Pathology

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Repair and Healing

Eighth Lecture

- Tissue Repair : Includes Two Processes.

  1- Regeneration

  2- Healing.

Repair :

- Host response to replace Dead tissue by Healthy tissue (Restoration of tissue architecture and function after an injury).
- Repair occurs by Two processes :
  1. Regeneration: Replacement of dead cells (tissues) by proliferation of parenchymal cells of same type (Return to Normal State).
  2. Healing: Replacement of dead tissue by connective (fibrous) tissue resulting in Permanent Scar formation.

Important factors in repair :

- ❖ Cellular Proliferation.
- ❖ Growth Factors.
- ❖ Extra- Cellular Matrix (ECM).

Cellular proliferation :

✓ Tissues of the body are divided into Three Types according to their Regenerative Capacity :

1. Labile (Continuously Dividing) Cells.
2. Stable (Quiescent) Cells.
3. Permanent (Non- Dividing) Cells.

1. Labile (Continuously Dividing) Cells (Tissues) :

✓ Cells are continuously proliferating.

✓ Can easily regenerate after injury.

✓ Contain a pool of stem cells.

✓ Examples: Cells of bone marrow, skin and mucosa of GIT, vagina, cervix, endometrium and urinary bladder.

2. Stable (Quiescent) Cells (Tissues) :

Cells which stop multiplication when growth is complete after birth but retain ability to multiply when there is a need for that Examples: Cells of liver, pancreas, kidney, fibroblasts, endothelial cells and smooth muscle cells.

3. Permanent (Non-Dividing) Cells (Tissues) :

Cells which stop multiplication early in neonatal life after birth. Examples: Neurons, nerves, cardiac muscles & skeletal muscles.

Growth factors :

✓ Very important in tissue repair.

✓ Actions:

- Stimulate cell Division and Proliferation.
- Promote cell Survival and Differentiation.

✓Huge list ! Usually have "GF" in name:

- EGF (Epidermal growth factor)
- TGF-α , TGF-β (Transforming growth factors)
- PDGF (Platelet-derived growth factor)
- FGF (Fibroblast growth factor)
- VEGF (Vascular endothelial growth factor)

Extra cellular matrix (ECM) :

- ECM is the network that surrounding the cells.
- Two forms:
  - Interstitial matrix
  - Basement membrane
- Does lots of things !
  - Sequesters water and minerals.
  - Gives cells a scaffold to adhere to.
  - Stores growth factors.
  - ECM regulates proliferation, movement, and Differentiation of the cells living in it.
  - Intact ECM is required for tissue regeneration, if ECM is damaged, repair only by scar formation.

Regeneration :

- ☒ It occurs all the time in labile tissues.
- ☒ Cells are continuously being lost and replaced by proliferation of residual cells (stem cells) .
- ☒ If demand increases, supply increases easily.
- ☒ It occurs in limited form in stable tissues.

- Examples: Remove one kidney : Other kidney undergoes compensatory hypertrophy and hyperplasia.
- Remove half of the liver: It will grow back to normal size.

☒ Regeneration only occurs if residual tissue is intact with the presence of stem cells.

Scarring :

✓ If injury is severe, regeneration can't happen. So, fibrosis (scarring) replaces the injured tissue, as in permanent tissues (non-regenerating tissues), chronic inflammations, excessive tissue damage and excessive fibrin deposition.

Four Components of Scar Formation :

- ❖ New blood vessel formation (Angiogenesis).
- ❖ Migration and proliferation of Fibroblasts.
- ❖ Synthesis of Collagen (Scar Formation).
- ❖ Remodeling of scar.

Healing of skin wounds

1. Healing by Primary Union (First Intention).
2. Healing by Secondary Union (Second Intention).

Healing by First Intention (Primary Union)

- It occurs in small and clean wounds that close easily.
- Epithelial regeneration predominates over fibrosis.
- Healing is fast, with minimal scarring and infection.
- Example: Well-approximated surgical incisions.

Timeline :

- ✓ By 24 hours.
- ✓ By 3-7 days.
- ✓ Weeks later.

By 24 hours :

- ☒ Formation of blood clot (Scab on the surface of wound).
- ☒ Acute inflammation ➔ Neutrophils come in.
- ☒ Epithelium (Epidermis) begins to regenerate.

By 3-7 days :

- ☒ Macrophages come in and replace neutrophils.
- ☒ Granulation tissue is formed :
  - ✓ New blood vessels (angiogenesis) .
  - ✓ Fibroblasts.
- ☒ Epithelium (Epidermis) increases in thickness.
- ☒ Collagen begins to bridge the incision.

Weeks later (by the end of the first month) :

- ☒ Granulation tissue is gone.
- ☒ Collagen is remodeled.
- ☒ Epidermis : full thickness and mature but without dermal appendages and No rete ridges at line of incision.
- ☒ Eventually, Scar forms.

By the End of First Month :

Scar consists of mature connective fibrous tissue without inflammatory cells and No blood vessels, and covered by normal Epidermis. Dermal appendages are lost in the line of incision and No rete ridges.

Granulation Tissue

- Tissue of Healing.
- It is formed by day 3-5.
- Soft, pinkish and granular appearance.
- It consists of proliferating fibroblast, newly-formed blood vessels or capillaries (Angiogenesis) in loose ECM and inflammatory cells (macrophage, lymphocytes and others)
- Progressively, granulation tissue change and mature into dense fibrous tissue (Fibrosis) and scar formation.