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Pathology

Doctor 2017 | Medicine | JU

◉ Sheet ○ Slides

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FACTORS THAT IMPAIR TISSUE REPAIR:

Are also called co-morbidities and can act individually or in combination. **All** can delay repair (causes 2nd intention healing to replace 1st intention healing) and/or increase risk of infections.

1. **Infections** (local or systemic):
    a. Prolong inflammation
    b. Potentially increase local tissue injury
    c. Increase risk of scar formation
    d. Common surgery problem, 1st intention healing window is lost → healing progresses by 2nd intention → scar develops at site of surgery.
2. **Diabetes mellitus** (a systemic disease)
3. **Nutritional status**: ex. Vit. C deficiency and protein malnutrition → less enzymes and structural proteins (collagen) for repair and remodeling.
4. **Steroids**: strong anti-inflammatory effects → immunosuppression → higher risk of infections.
5. **Mechanical factors**: such as increased local pressure (high intra-abdominal/thoracic pressure from intense cough or vomiting) or torsion (from obesity) may cause wounds to pull apart (dehiscence).
6. **Poor perfusion**: resulting either from arteriosclerosis and diabetes or from obstructed venous drainage (e.g., in varicose veins), causes ischemia and slower angiogenesis.
7. **Foreign bodies**: such as fragments of steel, glass, or even bone.
   *****Implants are not usually counted as foreign bodies but can sometimes have the same effects to much lower extents.
8. **Type and extent of tissue injury**: the magnitude of the injury, extensive injury will probably result in incomplete tissue regeneration and at least partial loss of function.
9. **Site of injury**: corresponds to the ability of the tissue to regenerate (squamous epithelium (labile) vs myocardium (permanent)) or the vulnerability of the location ex. Walking or even simply standing can affect repair of an injury at the sole of the foot.

Abnormal Wound Healing

Complications of tissue repair can arise from abnormalities in any of the basic components of the process, including deficient/excessive scar formation, formation of contractures, and organ fibrosis. **In some cases, failure of healing may lead to dehiscence (wound rupture).**

- Chronic wounds due to defective healing:
  a. **Venous leg ulcers:** occurs in patients with varicose veins (دوالي). Varicose veins (caused by long standing times ex.teachers) impede venous return → stasis of blood → back-pressure on arterial supply → **poor perfusion** → ulcer formation. Venous leg ulcers are characterized by their location on the medial side of the leg and the deposition of iron pigments (hemosiderin). These ulcers fail to heal because of poor perfusion.

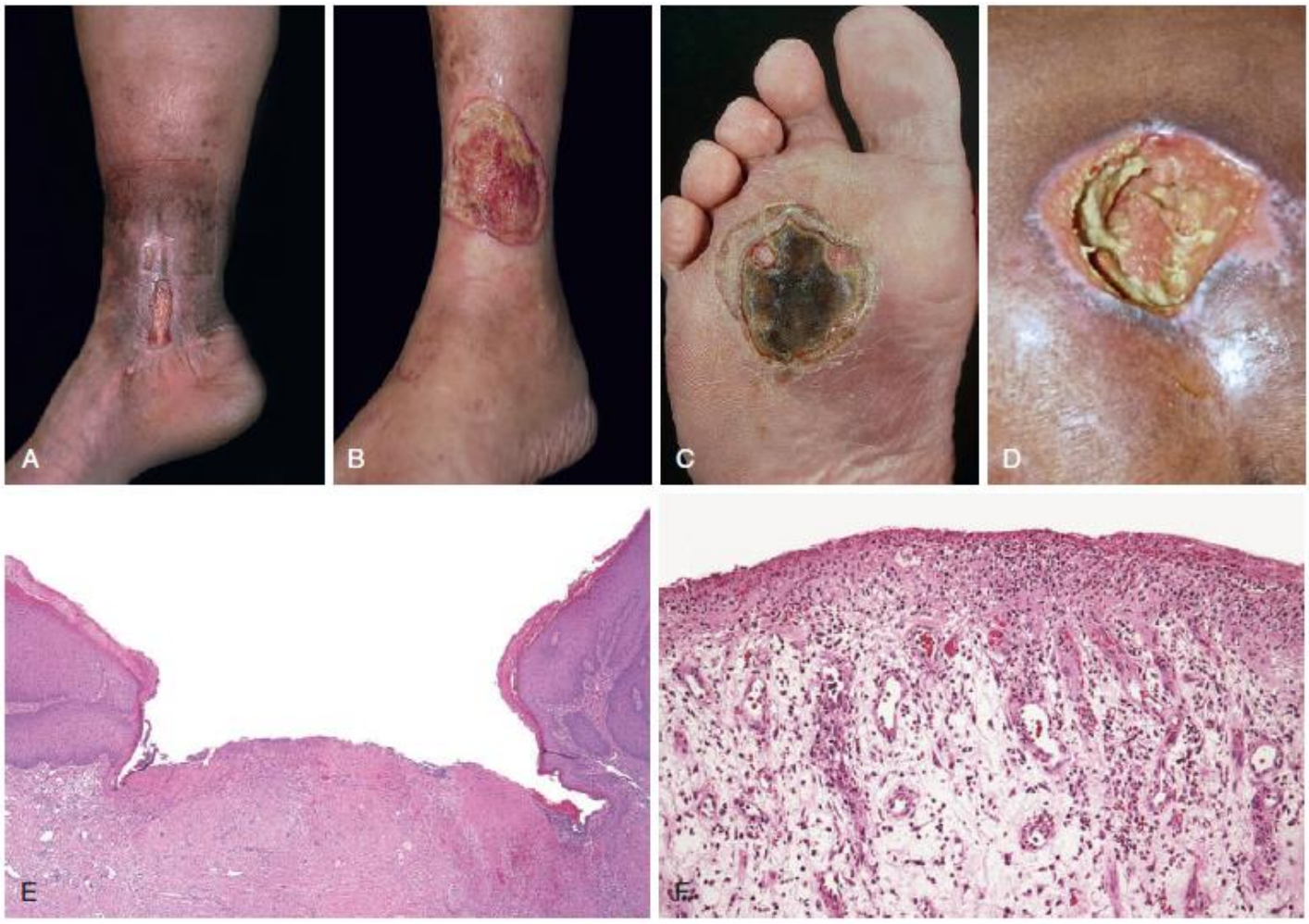


Fig. 3.27 Chronic wounds illustrating defects in wound healing. (A–D) External appearance of skin ulcers. *(From Eming SA, Margin P, Tomic-Canic M: Wound repair and regeneration: mechanisms, signaling, and translation,* Sci Transl Med *6:265, 2014.)* (A) Venous leg ulcer; (B) arterial ulcer, with more extensive tissue necrosis; (C) diabetic ulcer; and (D) pressure sore. (E–F) Histologic appearance of a diabetic ulcer. (E) ulcer crater; (F) chronic inflammation and granulation tissue.

Please read this

b. **Arterial ulcers**: develop in individuals with **atherosclerosis** of peripheral arteries, especially associated with **diabetes** or Buerger's disease. The ischemia results in atrophy and then necrosis of the skin and underlying tissues (more distant and deeper than venous ulcers).

c. **Pressure sores**: are areas of **skin ulceration and necrosis** of underlying tissues caused by prolonged compression of tissues against a bone, for example, on the backs of bedridden immobile patients. They are deep and difficult to treat and are indicators of poor nursing since they are easily preventable by moving the patient from time to time to relieve the pressure.

d. **Diabetic ulcers**: diabetes causes peripheral neuropathy (when peripheral nerves stop functioning due to high sugar content), which can stop sensations to pain due to injury → injury is ignored → no treatment → **inflammation → inability to heal due to ischemia → tissue necrosis** → can lead to gangrenous necrosis and a need for amputation.

- Excessive Scarring:

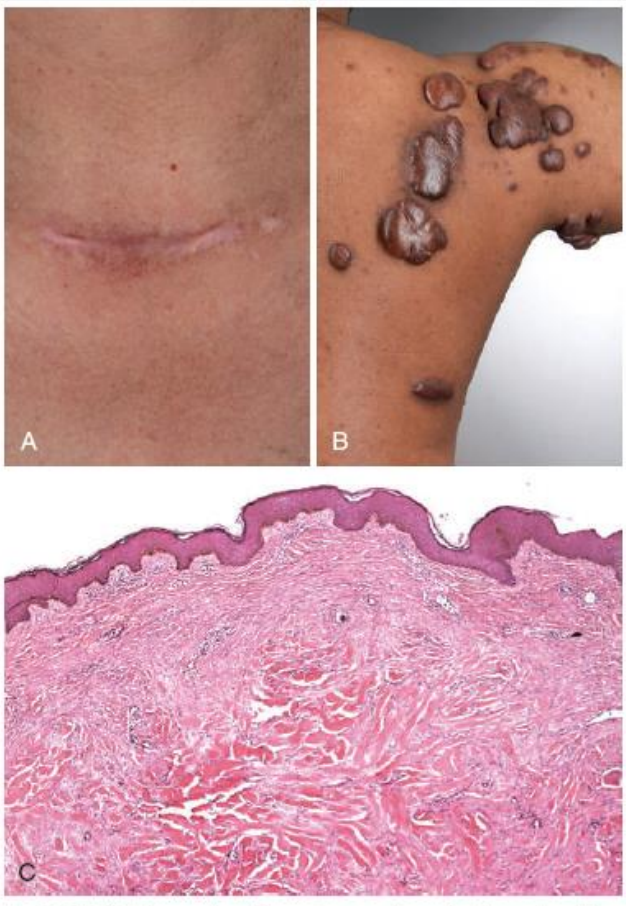


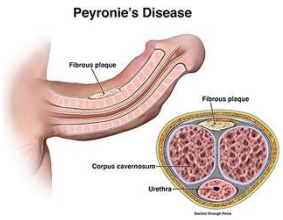
Fig. 3.28 Clinical examples of excessive scarring and collagen deposition. (A) Hypertrophic scar. (B) Keloid. (C) Microscopic appearance of a keloid. Note the thick connective tissue deposition in the dermis. *(A–B from Eming SA, Margin P, Tomic-Canic M: Wound repair and regeneration: mechanisms, signaling, and translation,* Sci Transl Med *6:265, 2014, p. 2.)*

a. **Hypertrophic scar**: excessive amounts of collagen and scar tissue ***within*** the boundaries of the original wound probably due to less MMP/collagenase activity or higher TGF-ß activity. Regresses over time.

b. Keloid: excessive amounts of collagen and scar tissue which grows ***beyond*** the boundaries of the original wound and does not regress over time. Those of **African descent** are predisposed (at higher risk) to keloid formation.

c. **Exuberant granulation** (proud flesh): much bigger than keloid (500g instead of 5g), characterized by the formation of **exaggerated** amounts of granulation tissue.

d. **Aggressive fibromatosis** (desmoid tumour): 2 types:



- Superficial: has 3 major syndromes, plantar (on the sole of the foot), palmar (on the palm of the hand), Peyronie's (the development of fibrous scar tissue inside the penis that causes curved, painful erections).
- Deep: in the abdomen, causes organ dysfunction and is fatal by local fibrous proliferation - associated with FAP (Familial Adenomatous Polyposis) syndrome.

*Desmoid tumours lie in the grey area between benign and metastatic tumours. Are NOT metastatic.

e. **Contractures**: Wound contraction is an important part of the normal healing process. An exaggeration of this process gives rise to *contractures.* They are commonly seen after **serious burns** and <u>can compromise the movement of joints.</u>

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- Organ Fibrosis:

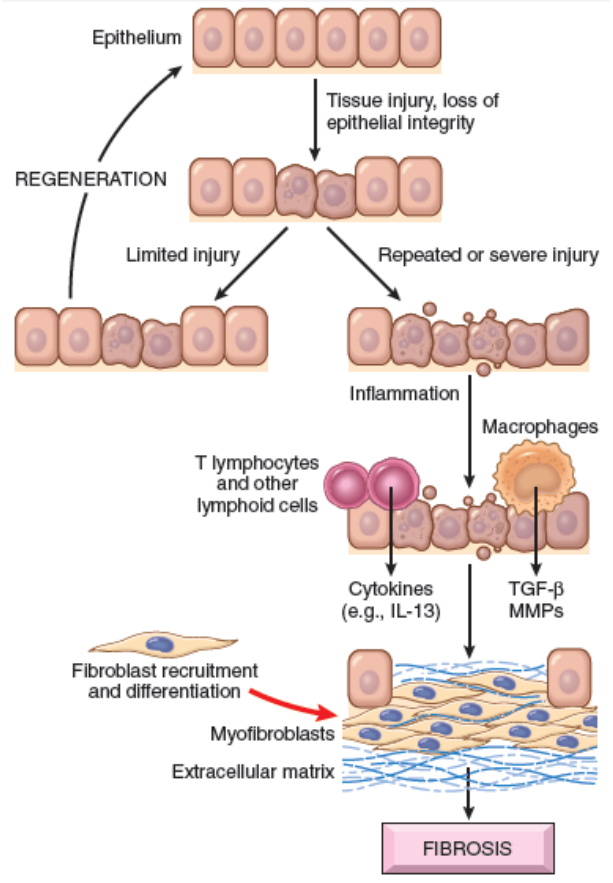

Fig. 3.29 Mechanisms of fibrosis. Persistent tissue injury leads to chronic inflammation and loss of tissue architecture. Cytokines produced by macrophages and other leukocytes stimulate the migration and proliferation of fibroblasts and myofibroblasts and the deposition of collagen and other extracellular matrix proteins. The net result is replacement of normal tissue by fibrosis.

Remember:

Scar and fibrosis: excessive deposition of collagen and ECM.

- Organ fibrosis is caused by a **<u>continuous cycle</u>** <u>of infections and immunologic injuries followed by fibrotic repair → accumulation of scar tissue which replaces functional parenchymal tissue → loss of function.</u>
- TGF-ß is the most common cytokine of fibrosis.
- Examples: liver cirrhosis, Idiopathic lung fibrosis, and ESKD (End-Stage Kidney Disease).

SUMMARY

CUTANEOUS WOUND HEALING AND PATHOLOGIC ASPECTS OF REPAIR

- The main phases of cutaneous wound healing are inflammation, formation of granulation tissue, and ECM remodeling.
- Cutaneous wounds can heal by primary union (first intention) or secondary union (secondary intention); secondary healing involves more extensive scarring and wound contraction.
- Wound healing can be altered by many conditions, particularly infection and diabetes; the type, volume, and location of the injury are important factors that influence the healing process.
- Excessive production of ECM can cause keloids in the skin.
- Persistent stimulation of collagen synthesis in chronic inflammatory diseases leads to tissue fibrosis, often with extensive loss of the tissue and functional impairment.

GOOD LUCK