected and are unlikely to heal without further treatment

Radiation

- Causes endothelial cell , capillary and arteriole damage
- Irradiated fibroblasts secrete less collagen and extracellular matrix
- Lymphatics are destroyed resulting in edema and risk of infection

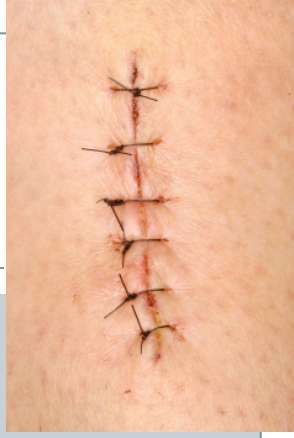
Blood supply

- Decreased tissue perfusion results in decreased wound oxygenation
- Fibroblasts are oxygen-sensitive and their function is reduced in hypoxic states

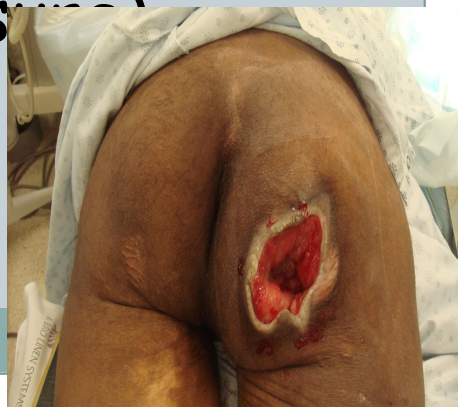
Decreased oxygen delivery to tissue reduces :

- Collagen formation
- Extracellular matrix deposition
- Angiogenesis
- Epithliazation

Types of wound healing



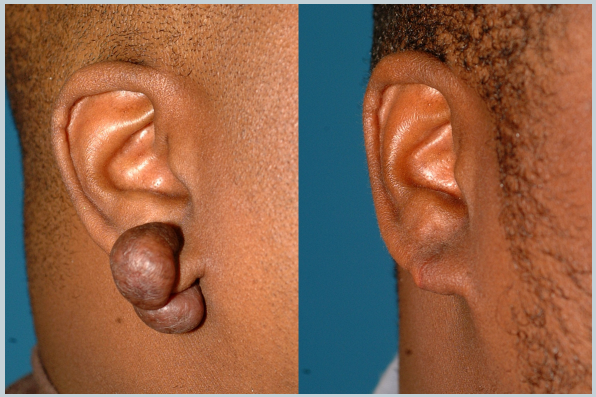
- Primary intention
  - Primary closure of the wound ∴ least amount of scarring
- Secondary intention
  - Heal by granulation, contraction and epithelialization
- Tertiary intention (delayed primary clos
  - Used for contaminated wounds



Abnormal scarring

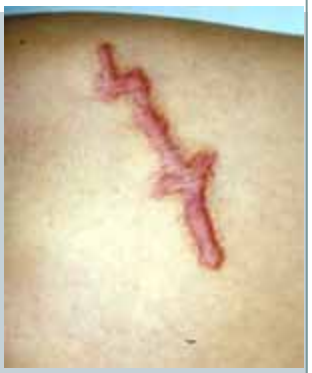
- Keloids
- Hypertrophic scars

Keloids



- Significant familial incidence
- Dark > light skin
- Females > males
- Most common 10 – 30 yrs of age
- Outgrows wound borders
- Appears months after surgery and rarely subsides
- Mostly in face earlobes and anterior chest & deltoid
- Possible autoimmune phenomenon

Hypertrophic scars



- Low familial incidence
- Low racial incidence
- Equal sex ratio
- Occur at nay age but mostly less than 2 yrs
- Remains within wound borders
- Appears soon after surgery and subsides with time
- Across flexor surfaces
- Due tension closure
- Treated as keloids with better outcome

Treatment

- Prevention by avoiding:
  - Unnecessary surgeries
  - High risk patients or sites
  - Closure under tension
  - Crossing joint likes
  - Rough tissue handling
  - Infections and hematoma
- Therapeutic:
  - Pressure garments
  - Silicon sheets
  - Steroid injections
  - Radiation
  - Revision

Fetal wound healing

- Tissue healing during the first 3 months of fetal life is by regeneration rather than scarring
- Defers from adult healing by :
  - Reduced inflammatory response
  - Epitheliazation is more rapid
  - Angiogenesis is reduced
  - Collagen deposition is more rapid , organized and not excessive
  - More water and HA content
  - More collagen type 3 rather than type 1
- These differences due to the lack of TGF-β