

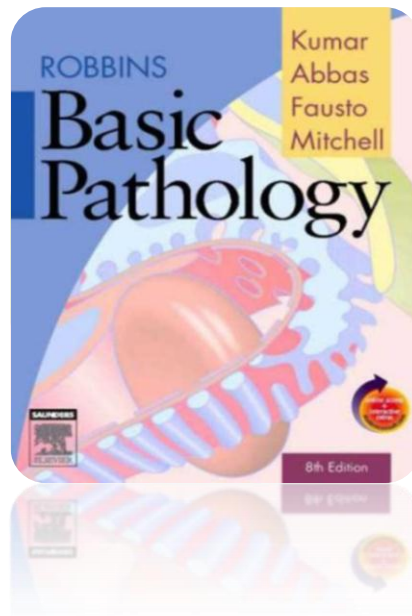


# INFLAMMATION 5

## Lecture 5

### Repair and healing

Notes on Dr. Ammar C. Al-Rikabi's handout,  
Dr. Maha Arafah



First year Medicine-Foundation Block  
Pathology Team  
September 2012

**Please note: This paper does not replace the main sources, it's only a facilitator.**

#### **Acknowledgement**

Dear colleague, this paper was a result of hours and days of hard work from both female & male pathology teams...  
All what they want from you is "Dua'a"



## Objectives

Upon completion of this lecture, the student should:

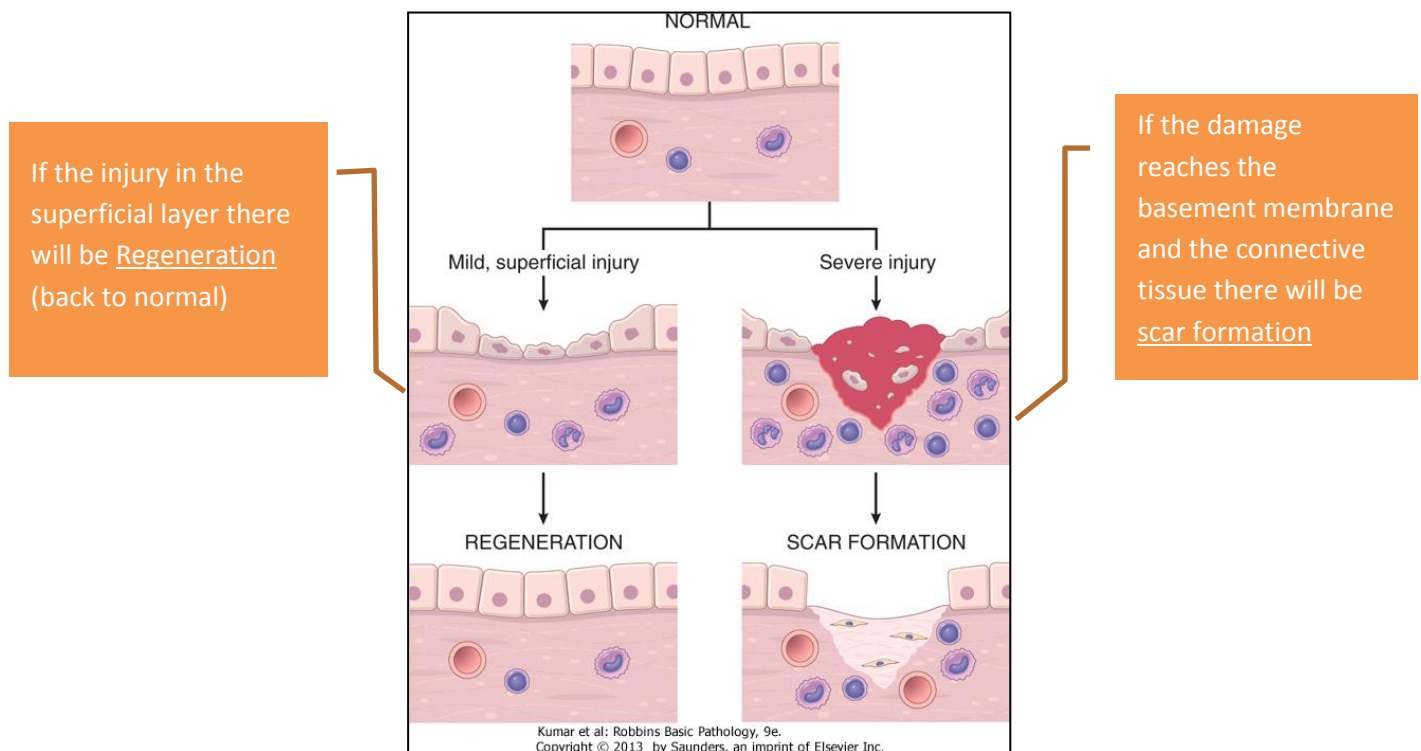
- Know that after inflammation there will be repair.
- Describe the differences between the various cell types (ie, labile, stable, and permanent cells) in terms of their regeneration potential. List examples of each cell type.
- Know the factors that are most important in determining whether regeneration will restore normal tissue architecture.
- List the three main phases of cutaneous wound healing.
- Compare and contrast the difference between healing by primary intention and healing by secondary intention.
- List factors which are associated with delayed wound healing.
- List complication of wound healing.

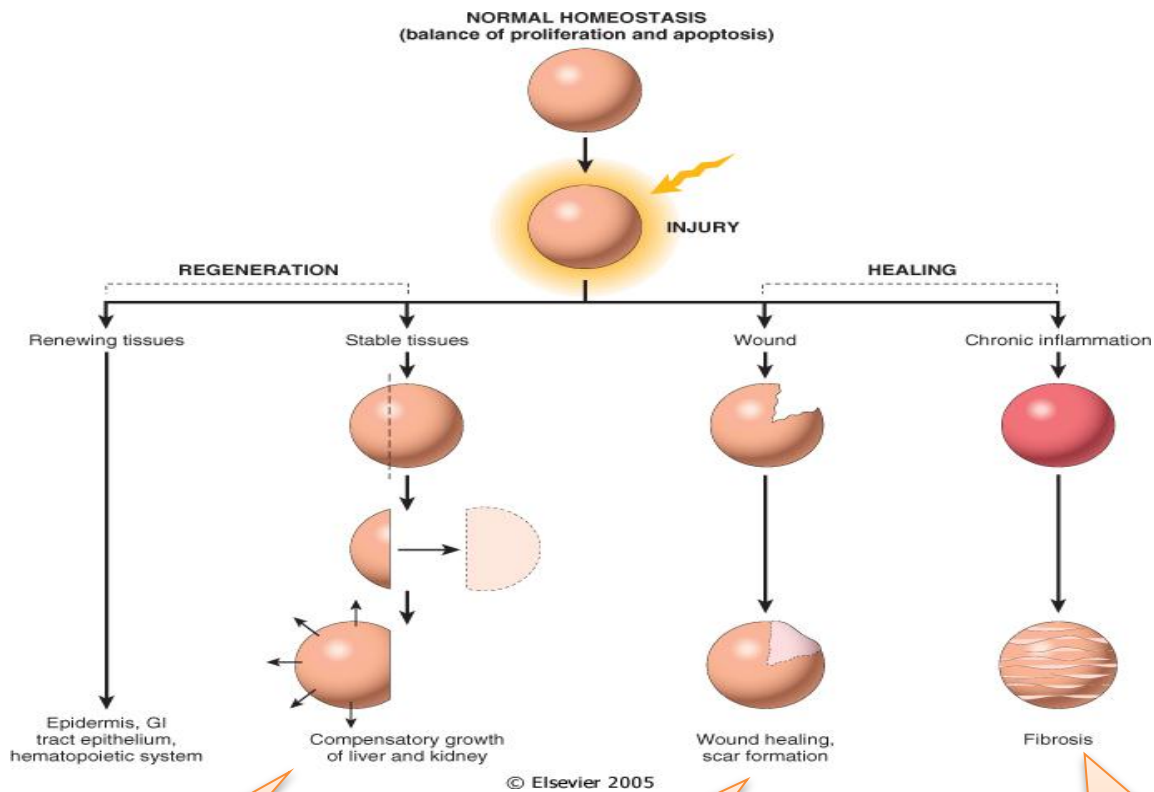


## Goal of the repair process

- to restore the tissue to its original state after inflammatory reaction
- Some tissues can be completely reconstituted after injury, such as the repair of bone after a fracture (كسر) or the regeneration of the surface epithelium in a cutaneous wound (جرح جلدي).
- For tissues that are incapable of regeneration, repair is accomplished by **connective tissue deposition**, producing a **scar**. (scar is localized area of fibrosis)
- If damage persists (استمر), inflammation becomes chronic, and tissue damage and repair may occur concurrently (بنفس الوقت). **Connective tissue deposition** in these conditions is usually referred to as **fibrosis**.

The term fibrosis applies to any abnormal deposition of connective tissue, regardless of cause.





When we remove part of liver or kidney the other part will regenerate totally.

If there was focal abscess formation with destruction of stroma, it will heal by focal fibrosis (scar).

If there is continuous chronic inflammation then the entire organ will go fibrosis and the scar well involve the entire organ (e.g. liver cirrhosis التليف الكبدي).

## Repair by tissue regeneration and healing depend on cell type and power of cell to divided

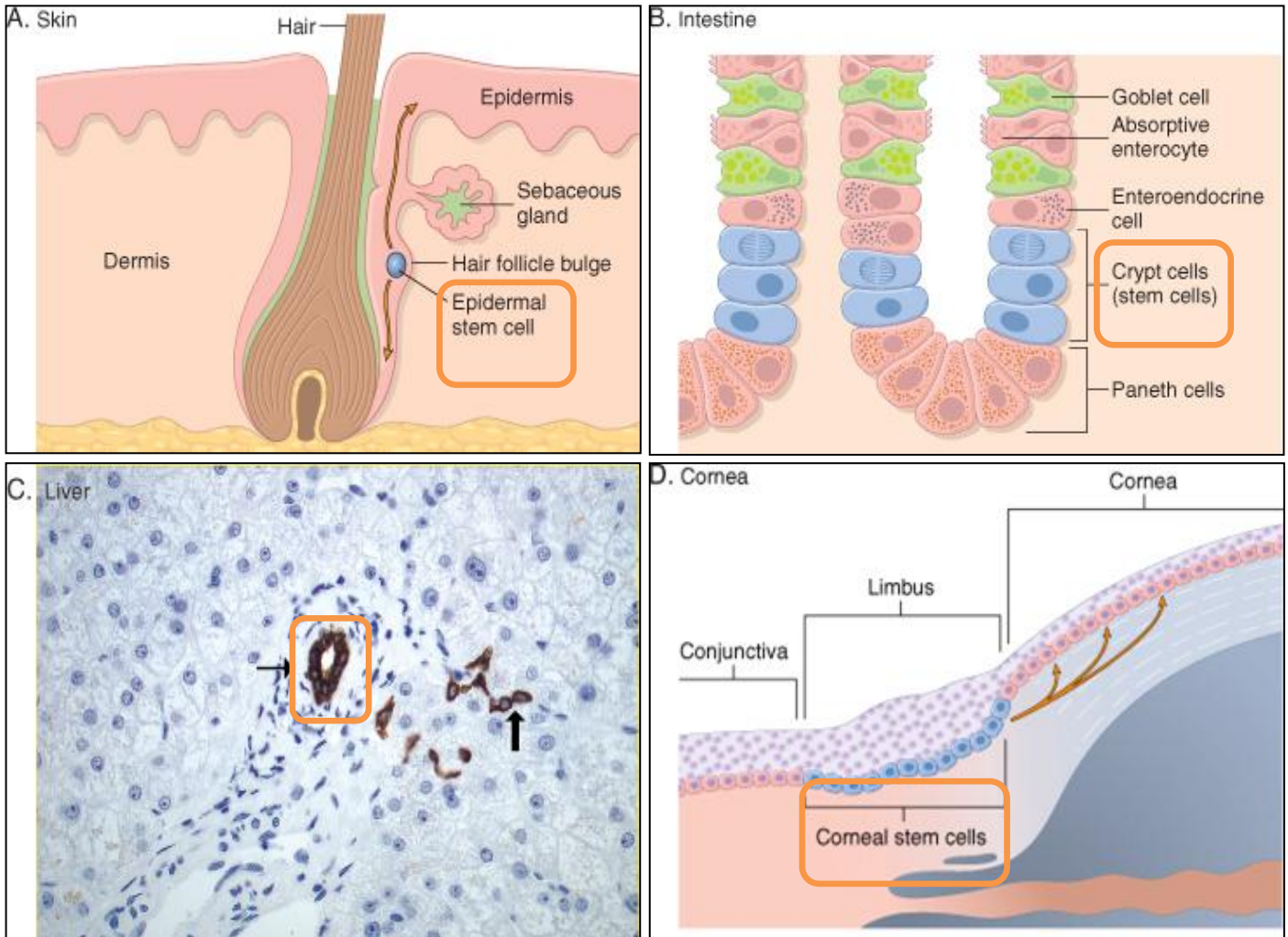
**Labile cells:** continue to proliferate throughout life : squamous, columnar, transitional epithelia; hematopoietic(RBC,WBC..) and lymphoid tissues

**Stable cells:** retain the capacity of proliferation but they don't replicate normally (they divided only if need) : parenchymal cell of all glandular organs & mesenchymal cells.

**Permanent cells:** cannot reproduce themselves after birth: neurons, skeletal muscle, cardiac muscle cells (if there ischemia to the heart then inflammation cause a scar this part of the heart with the scar will lose it's function)



e.g. of labile cells



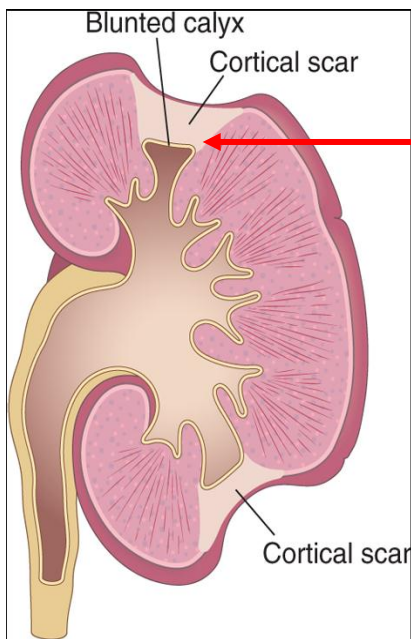
# Healing

to a wound  
(commonly in the skin)

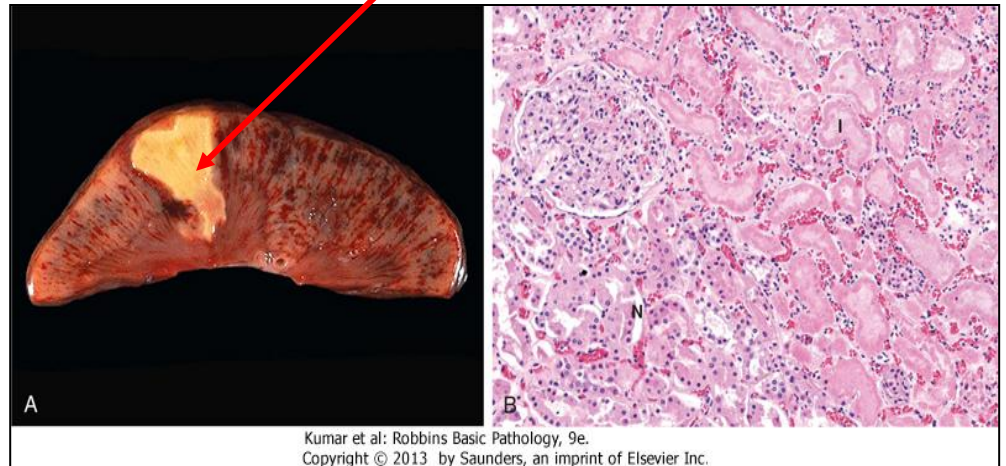
to inflammatory processes in internal organs

to cell necrosis in organs incapable (Can't) of regeneration





Coagulative necrosis if there damage of the basement membrane it will heal by localized fibrosis and scar formation. This part will lose its function.



## Mechanism of repair

- Repair begins early in inflammation.
- At site of inflammation, **fibroblasts** and **vascular endothelial cells** begin proliferating to form a specialized type of tissue called: **Granulation tissue**
- The process is called **Organization**

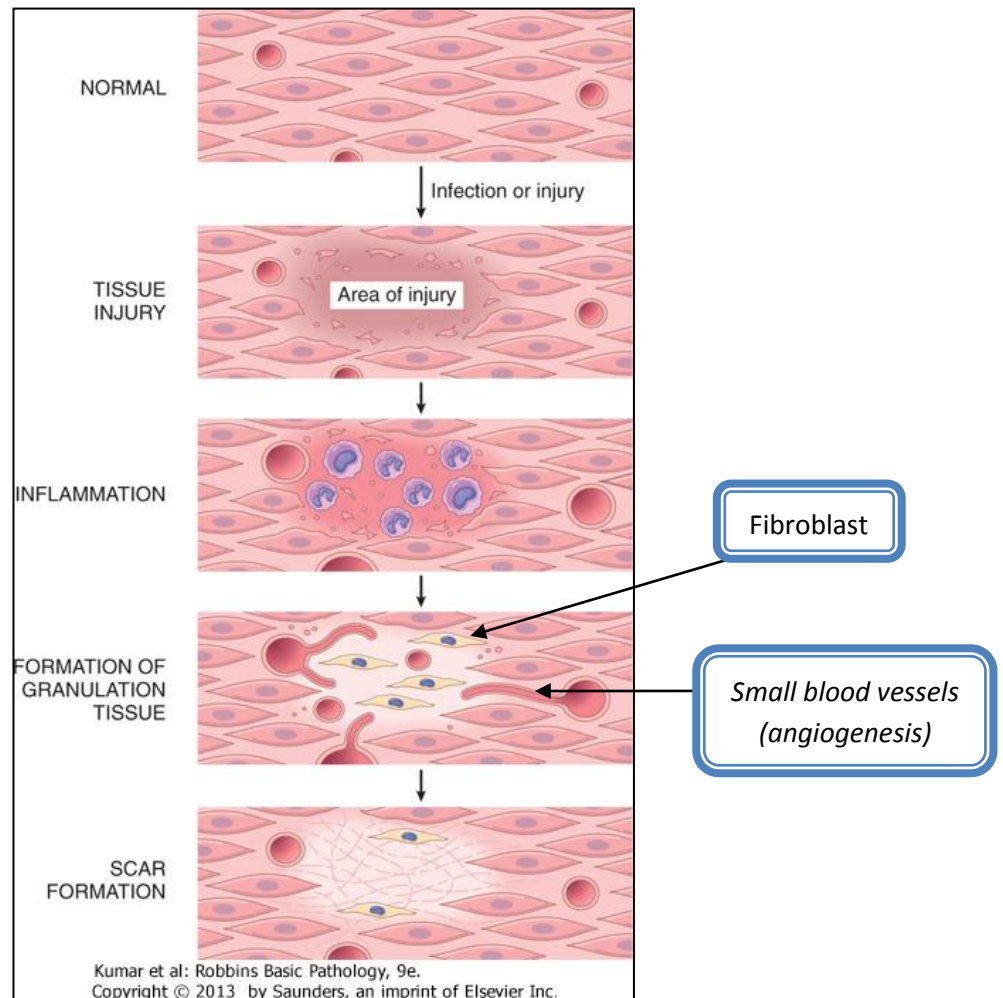
The term derives from its pink, soft, granular appearance on the surface of wounds and it is **hallmark of healing** (سمة مميزة للشفاء)

## granulation tissue

It consists of: fibroblasts surrounded by abundant extracellular matrix, newly formed blood vessels (**angiogenesis**) and scattered macrophages and some other inflammatory cells.

It is characterised by: *the formation of new small blood vessels (angiogenesis), the proliferation of fibroblasts and scattered macrophages and some other inflammatory cells.*

These new vessels are leaky (مرشح), allowing the passage of proteins and red cells into the extravascular space. Thus, *new granulation tissue is often edematous*



## Repair by connective tissue (granulation tissue)

- The term granulation tissue was used by ancient surgeons for the red, granular tissue filling the non-healing wounds.
- With the advent of microscopy, it was discovered that granulation tissue occurs in all wounds during healing, and it may occur in chronic inflammation.



# What is the role of macrophages in wound healing?

Cleanup of debris, fibrin, and other foreign material at the site of repair

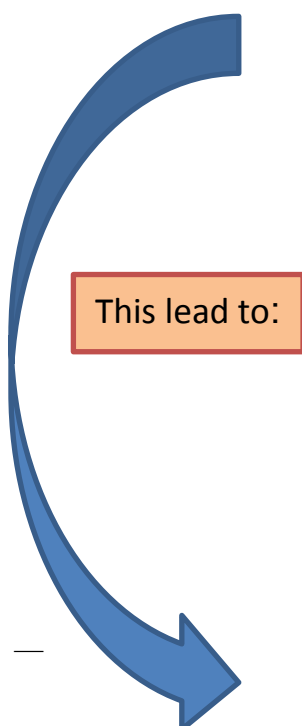
Macrophages recruit other cells: fibroblasts and angioblasts.

Stimulation of matrix production, **interleukins** that stimulate fibroblasts and angioblasts to produce the **extracellular matrix**. (collagene fiber, fibronectin...etc)

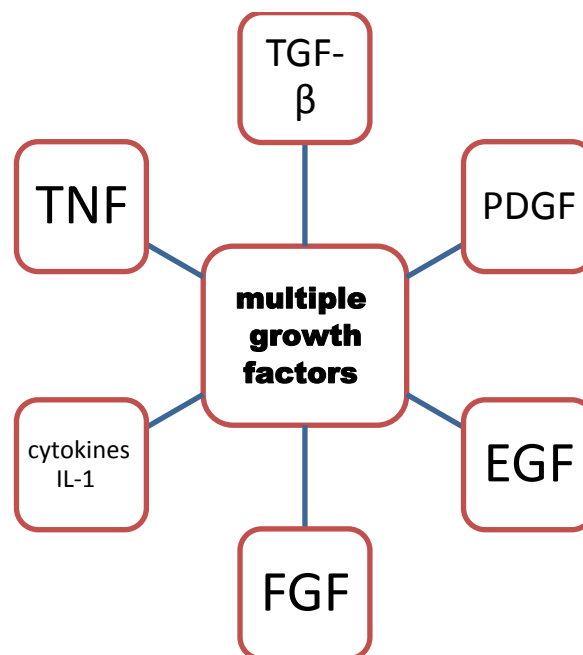
**Remodeling** of the scar. They secrete **collagenases** (enzyme that removes or digests extra collagen fiber in the scar)

## Fibroblast Migration and Proliferation

— *Migration* هجرة-نزوح-ارتحال of fibroblasts to the site of injury and their subsequent *proliferation* are triggered by :



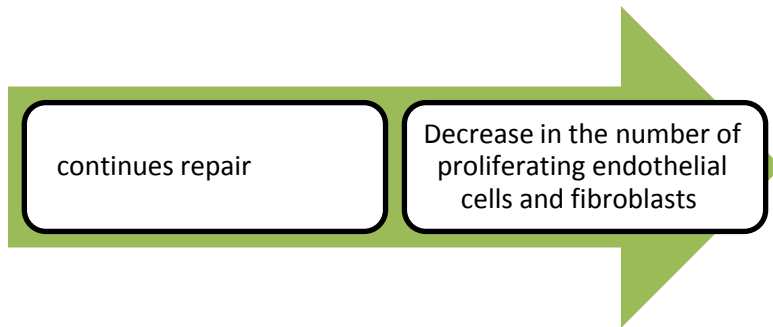
This lead to:







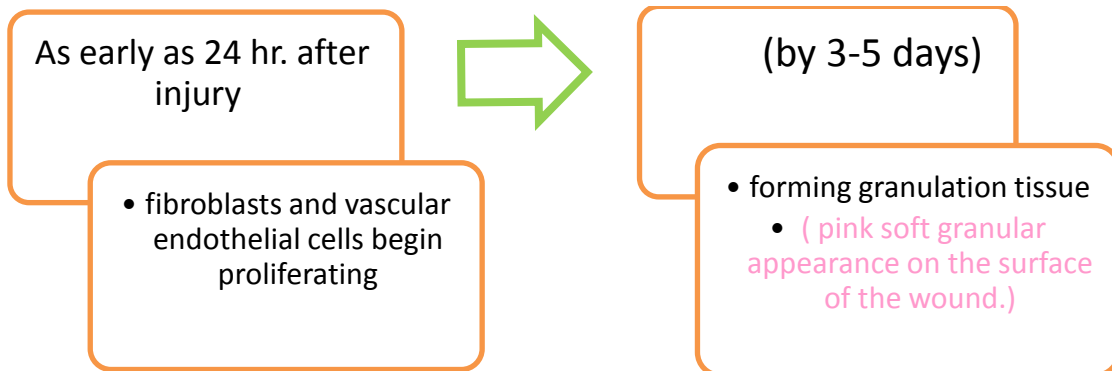
1. increased synthesis of **collagen and fibronectin**
2. decreased degradation of **extracellular matrix (ECM)** by **metalloproteinases**



### ECM Deposition and Scar Formation

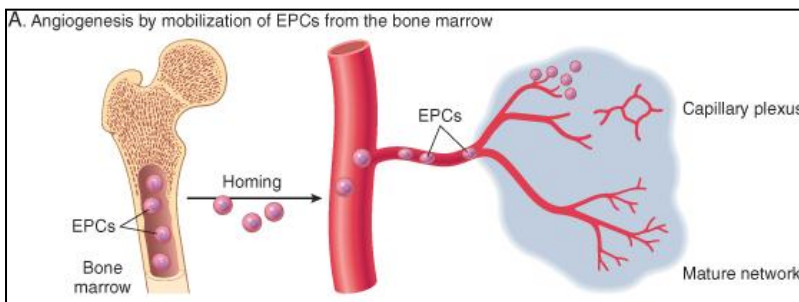
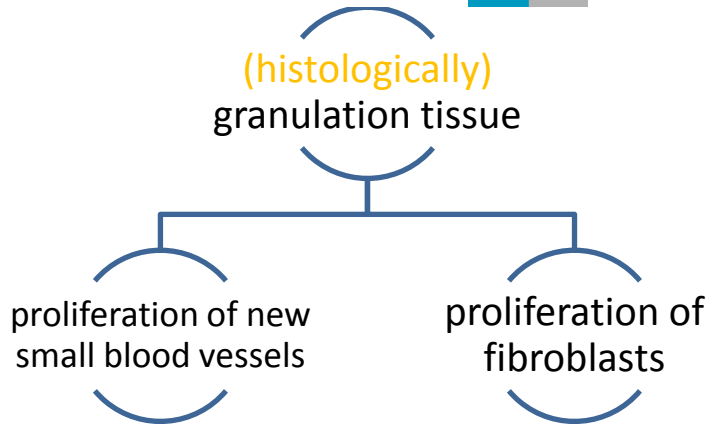
- Net collagen accumulation, however, **depends on**
  - ✓ Increased collagen synthesis
  - ✓ Decreased degradation.

### Repair by connective tissue granulation tissue

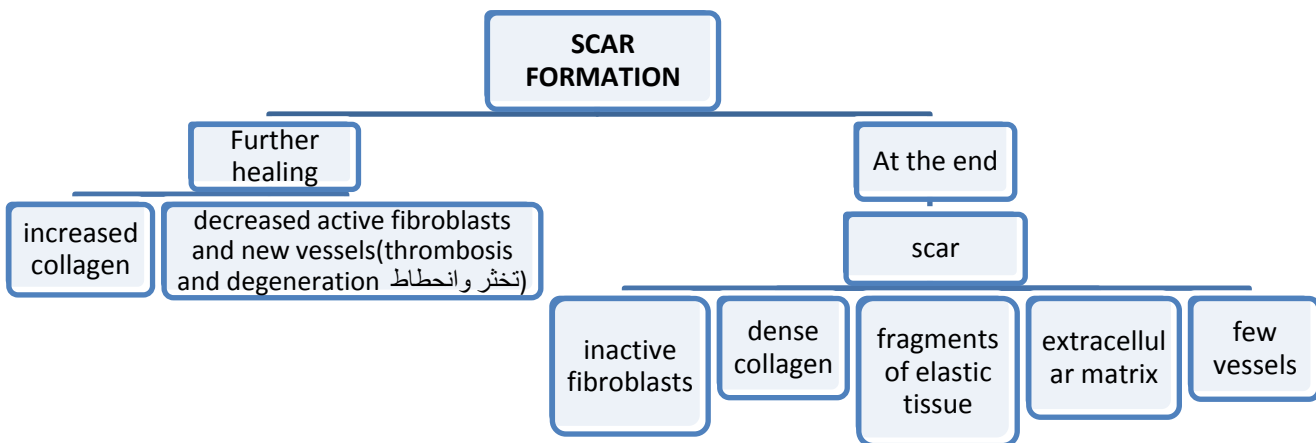


New granulation tissue is often **edematous**

Swollen with an excessive accumulation of fluid



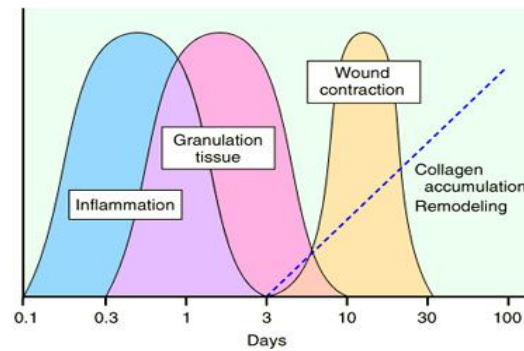
Angiogenesis from Endothelial Precursor Cells



▣ 3 processes that participate in the formation of a scar:



- (1) emigration and proliferation of in the site of injury
- (2) deposition of ECM
- (3) tissue remodeling.



## Cutaneous Wound healing

### التئام الجروح الجلدية

1. Primary union (healing by 1st intention)	2. Secondary union (healing by 2nd intention)
<ul style="list-style-type: none"> <li>clean surgical incision</li> <li>no significant bacterial contamination</li> <li>minimal loss of tissue</li> <li>clot, scab formation</li> </ul>	
	<ul style="list-style-type: none"> <li>more extensive loss of cells and tissue:                             <ul style="list-style-type: none"> <li>-infarction</li> <li>-inflammatory ulceration</li> <li>-abscess formation</li> </ul> </li> <li>surface wound with large defect</li> <li>large tissue defect that must be filled</li> </ul>

collagen **type III** is slowly replaced by collagen **type I** and the wound acquires tensile strength.

By the end of **third month**, the tissue has approximately **80%** of its original strength.



Difference between primary intention and secondary intention	the most common cause of delayed wound healing
<ul style="list-style-type: none"> <li>Require more time to close because the edges الحواف are far apart</li> <li>Show a more prominent inflammatory reaction in and around the wound تظهر ردود الفعل الالتهابية أكثر وضوحاً في و حول الجرح .</li> <li>Contain more copious granulation tissue inside the tissue defect</li> <li>wound contraction انكماش الجرح (5 to 10%) ? myofibroblasts</li> </ul>	<ul style="list-style-type: none"> <li>Infection</li> <li>Foreign bodies in the wound</li> <li>Mechanical factors</li> <li>Nutritional deficiencies</li> <li>Excess corticosteroids (steroid hormone that the adrenal cortex produces)</li> </ul>

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
- (3) formation of contractures.

يحدث عادة بالحروق →

ممكن مضاعفات في التئام الجروح تنشأ من خلل في أي من المكونات الأساسية لعملية الإصلاح. ويمكن تصنيف هذه الانحرافات إلى ثلاث فئات عامة:  
 (1) تشكل ندبة ناقصة  
 (2) تشكل المفرط لمكونات الإصلاح  
 (3) تشكل الاتكماشات.

**Keloids** are hyperplastic scars composed irregularly deposited collagen. They may bulging masses. كتل منتفخة – متورمة



of appear as



e.g : Case ..

if there is someone with dark skin and have scare above the skin , what is called ?

**Keloid**