FACTORS AFFECTING WOUND HEALING

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LEARNING OBJECTIVES

1. Factors affecting wound healing
2. Pathological aspects of wound healing
3. Scar formation
4. Fibrosis

DEFINITION

Wound healing refers to replacement of body's destroyed tissue by living tissue.

Can be achieved by 2 mechanisms:

1. Tissue regeneration

2. Scar formation

INTRODUCTION

During healing, a complex cascade of cellular events occur to achieve resurfacing, reconstitution and restoration of tensile strength of injured tissue.

Wound healing occurs in 3 phases

1. Inflammatory phase

2. Proliferative phase

3. Remodeling phase

WOUND HEALING

The replacement of granulation tissue with a scar involves changes in the composition of the ECM.

***The balance between ECM synthesis and degradation results in remodeling of the connective tissue framework – an important feature of tissue repair*.**

Some of the growth factors that stimulate synthesis of collagen and other connective tissue molecules also modulate the synthesis and activation of metalloproteinases, enzymes that degrade these ECM components.

WOUND HEALING

If tissue injury is severe or chronic, and results in damage of both parenchymal cells and the stromal framework of the tissue, healing can not be accomplished by regeneration. Under these conditions, the main healing process is *repair by deposition of collagen and other ECM components, causing the formation of* a *scar*.

STAGES OF REPAIR

Repair by connective tissue deposition includes the following basic features:

- ***inflammation***
- ***angiogenesis***
- ***migration and proliferation of fibroblasts***
- ***scar formation***
- ***connective tissue remodeling*.**

FACTORS THAT INFLUENCE WOUND HEALING

The adequacy of wound repair may be impaired by:

1.Systemic factors

2. Local host factors

SYSTEMIC FACTORS THAT INFLUENCE WOUND HEALING

Systemic factors include:

- ***Nutrition*** **has profound effects on wound healing. Protein deficiency, for example, and particularly vitamin C deficiency, inhibit collagen synthesis and retard healing.**
- ***Metabolic status*** **can change wound healing. Diabetes mellitus, for example, is associated with delayed healing, as a consequence of the microangiopathy that is a frequent feature of this disease**
- ***Circulatory status*** **can modulate wound healing. *Inadequate blood supply* , usually caused by arteriosclerosis or venous abnormalities (e.g., varicose veins) that retard venous drainage, also impairs healing.**

- ***Hormones*** **such as *glucocorticoids* have well-documented anti-inflammatory effects that influence various components of inflammation. These agents also inhibit collagen synthesis.**

LOCAL FACTORS THAT INFLUENCE WOUND HEALING

Local factors that influence healing include:

- ***Infection*** is the single most important cause of delay in healing, because it results in persistent tissue injury and inflammation.

- ***Mechanical factors***,

  Early motion of wounds, can delay healing, by compressing blood vessels and separating the edges of the wound.

- ***Foreign bodies***,

  Sutures or fragments of steel, glass, or even bone

- ***Size, location, and type of wound .***

Wounds in richly vascularized areas, such as the face, heal faster than those in poorly vascularized ones, such as the foot. we have small incisional injuries heal faster and with less scar formation than large excisional wounds or wounds caused by blunt trauma.

PATHOLOGIC ASPECTS OF REPAIR

COMPLICATIONS IN WOUND HEALING CAN ARISE FROM ABNORMALITIES IN ANY OF THE BASIC COMPONENTS OF
THE REPAIR PROCESS.

THESE ABERRATIONS CAN BE GROUPED INTO THREE GENERAL CATEGORIES:

1. *DEFICIENT SCAR FORMATION*,

2. *EXCESSIVE FORMATION OF THE REPAIR COMPONENTS* , AND

3.*FORMATION OF CONTRACTURES*.

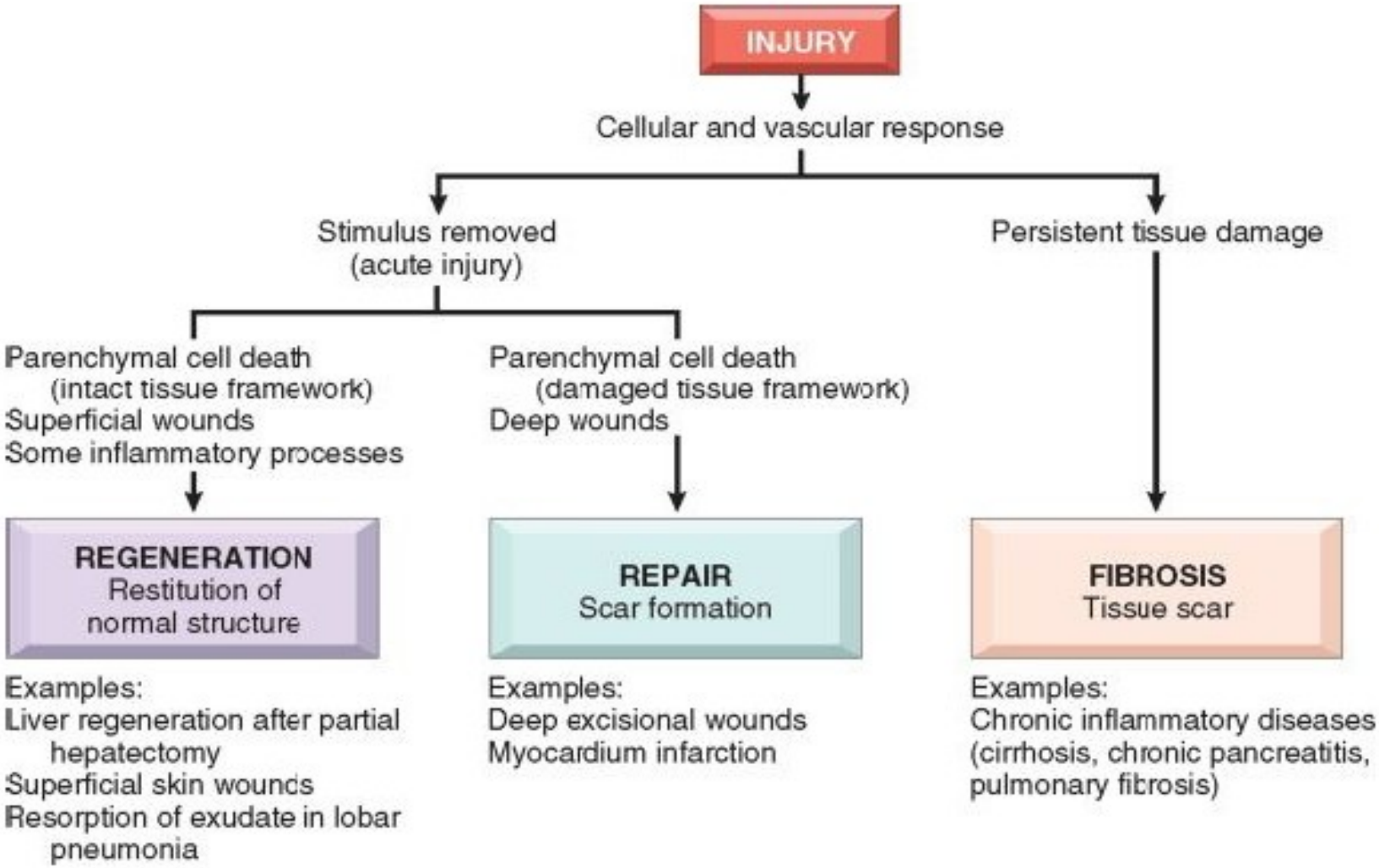


FIGURE 3-26 Repair, regeneration, and fibrosis after injury and inflammation.

- *INADEQUATE FORMATION OF GRANULATION TISSUE OR ASSEMBLY OF A SCAR*

Two types of complications:

1. *Wound dehiscence*

Dehiscence or rupture of a wound is most common after abdominal surgery and is due to increased abdominal pressure. Vomiting, coughing, or ileus can generate mechanical stress on the abdominal wound.

2. Ulceration.

Wounds can ulcerate because of inadequate vascularization during healing. For example, lower extremity wounds in individuals with atherosclerotic peripheral vascular disease typically ulcerate non-healing wounds also form in areas devoid of sensation. These neuropathic ulcers are occasionally seen in patients with diabetic peripheral neuropathy

EXCESSIVE FORMATION OF THE COMPONENTS OF THE REPAIR PROCESS

1.Excessive formation of the components of the repair process **can give rise to hypertrophic scars and keloids.**

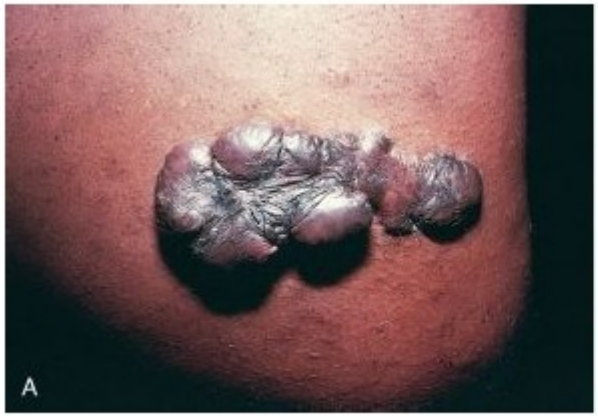
2. The accumulation of excessive amounts of collagen may give rise to a raised scar known as a *hypertrophic scar*; if the scar tissue grows beyond the boundaries of the original wound and does not regress, it is called a *keloid.*

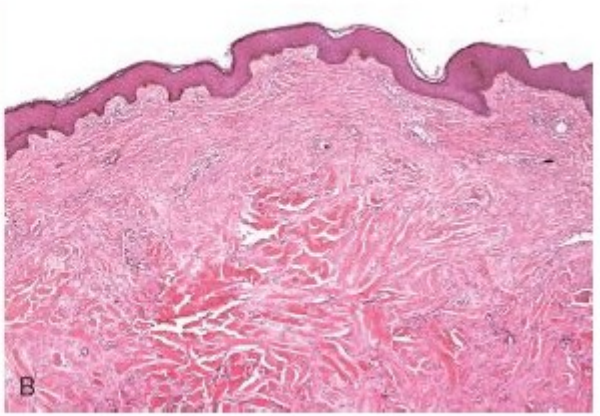
3. Keloid formation seems to be an individual predisposition, and for unknown reasons this aberration is somewhat more common in african- americans.

4. Hypertrophic scars generally develop after thermal or traumatic injury that involves the deep layers of the dermis.

5. Collagen is produced by myofibroblasts, which persist in the lesion through the autocrine production of tgf-β, and the establishment of focal adhesions.

...ent of joints (Fig. 3-24).





CONTRACTION

Contraction **in the size of a wound is an important part of the normal healing process.**

An exaggeration of this process gives rise to *contracture* and results in deformities of the wound and the surrounding tissues.

Contractures are particularly prone to develop on the palms, the soles, and the anterior aspect of the thorax.

Contractures are commonly seen after serious burns and can compromise the movement of joints

Wound contraction.

Wound contraction generally occurs in large surface wounds .

The contraction helps to close the wound by decreasing the gap between its dermal edges and by reducing the wound surface area.

it is an important feature in healing by secondary union.

The initial steps of wound contraction involve the formation, at the edge of the wound, of a network of *myofibroblasts* that express smooth muscle α-actin and vimentin.

These cells produce large amounts of ECM components

Type I collagen
Tenascin-c,
SPARC, and
Fibronectin.,
Myofibroblasts

SCAR FORMATION.

The leukocytic infiltrate, edema, and increased vascularity largely disappear during the secondweek.

Blanching begins, accomplished by the increased accumulation of collagen within the wound area and regression of vascular channels.

The original granulation tissue scaffolding is converted into a pale, avascular scar, composed of spindle-shaped fibroblasts, dense collagen, fragments of elastic tissue, and other ECM components.

The dermal appendages that have been destroyed in the line of the incision are permanently lost, although in rats new hair follicles may develop in large healing wounds under went stimulation.

This result suggests that, with appropriate treatment procedures, regrowth of skin appendages during wound healing might be achieved in humans.

***By the end of the first month, the scar is made up of acellular connective tissue devoid of inflammatory infiltrate, covered by intact epidermis*.**

FIBROSIS

Deposition of collagen is part of normal wound healing.

Fibrosis / Scar

Excessive deposition of collagen and other ECM components in a tissue.

The basic mechanisms that occur in the development of fibrosis associated with chronic inflammatory diseases.

Similar to the mechanisms of skin wound healing.

However, in contrast to the short-lived stimulus that triggers the orderly steps of wound healing.

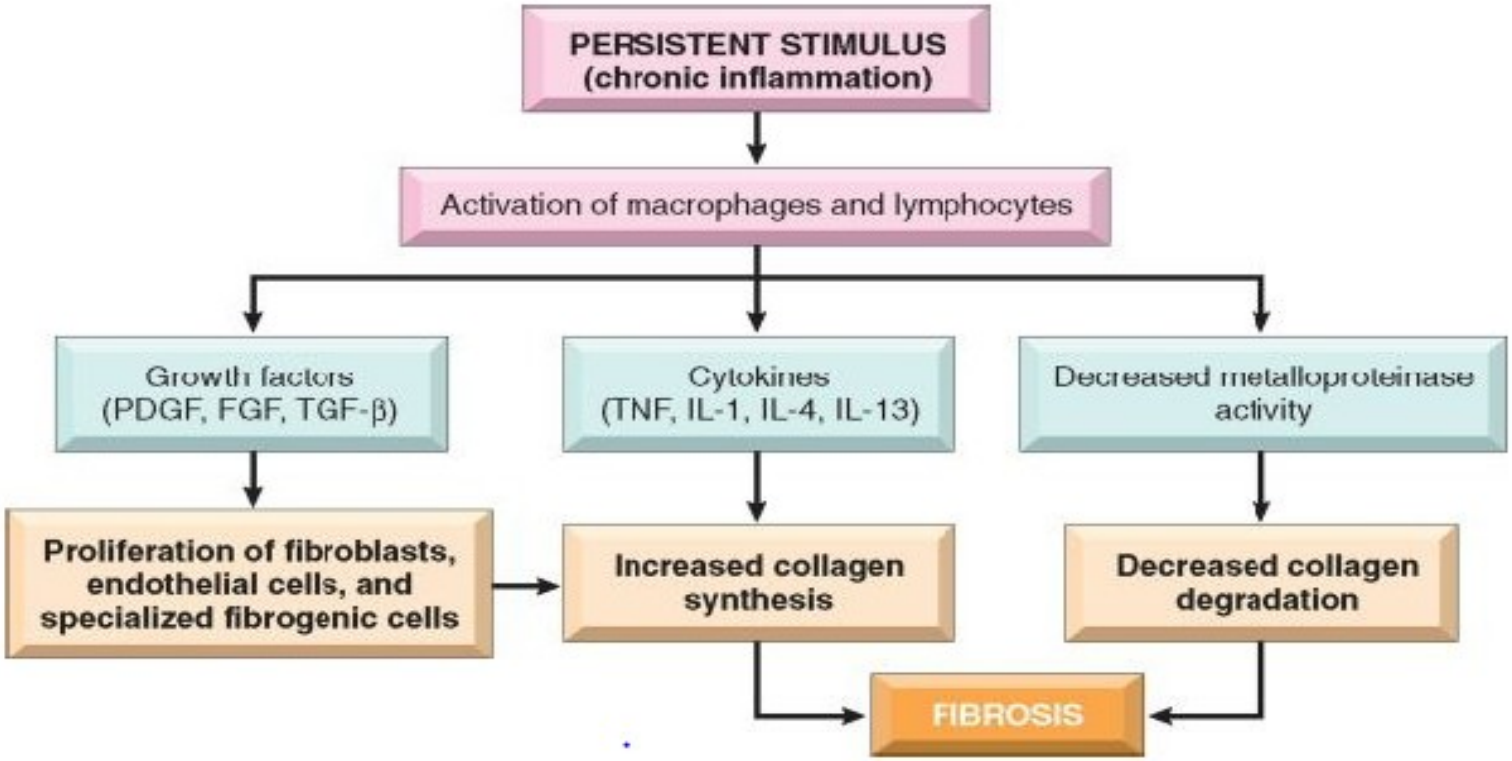
Stimulus caused by infections, autoimmune reactions, trauma, and other types of tissue injury persists in chronic diseases, causing organ dysfunction and often organ failure.

FIBROSIS

1. Development of fibrosis in chronic inflammation.

2. The persistent stimulus of chronic inflammation activates macrophages and lymphocytes, leading to the production of growth factors and cytokines, which increase the synthesis of collagen.

3. Deposition of collagen is enhanced by decreased activity of metalloproteinases.


PERSISTENT STIMULUS
(chronic inflammation)
Activation of macrophages and lymphocytes
Growth factors
(PDGF, FGF, TGF-β)
Cytokines
(TNF, IL-1, IL-4, IL-13)
Decreased metalloproteinase activity
Proliferation of fibroblasts, endothelial cells, and specialized fibrogenic cells
Increased collagen synthesis
Decreased collagen degradation
FIBROSIS