

Wound healing and repair

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Objectives

- acute versus chronic wounds
- phases of wound healing
- basic principles of wound management
- wound management
- summary

Acute versus chronic wounds

Acute wounds

orderly physiologic sequence of inflammation, proliferation and maturation

Chronic wounds

inadequate angiogenesis, impaired innervation, or impaired cellular migration (*ischemic ulcers, venous ulcers, neuropathic foot ulcers and infected wounds including surgical site infections*)

Risk factors for non-healing

- Peripheral artery disease
- Diabetes
- Chronic venous insufficiency
- Aging
- Immunosuppressive therapy
- Chemotherapy and Radiation therapy
- Spinal cord disease and immobilization
- Malnutrition
- Infection
- Smoking and nicotine replacement therapy

Phases of wound healing

1. hemostasis

platelets aggregation, activation of clotting cascade, release of growth factors and cytokines (PDGF, TGF- β ,...)

2. inflammation

increased vascular permeability, cellular recruitment:

- Accumulation of mononuclear leukocytes and transformation into macrophages
- Mast cells degranulate, releasing histamine and other mediators of vasodilation and cellular migration
- Release of vasoactive substances from stromal mast cells
- migration and concentration of polymorphonuclear leukocytes that digest bacteria, foreign debris, and necrotic tissue with lysosomal enzymes

3. epithelialization

basal cell proliferation and epithelial migration occurring in the fibrin bridgework inside a clot

4. fibroplasia

fibroblast proliferation, accumulation of ground substance, and collagen production

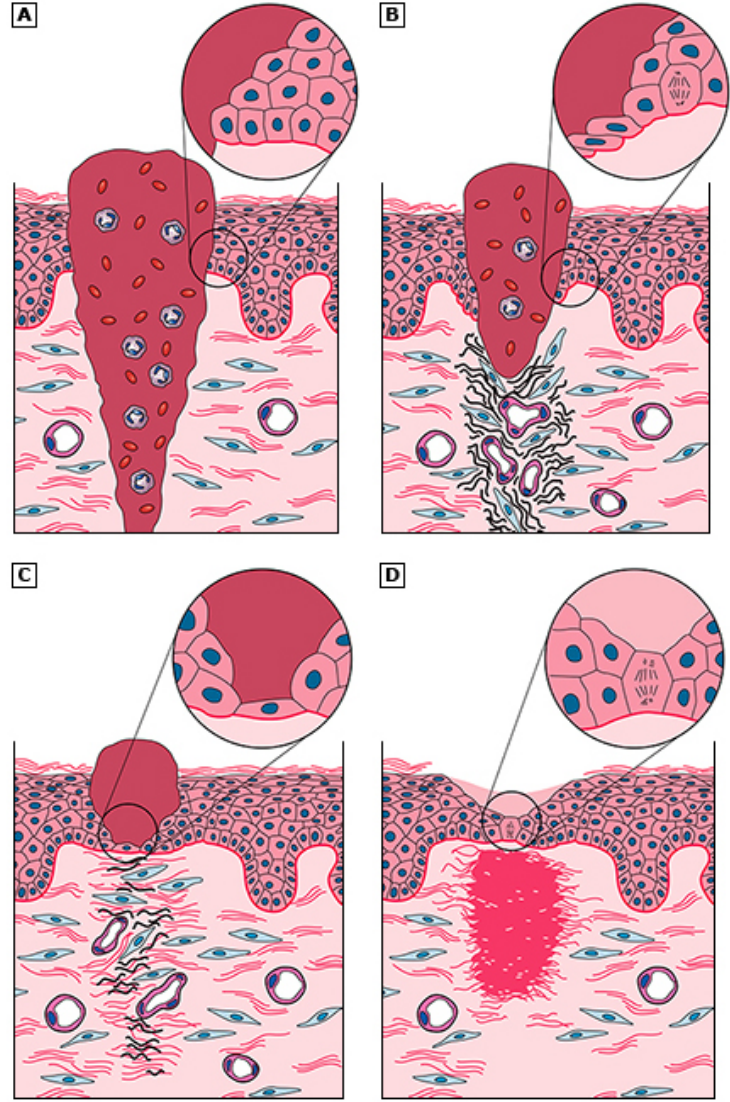
5. maturation

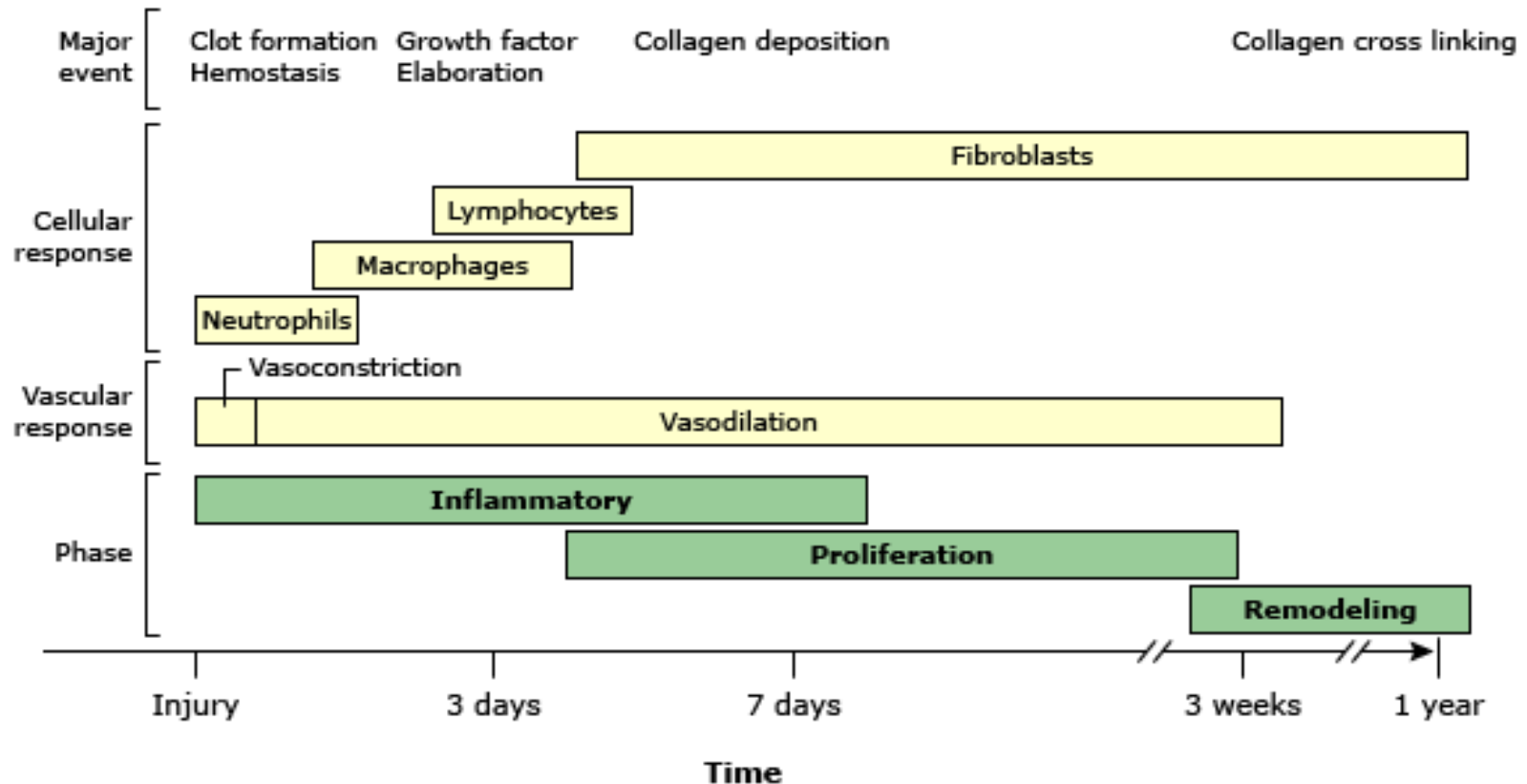
collagen cross-linking, collagen remodeling, wound contraction and repigmentation

Odland G, Ross R. Human wound repair. I. Epidermal regeneration. J Cell Biol 1968; 39:135.

Ross R, Everett NB, Tyler R. Wound healing and collagen formation. VI. The origin of the wound fibroblast studied in parabiosis. J Cell Biol 1970; 44:645.

Darby IA, Hewitson TD. Fibroblast differentiation in wound healing and fibrosis. Int Rev Cytol 2007; 257:143.





Basic principles of wound management

To ensure proper healing, the wound needs to be well *vascularized, free of devitalized tissue, clear of infection and moist!*

Wound dressings should eliminate dead space, control exudate, prevent bacterial overgrowth, ensure proper fluid balance, be cost-efficient, and be manageable for the patient.

Atiyeh BS, Ioannovich J, Al-Amm CA, El-Musa KA. Management of acute and chronic open wounds: the importance of moist environment in optimal wound healing. *Curr Pharm Biotechnol* 2002; 3:179.

Schultz GS, Sibbald RG, Falanga V, et al. Wound bed preparation: a systematic approach to wound management. *Wound Repair Regen* 2003; 11 Suppl 1:S1.

Wound management

Antibiotics

no evidence for antibiotic therapy as prophylaxis in non- infected chronic wounds
reserved for wounds that appear clinically infected (local or systemic symptoms)

Wound debridement

irrigation – decrease of bacterial load, remove of loose material

surgical

enzymatic – *Collagenase, Papain, Bromelain*

biologic – *maggot therapy with Australian sheep blow fly or green bottle fly*

Lipsky BA, Berendt AR, Deery HG, et al. Diagnosis and treatment of diabetic foot infections. *Plast Reconstr Surg* 2006; 117:212S.

Klasen HJ. A review on the nonoperative removal of necrotic tissue from burn wounds. *Burns* 2000; 26:207.

Andersen AS, Sandvang D, Schnorr KM, et al. A novel approach to the antimicrobial activity of maggot debridement therapy. *J Antimicrob Chemother* 2010; 65:1646.

Wound management

Topical therapy

- Growth factors –
- PDGF *Becaplermin* (approved for use in the United States as an adjuvant therapy for the treatment of diabetic foot ulcers)
 - GM-CSF (significantly higher rates of healing in 60 patients with venous ulcers)
 - EGF (not significantly associated with a greater reduction in ulcer size and higher ulcer healing rate compared with placebo)

Fang RC, Galiano RD. A review of becaplermin gel in the treatment of diabetic neuropathic foot ulcers. *Biologics* 2008; 2:1.
Falanga V, Eaglstein WH, Bucalo B, et al. Topical use of human recombinant epidermal growth factor (h-EGF) in venous ulcers. *J Dermatol Surg Oncol* 1992; 18:604.
Lipsky BA, Hoey C. Topical antimicrobial therapy for treating chronic wounds. *Clin Infect Dis* 2009; 49:1541.

Wound management

Antiseptics and antimicrobials

Cadexomer iodine (reduces bacterial load and provides a moist wound environment)

Silver sulfadiazine (antiseptic)

Lipsky BA, Hoey C. Topical antimicrobial therapy for treating chronic wounds. Clin Infect Dis 2009; 49:1541.

Vermeulen H, van Hattem JM, Storm-Versloot MN, Ubbink DT. Topical silver for treating infected wounds. Cochrane Database Syst Rev 2007; :CD005486.

Wound management

Wound dressings

general principles for chronic wound management

- Hydrogels for the debridement stage
- Foam and low-adherence dressings for the granulation stage
- Hydrocolloid and low-adherence dressings for the epithelialization stage

Films, alginates, hydroactives

Wound management

Wound closure

primary closure and delayed primary closure

negative pressure wound therapy



Mendez-Eastman S. Guidelines for using negative pressure wound therapy. *Adv Skin Wound Care* 2001; 14:314.

Kimball EJ, Adams DM, Kinikini DV, et al. Delayed abdominal closure in the management of ruptured abdominal aortic aneurysm. *Vascular* 2009; 17:309.

Wound management

Wound coverage

Full-thickness skin grafts

Split-thickness skin grafts

cell-based dressings (epidermal or dermal elements, collagen and fibroblasts)



Discussion

- To ensure proper healing, the wound needs to be well vascularized, free of devitalized tissue, clear of infection and moist!
- Wound dressings should eliminate dead space, control exudate, prevent bacterial overgrowth, ensure proper fluid balance, be cost-efficient, and be manageable for the patient.
- Topical agents such as antiseptics and antimicrobial agents can be used to control contamination
- Negative pressure wound therapy is frequently used to manage complex wounds prior to definitive closure.
- Acute wounds can often be closed primarily. Chronic wounds can undergo delayed closure or coverage with skin grafts or bioengineered tissues.