Cutaneous wound healing :- Cutaneous wound healing is a process involves both **epithelial regeneration (healing of the epidermis)** **and** **the formation of connective tissue scar (healing of the dermis) .** healing process in general has three main phases:

(1) inflammation,

(2) formation of granulation tissue,

(3) ECM deposition and remodeling .

Depending on the nature and size of the wound, the healing of skin wounds is occur by :-

1- healing by first intention (primary union).

2- healing by second intention (secondary union).

1- healing by first intention **(primary union).**

is the healing of a clean, uninfected small wound or surgical incision approximated by surgical sutures .This is referred to as *primary union,* or *healing by first intention.* The incision causes only focal disruption of epithelial basement membrane continuity and death of a relatively few epithelial and connective tissue cells. As a result,

- Epithelial regeneration predominates over fibrosis.
- A small scar is formed, but there is minimal wound contraction .

Steps of primary union

1- The narrow incisional space first fills with clotted blood containing fibrin and blood cells, dehydration of the surface clot forms scab that covers the wound and seals it from the environment .

2- Within 24 hours, neutrophils are seen at the incision margin, migrating toward the fibrin clot. Basal cells at the cut edge of the epidermis increased mitotic activity .

3-Within 24 to 48 hours, epithelial cells from both edges migrate and proliferate along the dermis, depositing basement membrane components as they progress. The cells meet in the midline beneath the surface scab, yielding a thin but continuous epithelial layer.

4- By 3rd day, neutrophils have been replaced by macrophages, and granulation tissue invades the incision space. Collagen fibers are evident at the incision margins, but these are vertically oriented and do not bridge the incision. Epithelial cell proliferation continues, yielding a thickened epidermal layer.

5-By 5rd day, neovascularization reaches its peak as granulation tissue fills the incisional space. Collagen fibrils become more abundant and begin to bridge the incision. The epidermis recovers its normal thickness as differentiation of surface cells yields a mature epidermal architecture with surface keratinization.

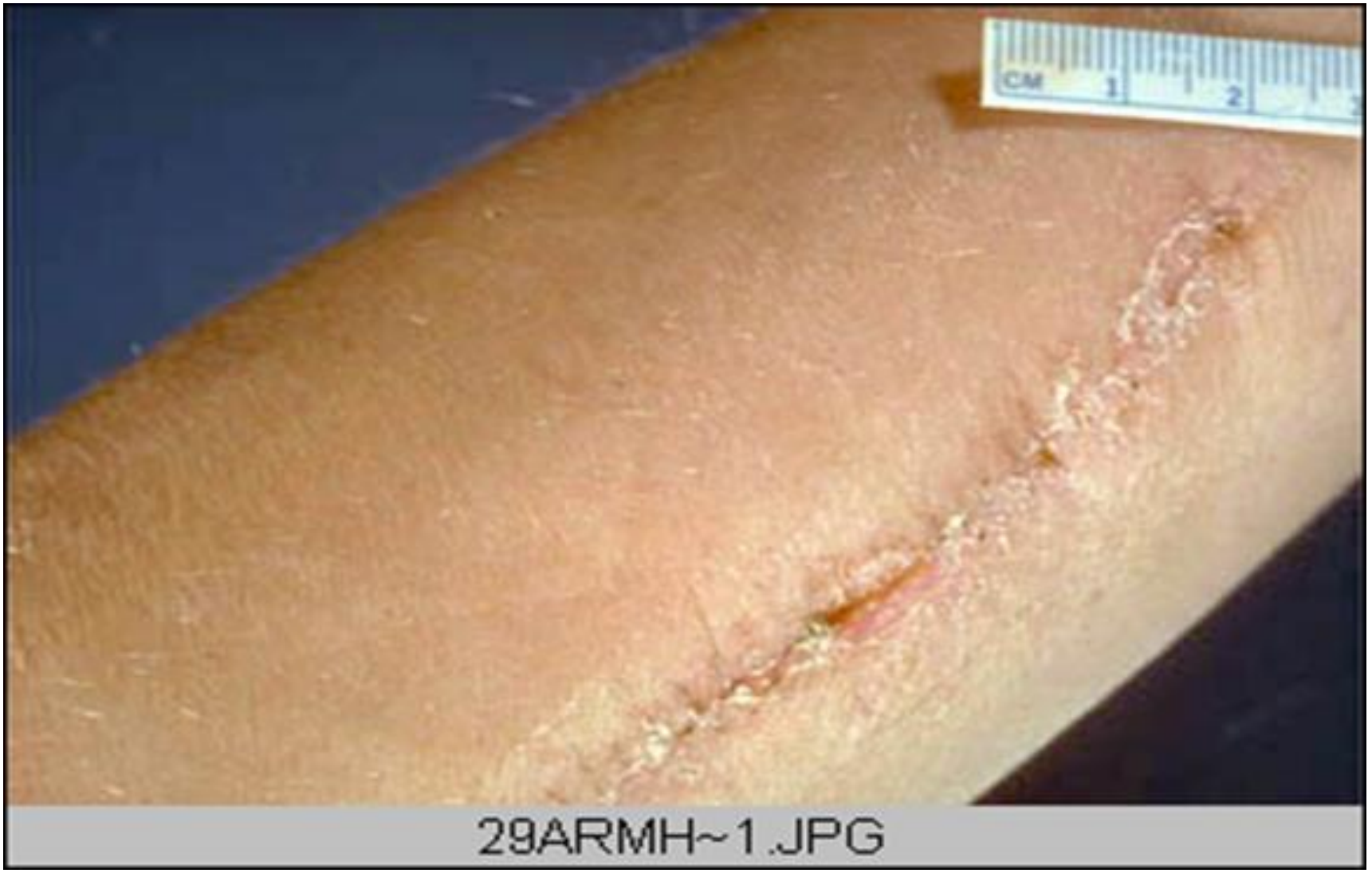
6-During the second week, there is continued collagen accumulation and fibroblast proliferation. The leukocyte substantially infiltrate, edema, and vascularity are diminished .

The process of "**blanching**" begins, accomplished by increasing collagen deposition within the incisional scar and the regression of vascular channels .

7-By the end of the first month, the scar consists of a connective tissue, devoid of inflammatory cells, covered by normal epidermis.

the dermal appendages in the line of the incision are lost.

The tensile strength of the wound increases with time .



Arm, healing surgical incision. This image demonstrates healing by first intention which occur in clean, un infected wounds that have apposed edges.

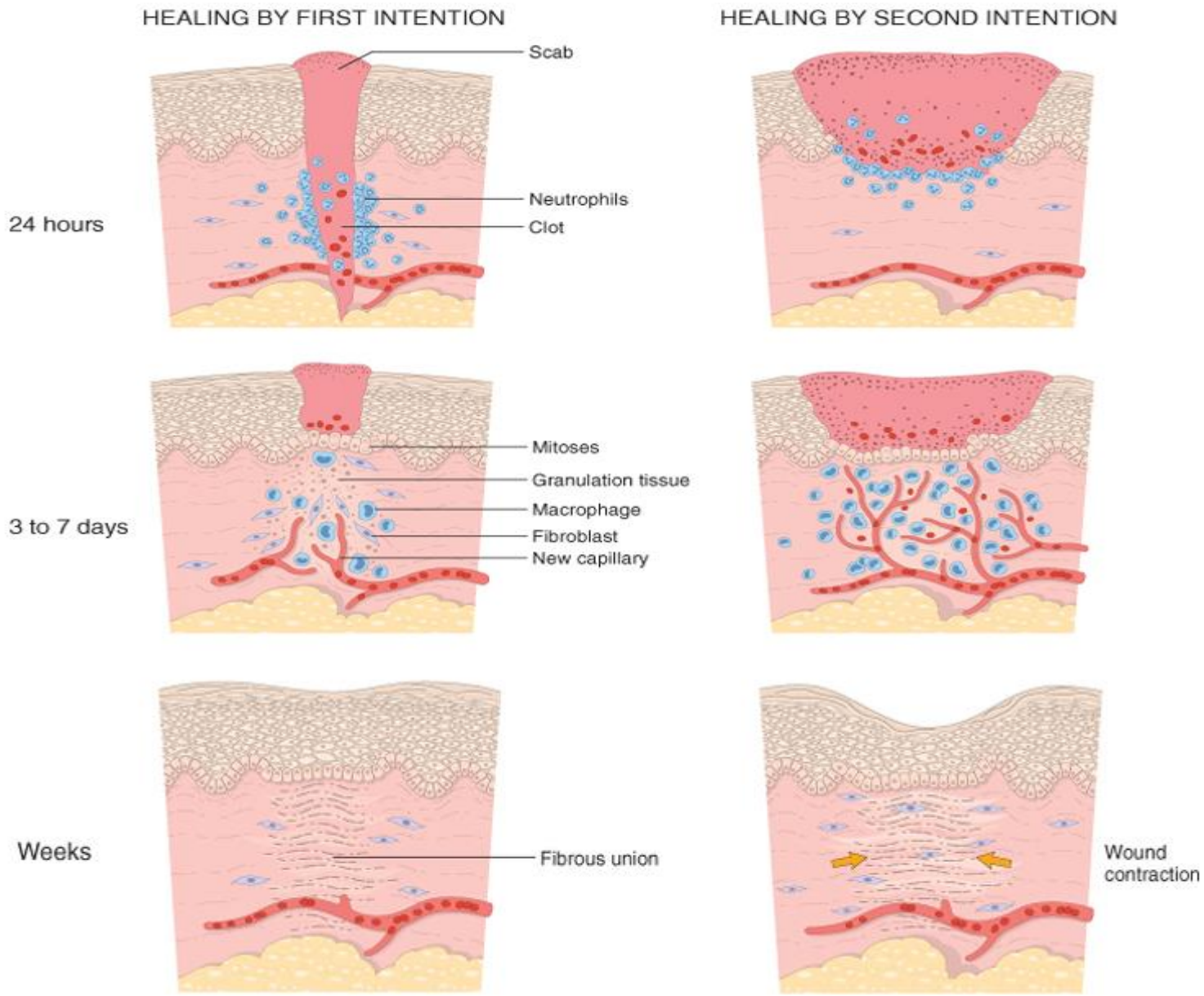


Figure 3-15 Steps in wound healing by first intention (*left*) and second intention (*right*). In the latter, note the large amount of granulation tissue and wound contraction.

2- Healing by Second Intention

When tissue loss is more extensive, such as in large wounds, abscess formation, and ulceration, and infarction in parenchymal organs, the repair process is more complex .

In **second-intention healing**, also known as *healing by secondary union,* the inflammatory reaction is more intense, and there is abundant granulation tissue, with accumulation of ECM and formation of a large scar, followed by wound contraction mediated by the action of **myofibroblasts** .

wound contraction

Secondary healing involves wound contraction. Within 6 weeks, for example, large skin wound may be reduced to 5% to 10% of their original size, largely by contraction. This process is due to the presence of ***myofibroblasts***, which are modified fibroblasts exhibiting many of the ultrastructural and functional features of contractile smooth muscle cells .

Healing by 1st intention	healing by2nd intention
1- small wound and few tissue loss .	1- large wound and tissue loss is more extensive
2- clean cut and un infected wound	2- not clean and infected cut wound
3- granulation tissue is small amount .	3- large amount of granulation tissue
4- cut a margins are closely opposite.	4- cut a margins are not closely opposite
5- small scar formed .	5- large scar formed .
6- there is minimal wound contraction	6- there is maximal wound contraction

Factors that impaired tissue repair

Tissue repair may be impaired by a variety of factors that reduce the quality or adequacy of the reparative process .

Factors that interfere with healing may be extrinsic (e.g.,infection) or intrinsic to the injured tissue, and systemic or local:

1- ***Infection*** is one of the most important cause that delay healing; it prolongs the inflammation phase of the process and potentially increases the local tissue injury .

2- Diabetes is a metabolic disease that compromises tissue repair for many reasons and is an important systemic cause of abnormal wound healing .

3- *Nutrition* has profound effects on repair ; protein malnutrition, and vitamin C deficiency, for example inhibits collagen synthesis and retards healing .

4- ***Glucocorticoids*** (steroids) have well-documented anti-inflammatory effects , and their administration may result in weak scars due to diminished fibrosis.

5- ***Mechanical factors*** such as increased local pressure or torsion may cause wounds to pull apart.

6- Poor perfusion, resulting either from arteriosclerosis and diabetes or obstructed venous drainage also impairs healing .

7- ***foreign bodies*** such as fragments of steel, glass, or even

bone impede healing .

Complications of Wound Healing

Abnormalities in any of the three basic components of healing processes – regeneration , repair, and contraction result in the complications of wound healing.

1. Infection

A wound may provide the portal of entry for many organisms. Infection may delay healing , and if severe stop it completely .

2. Deficient Scar Formation

Inadequate formation of **granulation tissue** or an inability to form a suitable **extracellular matrix** leads to deficient scar formation and its complications. The complications of deficient scar formation are:

a. Wound dehiscence & incitional hernias

b. Ulceration

3. Excessive Scar Formation

1- hypertrophic scar is t he accumulation of excessive amounts of collagen may result in a raised scar . Hypertrophic scars occur after thermal or traumatic injury that involves the deep layers of the dermis . Hypertrophic scars tend to regress after several months .
If the scar tissue grows beyond the boundaries of the original wound and does not regress, it is called a **keloid**

2- ***keloids*** An excessive formation of collagenous tissue results in the appearance of a raised area of scar tissue . It is an exuberant scar that tends to progress and recur after excision .

The cause of this is unknown. Genetic predisposition, repeated trauma , and irritation caused by foreign body , and burns, may play a part. It is common in areas of the neck & in the ear lobes .

3- ***exuberant granulation*** the formation of excessive amounts of granulation tissue that protrudes above the level of the surrounding skin and blocks re-epithelialization and restoration of epithelial continuity . This excessive granulation must be removed by cautery or surgical excision to permit restoration of epithelial continuity..

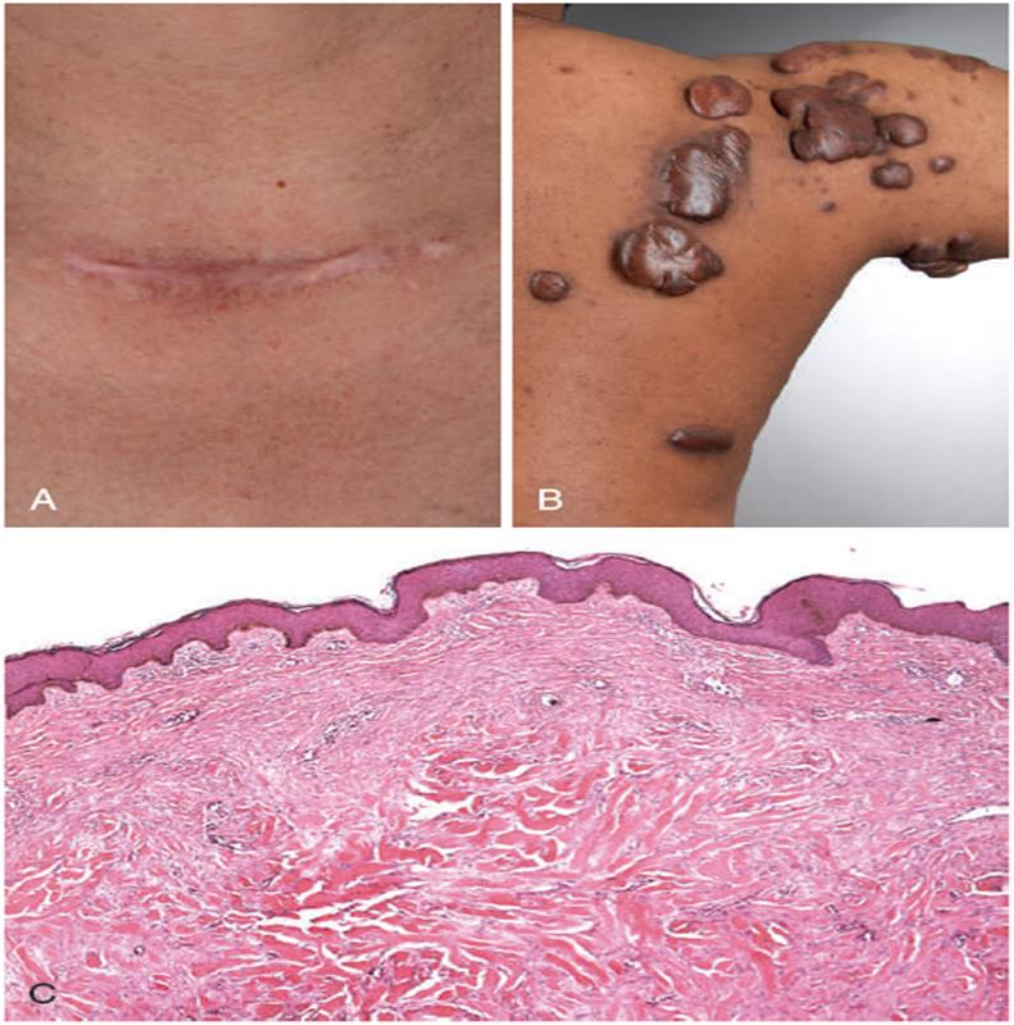


Fig. 3.28 Clinical examples of excessive scarring and collagen deposition. (A) Hypertrophic scar. (B) Keloid. (C) Microscopic appearance of a keloid. Note the thick connective tissue deposition in the dermis. *(A–B from Eming SA, Margin P, Tomic-Canic M: Wound repair and regeneration: mechanisms, signaling,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

4. Excessive contraction

Wound contraction 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 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 .

5. Miscellaneous (or epidermoid cyst)

Epithelial cells which flow into the healing wound may later sometimes persist, and proliferate to form an epidermoid cyst .

HEALING OF BONE FRACTURE

- Bone fracture is separation discontinuity of the bone caused by physical trauma,.

- The separation of fractured ends may be **complete or incomplete**. The latter is common in young children and called **greenstick fracture**.

- The fracture may be a **closed** with an intact overlying skin or **open** when the overlying skin is also injured so that the fractured bone is exposed through a gaping wound.

- A **comminuted fracture** is the fracture in which the bone is divided into multiple fragments .

Fracture healing

- Due to tearing of blood vessels in the medullary cavity, cortex and periosteum , **a hematoma** forms at the site of fracture .

-The haemopoietic marrow around the fracture site undergoes **ischemic necrosis**. Bone death is recognized histologically by loss of osteocytes from lacunae .

- hematoma is induce a local inflammatory response, with hyperemia, exudation of protein rich fluid, & migration of neutrophils & macrophages. These cells phagocytose the hematoma & necrotic debris. This is followed by in-growth of capillaries & fibroblasts, producing **fibrovascular granulation tissue.**

- **At the end of the 1st week**, osteoblasts derived from osteoprogenitor cells of the inner layer of the periosteum will migrate into the granulation tissue and deposit larger quantities of osteoid producing a **woven bone pattern**.

- **External callus** is formed by the periosteum and tends to immobilize the bone fracture site. The two enlarging callus advance towards each other until finally unite to bridge the fracture gap from outside .

- **The internal callus** derived from endosteal osteoprogenitor cells bridges the fracture from within the medullary cavity, and contains cartilage due to better vascularization.

The cartilaginous component of callus is converted to bone by **endochondral ossification.**

Callus is usually formed by the 3rd week after the incident of fracture which is mechanically weak.

The amount of external callus depends on the site of fracture & the degree of immobilization. It tends to be abundant in poorly immobilized fracture e.g. clavicle & ribs.

Remodeling of callus

Remodeling is done by the osteoblasts & osteoclastes. This process may take about a year, although the time varies from site to site. It is also more rapid and more complete in children .

Factors Affecting Fracture Healing

These are basically similar to those of affecting healing in general.

1- mobility of fracture ends and mal-alignment may interfering with fracture healing .

2- Vitamin D deficiency leads to abundant callus, which fails to calcify & remains soft .