

Tissue repair

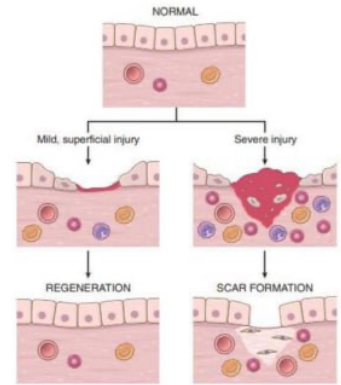
← قدرة الكائن على إصلاح نفسه، ندى تتعجب به

Is Critical for survival ← Toxins

← التهاب من بس استجابة الأضرار بل يتضمن به، عليه يصح إصلاح الأضرار

1. Regeneration by proliferation of residual (uninjured) cells and maturation of tissue stem cells.

2. Deposition of connective tissue to form a scar



تشوف الموضوع كله يعتمد على النسيج يلي حالك ودرجة الضرر



Proliferation of cells that survive the injury and retain the capacity to proliferate leading to restoration of damaged tissues, may seen in:

1. Rapidly dividing epithelia of the skin and intestines.
2. Some parenchymal organs, notably the liver.
3. Tissue stem cells.

B. CONNECTIVE TISSUE DEPOSITION (SCAR FORMATION) → Repair occurs by the laying down of connective (fibrous) tissue, a process that may result in formation of a scar, it occur in:

1. Injured tissues are incapable of complete restitution.
2. If the supporting structures of the tissue are severely damaged

لا نرى في FIBROUS scar من نسيج طبيعي ولكن

PROVIDES Enough structural Stability → The tissue will still functioning

بس لو زاد، لوضع عن حده و أكثرنا Collagen فيه
داخليه بـ Chronic inflammation هو وقت احسن

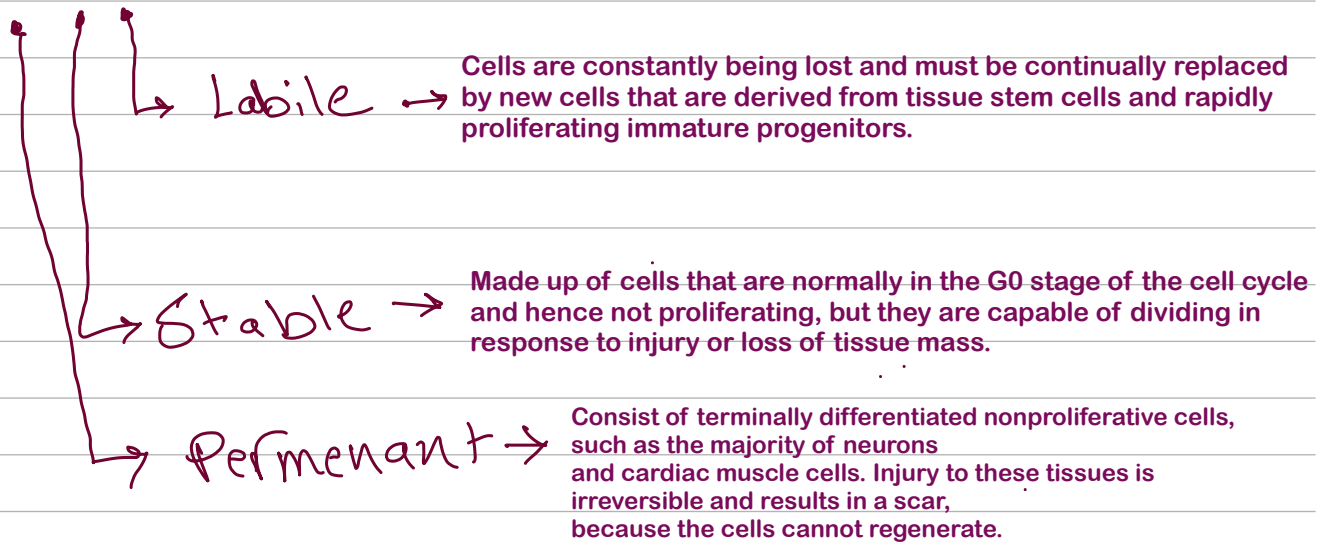
FIBROSIS و نسيج لوطيفة

Fibrosis → Extensive deposition of collagen that occurs in:
A. Lungs, liver, kidney, and other organs as a consequence of chronic inflammation.
B. In the myocardium after extensive ischemic necrosis (infarction).

The ability of tissues to repair themselves is determined, in part, by their intrinsic proliferative capacity.

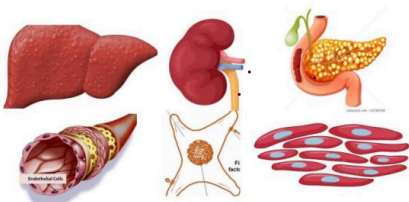
ولا يبرهنونها لها هاي الجدة!

الأنسجة تقسم بناءً على قدرتها على الانقسام



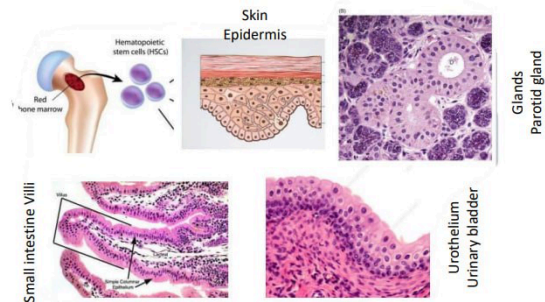
Stable tissues

Made up of cells that are normally in the G0 stage of the cell cycle and hence not proliferating, but they are capable of dividing in response to injury or loss of tissue mass.

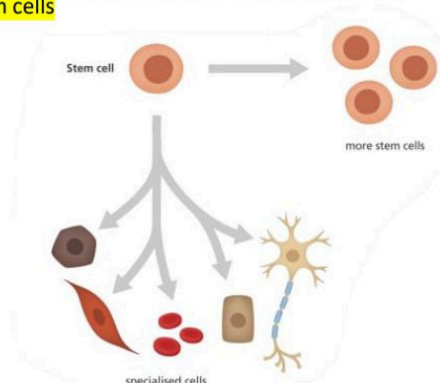


Labile tissues:

Cells are constantly being lost and must be continually replaced by new cells that are derived from tissue stem cells and rapidly proliferating immature progenitors.



In the process of regeneration, proliferation of residual cells is supplemented by development of mature cells from stem cells



Liver Regeneration

بصورتين :-



1. Proliferation of remaining hepatocyte → لو (٩٠٪) من الكبد متضرر ينجح (حودون)
2. Repopulation from progenitor cells → لو كامل الوضع هتوي

- Restoration of normal tissue architecture can occur only if the residual tissue is structurally intact.

- If the entire tissue is damaged, regeneration is incomplete and is accompanied by scarring.

1. Proliferation of hepatocytes following partial hepatectomy.

• In humans, resection of up to 90% of the liver can be corrected by proliferation of the residual hepatocytes.

• This process is driven by:

A. Cytokines such as IL-6 produced by Kupffer cells.

B. Hepatocyte growth factor (HGF) produced by many cell types.

2. Liver regeneration from progenitor cells.

• In situations in which the proliferative capacity of hepatocytes is impaired, progenitor cells in the liver contribute to repopulation, such as:

A. After chronic liver injury.

B. Inflammation.

- انتو عارفين انه ال Regeneration ليا نرجع الخلايا الا صلبة و صج !! ؟

- طيب لو ال Regeneration كانه مو نافع و اكل ؟

(ارقه) ايجوب التي هي SCAR !!

If repair cannot be accomplished by regeneration alone, it occurs by:

✓ Replacement of the injured cells with connective tissue, leading to the formation of a scar,

✓ Or by a combination of regeneration of some residual cells and scar formation.

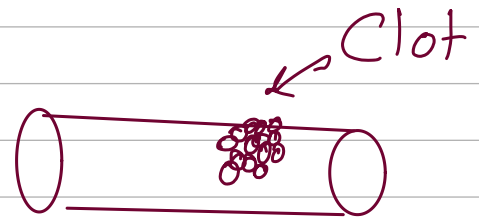
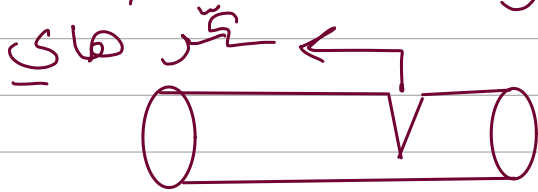
• The term scar is most used in connection to wound healing in the skin.

• Replacement of parenchymal cells in any tissue by collagen, as in the heart after myocardial infarction.

تير تاع (SCAR) ؟



1. لماذا في اصابة يفي في
 نيو صبح؟
 So, Stop Bleeding



Within minutes after injury, a hemostatic plug comprised of platelets is formed:

- ✓ Stops bleeding .
- ✓ Provides a scaffold for infiltrating inflammatory cells.

2. لماذا في جرحنا صونا وينا
 Inflammation
 !! امو !!

Inflammation:

- Include acute and chronic inflammatory responses.
- The inflammatory cells aimed to:
 - ✓ Eliminate the offending agents
 - ✓ Clear the debris

Macrophages are the central cellular players in the repair process:

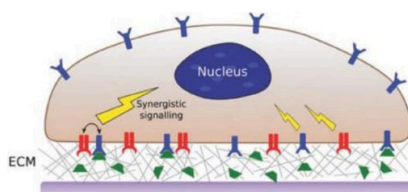
1. M1 macrophages:
 - ✓ Clear microbes and necrotic tissue and promote inflammation.
2. M2 macrophages:
 - ✓ Produce growth factors that stimulate the proliferation of many cell types in the next stage of repair.

3. من في جرح وتنظيف مكانه؟ مناه عوصها

Cell proliferation.

- ✓ In the next stage, which takes up to 10 days, several cell types migrate to close the now-clean wound, including:
 - A. Epithelial cells: migrate over the wound to cover it.
 - B. Endothelial and other vascular cells: proliferate to form new blood vessels, a process known as angiogenesis
 - C. Fibroblasts: proliferate and migrate into the site of injury and lay down collagen fibers that form the scar.

Cell proliferation is driven by signals provided by growth factors and from the extracellular matrix.



Granulation tissue

The combination of proliferating fibroblasts, loose connective tissue, new blood vessels and scattered chronic inflammatory cells, forms a granulation tissue.

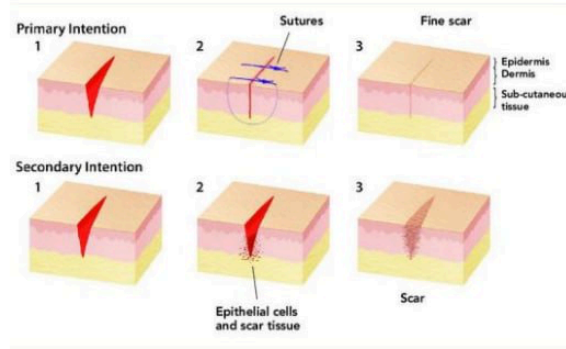
REMODELING.

The connective tissue that has been deposited by fibroblasts is reorganized to produce the stable fibrous scar.

This process begins 2 to 3 weeks after injury and may continue for months or years



- Healing of skin wounds can be classified into healing by :
 - A. First intention (primary union).
 - B. Second intention (secondary union).



- زرع جدید بہہ ہی

- نیچ جدید بہہ دم !



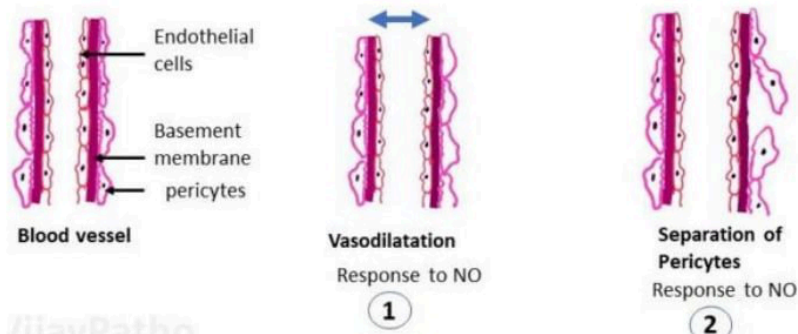
Angiogenesis

Angiogenesis is the process of new blood vessel development from existing vessels.

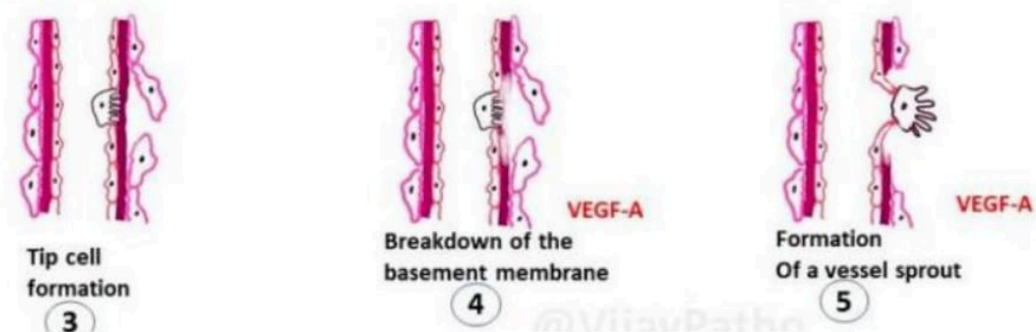
• It is critical in:

1. Healing at sites of injury.
2. Development of collateral circulations at sites of ischemia.
3. Allowing tumors to increase in size

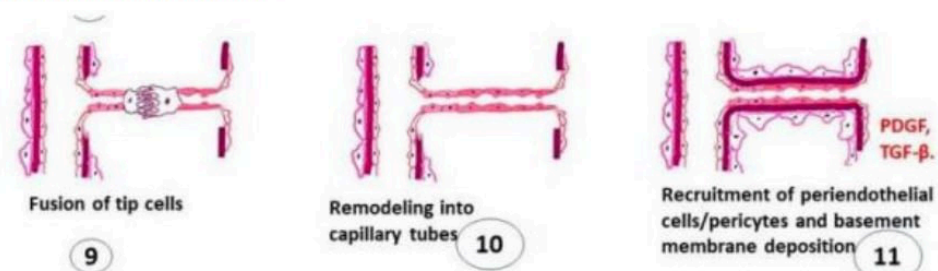
- Angiogenesis involves sprouting of new vessels from existing ones, and consists of the following steps:
- Vasodilation in response to NO and increased permeability induced by VEGF
- Separation of pericytes from the abluminal surface



- Migration of endothelial cells toward the area of tissue injury.
- Proliferation of endothelial cells just behind the leading front ("tip") of migrating cells.
- Breakdown of the basement membrane to allow formation of a vessel sprout .

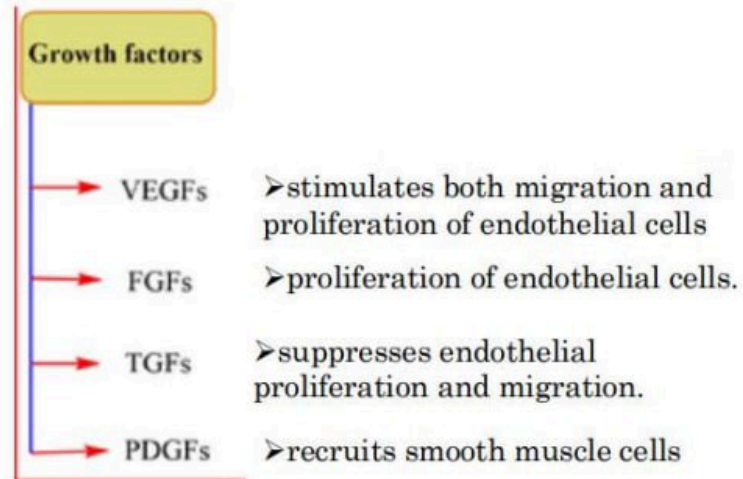


- Remodeling into capillary tubes.
- Recruitment of peri-endothelial cells (pericytes for small capillaries and smooth muscle cells for larger vessels) to form the mature vessel.
- Suppression of endothelial proliferation and migration and deposition of the basement membrane



- The process of angiogenesis involves several signaling pathways, cell–cell interactions, ECM proteins, and tissue enzymes:

1. Growth factors:



- So PDGF and TGF-B participate in the stabilization process

2. Notch signaling:

- Regulates the sprouting and branching of new vessels.

3. ECM proteins:

- Participate in the process of vessel sprouting in angiogenesis, through interactions with integrin receptors.
- Enzymes in the ECM, notably the matrix metalloproteinases (MMPs), degrade the ECM to permit remodeling and extension of the vascular tube.