PATHOLOGY

◉ Sheets ○ Slides

Number: 13

Done by: Hashim A. Mohammad

Corrected by: Noor Isbeih

Subject: Repair 3 & Amyloidosis

Doctor: Heyam Awad

00/00/0000

.....

Last lecture , we talked about scar formation.
Now , we will discuss examples of healing of surgical wounds.

- We have two types of skin wounds :
1- Clean incisions :
- not deep
- minimal tissue destruction
→ So , it can be repaired easily.

2- Deep incisions :
- have irregular borders
- can be infected
So , they cannot regenerate completely and will end in a scar formation.

Healing of such incisions can be through one of these two forms :
a- Healing by first intention (primary union)
b- Healing by second intention.

Healing by first intention (primary union)

- healing of a clean, uninfected surgical incision approximated by surgical sutures.
- there's very minimal destruction to basement membranes.

- **focal disruption of epithelial basement membrane continuity so.. A small scar is formed, with minimal wound contraction**

- epithelial regeneration is the principal mechanism of repair. (Everything will go back to normal) And Going back to normalcy will be an easy job since there's only minimal tissue damage.

Healing by second intention or "second Union"

- Occurs when cell or tissue loss is extensive, e:g in large wounds, at sites of abscess formation , ulceration and ischemic necrosis (infarction) in parenchymal organs.
- The repair process is more complex and involves a combination of regeneration and scarring.

Healing by second intention isn't only characterized by scar formation. It's also characterized by the following:

1. More intense inflammatory reaction.
2. Development of abundant granulation tissue.
3. Accumulation of ECM and formation of a large scar.
4. wound contraction mediated by myofibroblasts

- During healing , the injured area shrinks (becomes smaller). Why ?
  Because fibroblasts are associated with myofibroblasts that help the functioning fibroblasts contract , minimizing the sized of the injured area.

Wound contraction:

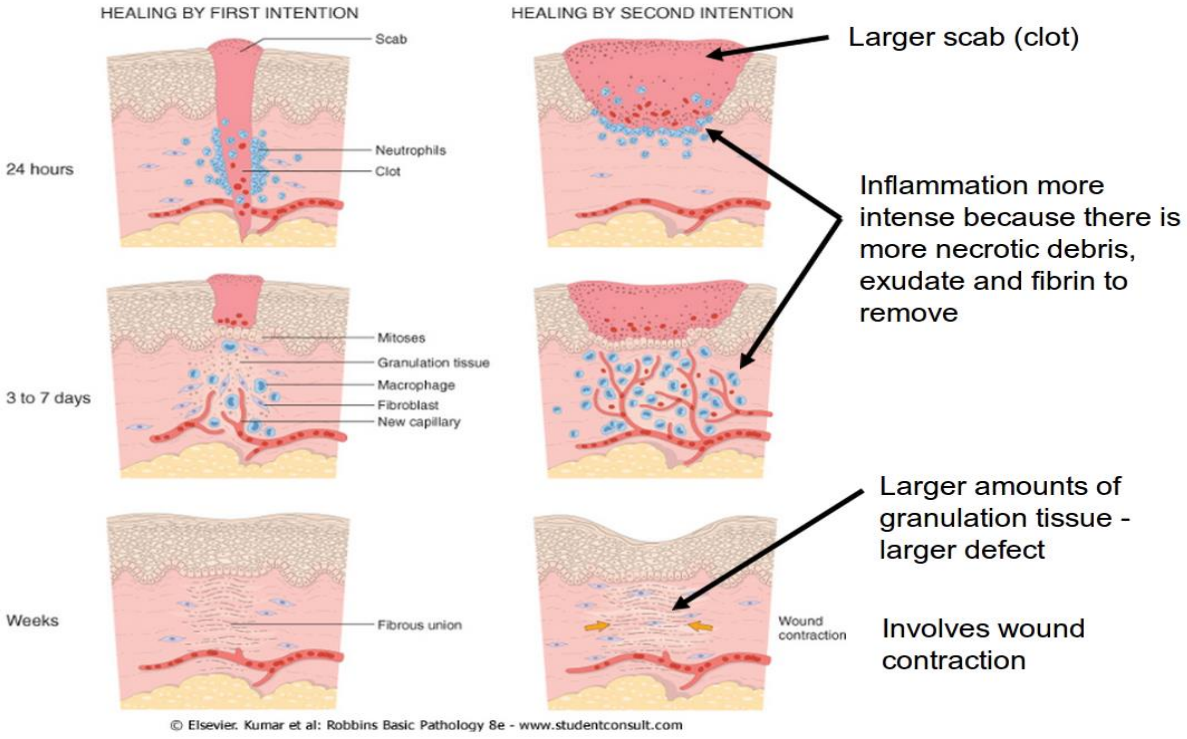
- mediated by myofibroblasts.
- Within 6 weeks, large skin defects may be reduced to 5% to 10% of their original size. Most of this reduction is due to wound contraction.

From Robbins (wasn't mentioned in the lecture)

- Why is the inflammatory reaction more intense when a wound is healed by secondary intention?
  Because healing by secondary intention is associated

with large tissue defects , so the amount of tissue debris , exudates and fibrin that is released and needs to be removed by inflammation is much larger than small tissue defects associated with healing by first intention.

Figure 1: Steps in wound healing by first intention(left) and second intention(right). In the latter case, Note the large amount of granulation tissue and wound contraction



Woung Strength

- Carefully sutured wounds have approximately 70% of normal skin strength due to the sutures.

-At 1 week (sutures removed) → 10% of normal.

- strength then increases as a result of collagen synthesis exceeding degradation during the first 2 months and by structural modification of collagen.

- These structural modifications are :
a- cross-linking
b- increased fiber size

- Maximum strength reached: 70% to 80% of normal by 3 months and usually doesn't improve substantially beyond that point.

-

Amyloidosis

- This is just a brief explanation of amyloidosis just to take a general idea about this term.

Amyloids :

Several proteins that share the same physical characteristics but with different chemical composition.

- They are misfolded proteins.
- They accumulate extracellularly and when they accumulate , they compress cells causing functional derangements.
→ they can cause disease.

- Amyloidosis isn't a disease by itself but a condition associated with many diseases.
- These diseases can be inherited ,inflammatory or neoplastic.

- Amyloids always have beta-pleated sheet configuration.
- Congo red stain is used to characterize amyloids.
-When viewed under the polarized light microscope, they demonstrate apple-green birefringence.

- All types of amyloid consist of continuous, non-branching fibrils with a diameter of approximately 7.5 to 10 nm. With a cross-β-pleated sheet conformation

This part is taken from Robbins:
(not included)

Amyloidosis is a condition associated with a number of inherited and inflammatory disorders in which extracellular deposits of fibrillar proteins are responsible for tissue damage and functional compromise. These abnormal fibrils are produced by the aggregation of misfolded proteins (which are soluble in their normal folded configuration) or protein fragments. The fibrillar deposits bind a wide variety of proteoglycans and glycosaminoglycans, including heparan sulfate and dermatan sulfate, and plasma proteins, notably serum amyloid P component (SAP). The presence of abundant charged sugar groups in these adsorbed proteins gives the deposits staining characteristics that were thought to resemble starch (amylose). Therefore, the deposits were called “amyloid,” a name that is firmly entrenched despite the realization that the deposits are unrelated to starch.

Summary of Amyloidosis:
Amyloidosis

- Amyloidosis is a disorder characterized by the extracellular deposits of misfolded proteins that aggregate to form insoluble fibrils.
- The deposition of these proteins may result from excessive production of proteins that are prone to misfolding and aggregation; mutations that produce proteins that cannot fold properly and tend to aggregate; or defective or incomplete proteolytic degradation of extracellular proteins.
- Amyloidosis may be localized or systemic. It is seen in association with a variety of primary disorders, including monoclonal plasma cell proliferations (in which the amyloid deposits consist of immunoglobulin light chains); chronic inflammatory diseases such as RA (deposits of amyloid A protein, derived from an acute-phase protein produced in inflammation); Alzheimer disease (amyloid B protein); familial conditions in which the amyloid deposits consist of mutants of normal proteins (e.g., transthyretin in familial amyloid polyneuropathies); amyloidosis associated with dialysis (deposits of β_2-microglobulin, whose clearance is defective).
- Amyloid deposits cause tissue injury and impair normal function by causing pressure on cells and tissues. They do not evoke an inflammatory response.

-