

PATHOLOGY

Sheet no.

Writers : 2021 Doctors

Corrector: Aram Al Nashash & Alaa Khader

Doctor : Mousa Al-Abbadi



TISSUE REPAIR:

Note: we finished the lectures of inflammation and we will start the tissue repair lectures and they 're much more easier

Quick reminder ... (R1) recognition (R2) recruitment (R3) elimination (R4) regulation

(R5) repair (which is the topic of our lecture today)

Repair is part of the inflammatory response (R5), but comes at the end and sometimes it's given a separate entity. In repair, growth factors = chemical mediators of repair.

- Inflammation may cause injury and repair is critical after eliminating the enemy
- Repair can be achieved by:
 1. Regeneration
 2. Scar & fibrosis
- Both require mediators and cellular proliferation. And interactions with ECM.

When there is an accident, there will be tissue loss, and the body must replace it due to the injury.

So, the top mechanism is regeneration only if the tissue is capable of regeneration. When we get ulcers in the oral mucosa can regenerate and **reepithelization**. Only if the injury was mild and superficial and the amount of tissue loss is little.

But in perianal abscess, all tissues of cavity are damaged (pus, bacteria, exudate); what is the treatment? Is by draining the wound or otherwise the patient won't heal. Once you drain the abscess, the body starts to form new tissues and scar tissues and fibrosis, because tissues of this cavity can't make regeneration or

وَأَنْ لَيْسَ لِلإِنْسَانِ إِلَّا مَا سَعَى وَأَنْ سَعْيُهُ سَوْفَ يُرَى ثُمَّ يُجْزَاهُ الْجَزَاءَ الْأَوْفَى

revascularization. Also, it depends on amount and severe of the tissue injury.

NOTE: Both require mediators (GROWTH FACTORS)

ECM (Extra cellular matrix), there are many collaborations between ECM and cells, which lead to the understanding of the role of the proteins of the ECM (collagens, GAGs)

TISSUE REGENERATION:

- Regeneration requires growth factors and interactions between cells and matrix (ECM).
- **Tissue types:** we have 3 types depending on there ability to regenerate

Labile tissue

**Continuous regeneration :
epithelia of mucosal surfaces**

- its basement cell layer which induces replication and replacement of tissues. In addition to the epithelial surfaces, **the bone marrow** most of the elements of body comes from bone marrow; Lymphocytes, leukocytes, RBCs all from stem cells (progenitor) → which are continuously capable of regeneration.

Stable tissue

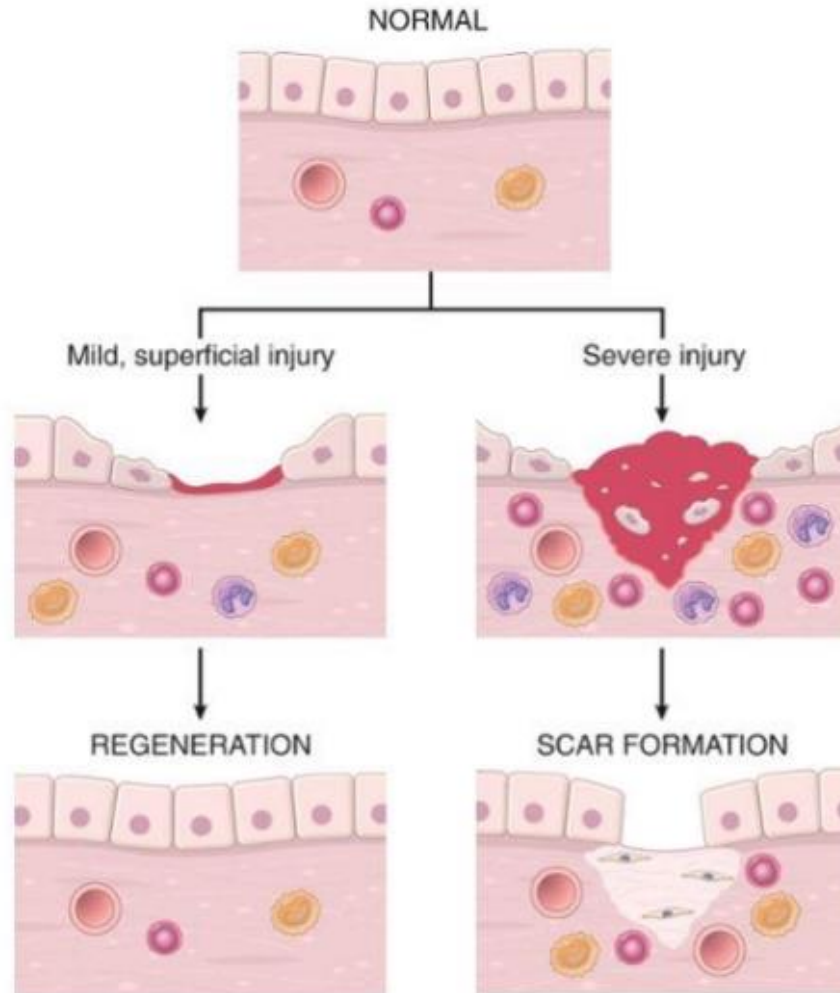
Normally in G₀, but can be stimulated to regenerate when injured (liver, Kidney, pancreas)

- they are in G₀ won't replicate, but when injured, these solid organs **will be stimulated** by different mediators and start their cycle (G₁→S→G₂).

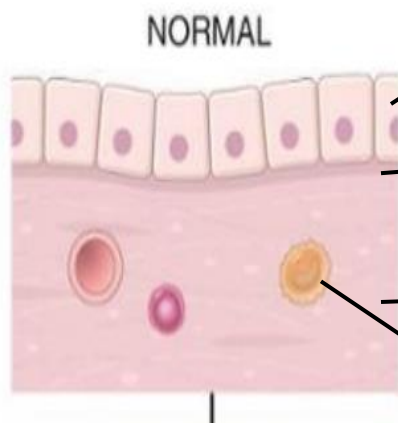
Permanent tissue

Terminally differentiated, non proliferative (neurons and cardiac muscle, skeletal muscle)

their DNA is switched off, there won't be any replication. So, when stroke or MI (myocardial infarction) and we didn't give the proper reperfusion → we can't replace the tissue and scar will form and will interfere with functions of the organ. It is because we can't replace cardiac myocytes or brain cells with new ones due to its low regenerative ability.



LET'S EXPLAIN THEM:



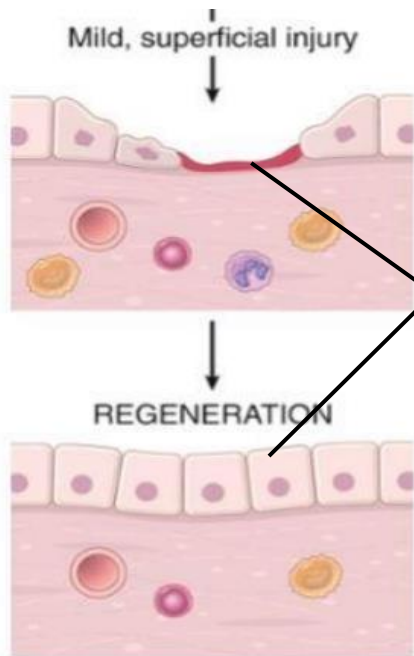
this may skin or any mucosal surface.

this is the basement membrane: collagen IV and Laminin

This is a submucosal matrix tissue.

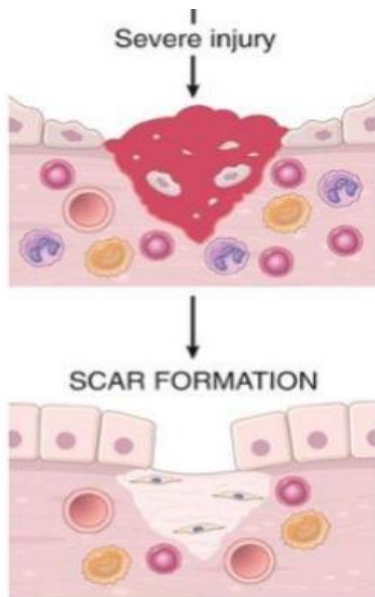
inflammatory cells: PMN and Macrophages (found in blood vessels)

وَأَنْ لَيْسَ لِلإِنْسَانِ إِلَّا مَا سَعَى وَأَنْ سَعْيَهُ سَوْفَ يُرَى ثُمَّ يُجْزَأُ الْجَزَاءَ الْأَوْفَى



repairing by first intention.

- Quick response
- Takes less time and the tissue is reborn (back to normal state)
- Growth factors are stimulated and whole loss of superficial epithelium is replaced by regenerating cells from the sides and filling the gap.



repairing by secondary intention

- There is a lot of tissue lost including the basement membrane, the tissue healing will take longer time.
- The regeneration alone isn't enough to fill the gap.
- This mechanism is called granulation tissue formation or healing by secondary intention.
 - Takes more time and scars are larger.
- Scars may interfere with the function of the organ.

1 st (primary) intention	Healing by Granulation tissue formation (secondary intention)
<ul style="list-style-type: none"> ➤ Regeneration is faster. ➤ Tissue reborn (gets back to normal) ➤ Includes clean surgical wounds. ➤ More reepithelization ➤ less scars formation 	<ul style="list-style-type: none"> ➤ Granyolation tissue forms ➤ Leads to scar tissue: which is cosmetically unpleasant. ➤ if it is big enough may interfere in function.
<p>NOTE: BOTH have granulation tissues, both lead to bleeding and scar formation. (differs in amount)</p>	

We will talk about granulation tissues in upcoming lectures!

LIVER REGENERATION:

- As we said previously live is a solid organ which mean it is **a stable tissue** that can regenerate upon stimulation

- **Liver can regenerate in 2 ways:**

– **1.Hepatocytes proliferation, post partial hepatectomy**

(The major mechanism)

If there was liver parenchymal tissue damage regardless of the injurious agent ; whether it's a trauma or viral infection , the hepatocytes can proliferate and if we come back after six months the lost part of the

liver has been replaced by a new liver tissue (REGENERATION)

وَأَنْ لَيْسَ لِلإِنْسَانِ إِلَّا مَا سَعَى وَأَنْ سَعْيُهُ سَوْفَ يُرَى ثُمَّ يُجْزَاهُ الْجَزَاءَ الأَوْفَى

– 2. Progenitor cells get activated and proliferate and differentiate Both need growth factors & cytokines and cell matrix interactions.

by recruitment of stem cells or Progenitor cells (found mainly in the bone marrow, and it is very complicated), they get recruited and enter the microenvironment of the parenchyma then they have specific proper growth factors and mediators of that specific tissue, so they get activated then proliferate and differentiate.

**** Both need growth factors & cytokines and cell interactions and matrix surrounding this tissue (proper environment)**

And now let's talk about the second mechanism of repair after regeneration:

REPAIR BY SCARRING:

- Large amount of tissue damage
- “Patching”, wound healing and Scarring
- Healing by first and second intention (we have talked about it before –go back to the table above-)

Steps:

– Hemostatic plug (platelets)...minutes

This step is very important to stop the bleeding after you get injured

At first a soft hemostatic plug will be formed (if you try to remove it bleeding will start again) then it is going to be hard (Eschar)

– **NOTE:** this eschar upon the time it will be avascular and acellular then will fall by itself.

– Inflammation (Macs, M1 and M2)...6-48 hours

وَأَنْ لَيْسَ لِلإِنْسَانِ إِلَّا مَا سَعَى وَأَنْ سَعْيُهُ سَوْفَ يُرَى ثُمَّ يُجْزَاهُ الْجَزَاءَ الْأَوْفَى

Switching between M1&M2 depends on (intensity & degree)

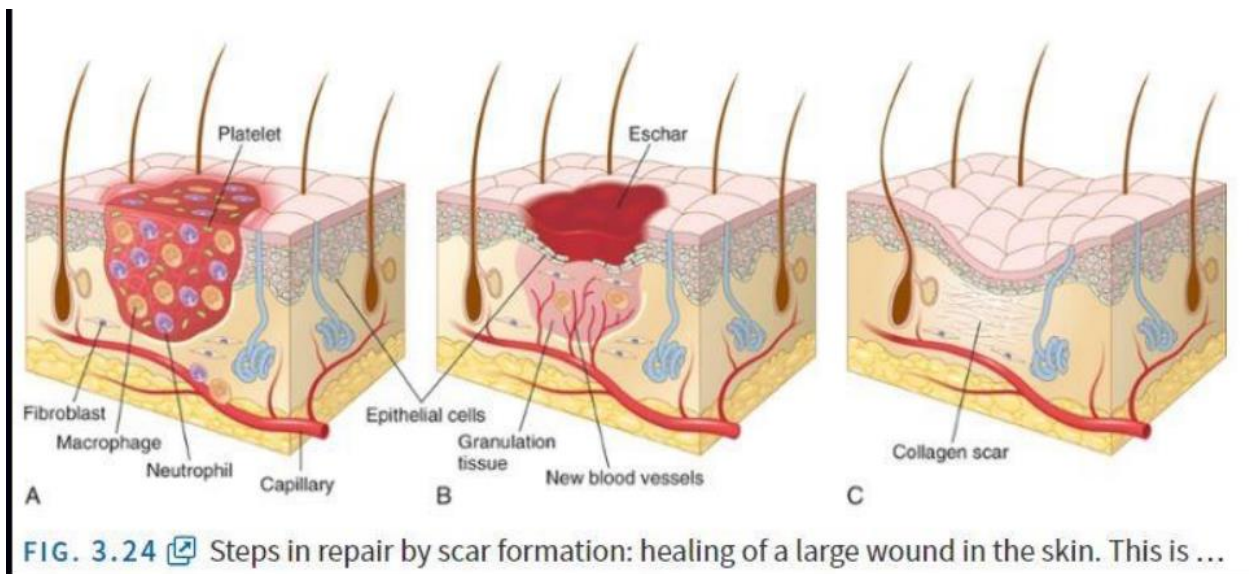
– Cell proliferation (granulation tissue)...10 days

If the wound was clean granulation will be minimal, this step include new blood vessel formation (angiogenesis), granulation tissue formation

– Remodeling.... 2-3 week

The extra tissue and material will be cleaned out and removed before the formation of strong scar tissue composed of strong collagen replacing the damaged parenchyma.

Note: the amount of scar comparable to the amount of tissue produced.



The End

لا تنسوا أخوتنا في غزة من صالح دعاءكم وفقنا الله واياكم

وَأَنْ لَيْسَ لِلإِنْسَانِ إِلَّا مَا سَعَى وَأَنْ سَعْيُهُ سَوْفَ يُرَى ثُمَّ يُجْزَاهُ الْجَزَاءَ الأَوْفَى