Cutaneous Wound Healing

• Phases:

1-**Inflammation**

2-Formation of **granulation tissue**

3-ECM **deposition & remodeling**

• Depending on the nature of the wound, the healing of cutaneous wounds can be **of 2 types:**

1-**Healing By First Intention (Primary Union).**

2-**Healing By Second Intention (Secondary Union).**

• Sequence Of Processes:

1. Induction of an **acute inflammatory response** by the initial injury.
2. **Parenchymal** cell **regenertation**
3. **Migration** & **Proliferation** of both **parenchymal & connective tissue cells.**
4. **Synthesis of ECM** proteins
5. **Remodeling of parenchymal elements** to restore tissue functions.
6. **Remodeling of C.T** to achieve wound strength.

1- Healing By First Intention

• Healing of **clean, Uninfected surgical incision** approximated by **surgical sutures** = **primary union.**

• Cell death & loss is **minimal**.

• **Epithelial regeneration** predominated **over** **fibrosis**.

• **Dehydration of blood clot** at the surface of incisional gap → scab → **protection of healing site.**

Steps Of Healing

First 24 Hours:

- **Neutrophils** at the margin of the incision migrate **toward the fibrin clot.**
- ⇧⇧ **mitotic activity** in **epidermal basal cells** at the **edge** of the incision.

24 -48 Hours

- **Epithelial cell proliferation & migration** from **both edges** along the dermis.
- **Deposition of BM.**
- **Formation of thin** but **continuous epithelial layer beneath** the **surface scab**.

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By Day 3

- Neutrophils **are replaced by macrophages**.
- **Granulation tissue formation.**
- **New vessels show increase permeability** due to incompletely formed interendothelial junctions & VEGF-induced increased vessel permeability.
- **Deposition of collagen** at the incision **margins** but **without bridging** the incision.
- **Thickening of epidermal covering** due to **continuous epithelial cell proliferation**.

By Day 5

- **Peaks of neovascularization**.
- Granulation tissue **fills the incisional gap.**
- **Abundance of collagen fibrils**
- Collagen fibrils **begin to bridge** the gap.
- Epidermis **recovers its normal thickness** with **surface keratinization**.

During the second week

- Continuous **collagen accumulation** & **fibroblast proliferation.**
- ⇩⇩ **Inflammatory infiltrate**. & **Edema**. & **Vascularity.**
- ⇧⇧ collagen deposition within the incision & **regression of vascular channels**.

By the end of the First month:

- The scar composed of cellular connective largely **devoid of inflammatory cells.**
- **Normal epidermis** covering.
- The **dermal appendages** in the line of incision are **permanently lost.**
- The tensile strength of the wound **increases with time.**

Duration	Features
Immediately after injury	Fibrin & platelets to form clot
Day 1	Neutrophils & blood clots
Day 3	• Neutrophils replaced by macrophages •Early granulation tissue • No bridging of incision gap
Day 5	• Maximum granulation tissue deposition • Collagen bridges the incision gap • Recovery of epidermal thickness • Neovascularization is maximum
Day 14	• Maximum collagen deposition
Day 28	• Scarring completed

2- Healing by Second Intention

• Healing by **secondary union**.

• **Extensive** tissue loss.

• E.g :

1- large wounds 2- abscess formation 3- ulceration 4- infarction of parenchymal organs

- **Regeneration of parenchymal cells** alone **cannot** restore the **original architecture.**

- Secondary Healing differs from Primary Healing in different aspects:

1. **A larger clot or scab** rich in **fibrin** & **fibronectin** forms at the surface of the wound.
2. **Inflammation is more intense** because the **volume of necrotic tissue is large**.
3. **Larger amount of granulation tissue**
4. Leading to formation of **greater mass of scar tissue**.
5. **Wound contraction**

Large skin defect maybe **reduced by 5-10%** of their original size due to wound **contraction within 6 weeks** largely due to **the presence of Myofibroblasts.**

Wound Strength

• **Carefully sutured wounds** have **70%** of the strength of **unwounded skin** mainly due to **the presence of surgical sutures**.

• When **sutures removed (at one Week),** the wound strength is **around 10%** of **that of unwounded skin.**

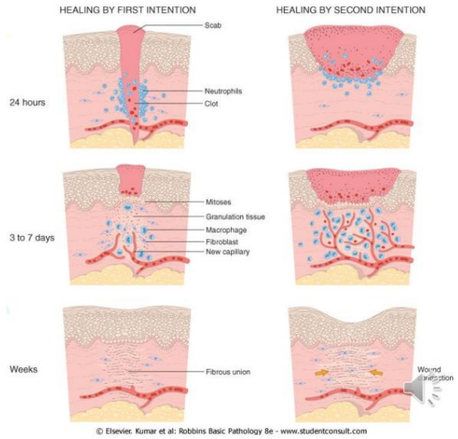
• The wound strength ⇧⇧ **rapidly over the following 4 weeks**.

• Wound strength reaches **around 70–80%** of normal **by 3 months** and **does not improve** beyond that.

• The **increasing tensile strength** results from :

- **collagen synthesis during the first 2 months**.
- **structural modifications of collagen** (cross linking & increase fiber size).

Primary Union (Healing by 1st intention)	Secondary Union (Healing by 2ry intention)
▪ E.g., surgical wound	▪ E.g. traumatic wound
▪ Narrow incision space resulting in a limited inflammatory reaction	▪ Large tissue defect resulting in a more intense inflammatory reaction
▪ Granulation tissue invade incision space	▪ Large amount of granulation tissue
▪ Limited amount of wound contraction	▪ More amount of wound contraction
▪ Healing in short time	▪ Healing take long time



Factors affecting Wound Healing

✓ **First: Extrinsic Factors causing delay in healing:**

1- **Infection**

2- **Nutrition** (protein deficiency, vit. C)

3- **Drugs (steroids)** → poor wound strength due to decreased fibrosis.

However in **corneal infections**, glucocorticoids are sometimes prescribed (along with antibiotics) to **reduce the likelihood of opacity that may result from collagen deposition .**

4- **Mechanical factors** → wound dehiscence.

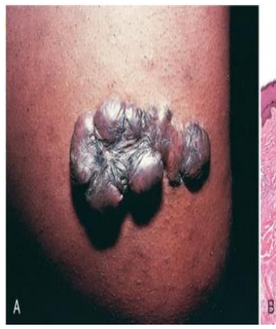
5- **Poor Perfusion** due to DM, atherosclerosis, varicies.

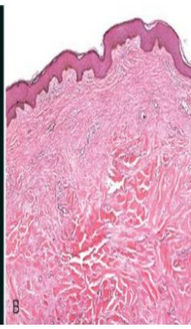
6- **Foreign bodies**.

✓ **Second: Intrinsic Factors**

1. **Type** of injured tissue
2. **Location** of the injury (body cavities).
3. **Chronic inflammatory disease**. LIKE autoimmune Ds.

- Aberrations of cell growth & ECM production.
- e.g 1. **keloid** 2. exuberant granulation(**Proud Flesh**).





Factors affecing the out come of healing:

1-The **type** and **volume** of tissue injured is critical.

- Complete **restoration of normal** can occur **only** in tissues composed of **stable and labile cells.**
- Injury to tissues composed of **permanent cells** must inevitably **result in scarring.**

2-**The location of the injury** and **the character of the tissue** in which the injury occurs are also important.

• **E.g:** inflammation arising in tissue spaces (**e.g., pleural, peritoneal, synovial cavities**) develops **extensive exudates** → **resolution ORGANIZATION**.

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