Lec 7,8,9

Tissue Repair Process (Resolution)

Tissue repair consists of two main pathways: **regeneration** and **scar formation**.

- **Tissue Regeneration:**
- Regeneration occurs when tissues recover completely through the interaction of growth factors and the extracellular matrix, depending on the tissue's regenerative capacity:

1. Labile tissues: Continuously regenerate (e.g.skin).
2. Stable tissues: Cells in G_0 phase proliferate upon damage (e.g., liver, kidney, pancreas).
3. Permanent tissues: No regeneration (e.g., neurons, cardiac and skeletal muscle).

- Liver Regeneration:
- Via hepatocyte proliferation or progenitor cell differentiation.

- Complete regeneration without scarring occurs in mild injuries (first intention).
- Severe injuries lead to scarring (second intention).

- **Scar Formation:**

Scar formation occurs when regeneration is insufficient, involving fibrosis (granulation tissue formation and remodeling).

Steps in Scar Formation:

1. Hemostatic Plug: Clot formation to control bleeding.
2. Inflammation: Macrophages release mediators that induce repair process.
3. Cell Proliferation:

- Angiogenesis: Formation of new capillaries via:
- VEGF-A, FGF-2, and TGF-β.
- Steps include degradation of the basement membrane, pericyte detachment, sprouting, and capillary stabilization.
- Fibroblast Activation and ECM Deposition:
- Driven by PDGF, FGF-2, and TGF-β (potent fibrogenic agent).
- Fibroblasts migrate, proliferate, and deposit type III collagen.

4. Tissue Remodeling:

- Cross-linking of collagen and conversion from type III to type I.
- Matrix metalloproteases (MMPs), inhibited by TIMPs, regulate ECM degradation.
- Reduction in blood vessels and scar maturation.

Factors Impairing Repair:

1. Infection: Prolongs inflammation.
2. Diabetes Mellitus: Impairs angiogenesis.
3. Malnutrition: Deficiency in essential nutrients (e.g., vitamin C).
4. Mechanical Factors: Wound dehiscence in obese patients.
5. Foreign Bodies: Persist at injury sites.
6. Injury Severity: Extensive damage delays repair.
7. Site of Injury: Dependent on blood supply.
8. Poor Perfusion: Reduces oxygen and nutrient delivery.
9. Steroids: Decrease inflammation.

Defective Repair:

Defective repair results in complications due to:

1. **Defective Scar Formation:**

- Examples:
- Venous leg ulcers (superficial).
- Arterial ulcers (deep).
- Diabetic ulcers (deep).
- Pressure sores (bed sores in back)
- Wound dehiscence.(like abdominal wound in obese pateint (Mech.factors))

2. **Excessive Scar Formation:**

- Examples:
- Hypertrophic Scars: Excess ECM
- Keloids: Consist of excess collagen type I, common in darker-skinned individuals.
- Exuberant Granulation Tissue: (proud flush)
- Desmoid Tumors: Aggressive fibromatosis.

3. **Contractures:**

- Excessive wound contraction leading to deformities (e.g., in hands and legs).

Organ Fibrosis:

Severe or continuous injury results in excessive scarring and loss of organ function, seen in:

- Liver Cirrhosis
- Idiopathic Pulmonary Fibrosis
- End-Stage Kidney Disease (ESKD)