



SHEET NO. 13



PATHOLOGY

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we finished the lectures of inflammation and we will start the tissue repair lectures

Tissue repair

Remember: the tissue repair process is part of the inflammatory response but comes at the end and sometimes it's given a separate entity

- The inflammation may cause injury and after tissue injury we need to repair what has been destroyed depending on the **amount** and the **degree** of damage
- We need mediators which are called GROWTH FACTORS.
- It is **critical step** to eliminate the enemy and its consequences

There are two major mechanisms for repair

1. **Regeneration**: the preferred and the main mechanism of repair.

2. **Scar and fibrosis** : replacement of the damaged tissue or parenchyma ;when regeneration is not possible

Both of mechanisms requires **chemical mediators of inflammation** , **cellular growth** , **cellular proliferation** and **critical complex interaction between the intravascular compartment , the cellular process of the inflammatory process , ECM and ECM proteins**

Depending on the tissue type , regeneration can insure

Tissue types	Notes
Labile tissue Epithelial cells of mucosal surfaces , bone marrow	Continuous regeneration ,
Stable tissue Solid organs (Liver , kidney and pancreas)	-More stable , slightly more differentiated - Normally in stable G0 phase (no inflammation, injury or stimulation) - Can be stimulated to regenerate upon stimulation with injury
Permanent tissue Cardiac muscle , skeletal muscles and neurons (once lost you can't replicate them, it will be replaced by scar tissue)	-Terminally differentiated Non proliferative - Cannot regenerate - The most dangerous

Let's take the skin as an example

Repair by first intention

In Small , mild superficial injury

Like first degree of burn , scratch and surgical wound

- The reparative regenerative mediators will be stimulated

- The whole loss of superficial epithelium will be replaced by regenerating epithelial cells from the sites and they will fill into the gap specially if *basement membrane is not injured or no deep injury was associated*

- its *quick* and takes less time

- most of the tissue will go back to pre-injury state (almost 98%)

Repair by secondary intention

In severe injury

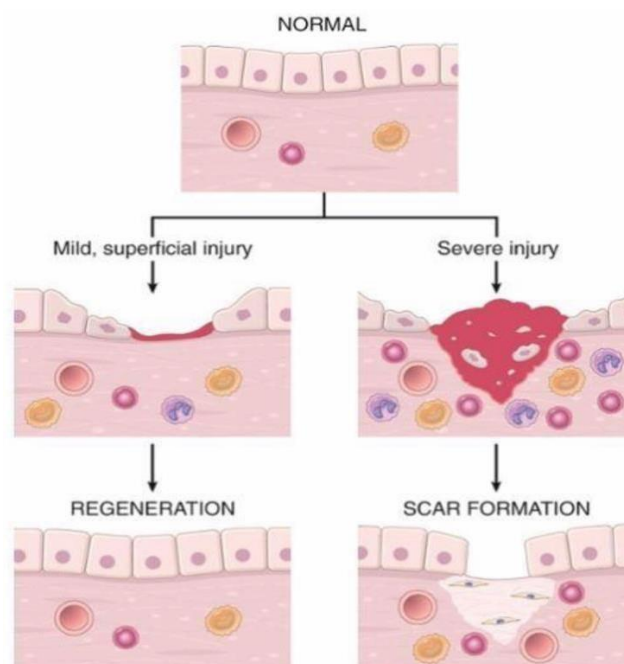
- if somebody has crush accident with crush injury where there is a lot of tissue lost including the basement membrane , superficial epithelium, matrix and sub mucosal tissue

- The healing require **granulation tissue formation** and the amount of scar tissue which has been produced will be a little bit larger

- sometimes disfiguring and embarks on the function of that organ

- it takes *longer* time

- The regeneration alone is not enough to fill in the gap



Liver can regenerate in 2 ways: -

1. Hepatocytes proliferation after injury, post partial hepatectomy

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

2. **The liver can replace itself** by recruitment of stem cells or Progenitor cells (found mainly in the bone marrow), (they get recruited and enter the microenvironment of the parenchyma then they have specific proper growth factors and mediators of that specific tissue), get activated then proliferate and differentiate

*** Both need growth factors & cytokines and cell interactions*

and matrix surrounding this tissue



Summary

Repair by Regeneration

- Different tissues consist of continuously dividing cells (epithelia, hematopoietic tissues), normally quiescent cells that are capable of proliferation (most parenchymal organs), and nondividing cells (neurons, skeletal and cardiac muscle). The regenerative capacity of a tissue depends on the proliferative potential of its constituent cells.
- Cell proliferation is controlled by the cell cycle, and is stimulated by growth factors and interactions of cells with the extracellular matrix.
- Regeneration of the liver is a classic example of repair by regeneration. It is triggered by cytokines and growth factors produced in response to loss of liver mass and inflammation. In different situations, regeneration may occur by proliferation of surviving hepatocytes or repopulation from progenitor cells.

Repair by scarring

Quick recap

- ❖ As we mentioned before , if there is a large amount of tissue lost or damaged during the initial phase of injury ; this require a longer process of repair initially by patching the wound , preventing the further bleeding , the wound healing will be more and the scare tissue which is formed from this reparative process will be much more and more
- ❖ **Healing by first (primary) intention** is **quick** and it is predominantly by **repletion and proliferation** and the **amount of tissue lost is small** and **the amount of scare tissue** which is formed **is minimal** and most of time this **will not embark the bodily function** of that injured tissue
- ❖ **Healing by secondary intention** when there is **a bigger wound** and **more tissue damaged** and the **scare tissue is big** and more (repair by granulation tissue formation then scar formation).

Steps of repair

Hemostatic plug

Mainly composed of **platelets** that aggregate and (some proteins), both of them close the loss of tissue to prevent further bleeding (stabilization of your blood condition).

- Underling matrix fibroblast and blood vessels will be in touch of the injury

-Cytokines and growth factors will be released

- It is formed **after minutes** from falling down or when you injure your leg or hand

Inflammation

Inflammation starts by stimulating the macrophages , M1 and M2 phase

-Takes (6-48) hours

Cell proliferation

Include new blood vessel formation (angiogenesis), granulation tissue formation

-Takes (1-10) days to ensure

Remodeling

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

-Takes (2-3) weeks

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

Eschar : hard dry fibrin clot mostly acellular which covers the lost tissue and prevents further bleeding

