**Lecture 7 General pathology Dr. Ali H. Murad**

***Types of repairs according to the type of the tissue:***

**1- Repair by regeneration:**

Cell renewal occurs continuously in **labile tissues,** such as the bone marrow, gut epithelium, and the skin. Damage to epithelia or an increased loss of blood cells can be corrected by the proliferation and differentiation of stem cells and, in the bone marrow, by proliferation of more differentiated progenitors.

The renewal of hematopoietic cells is driven by growth factors called colony-stimulative factors (CSFs), which are produced in response to increased consumption or loss of blood cells.

Tissue regeneration can occur in parenchymal organs with **stable cell** populations, but with the exception of the liver, this is usually a limitedprocess. Pancreas, adrenal, thyroid, and lung tissues have someregenerative capacity. Extensive regeneration or compensatoryhyperplasia can occur only if the residual tissue is structurally andfunctionally intact, as after partial surgical resection. By contrast, if thetissue is damaged by infection or inflammation, regeneration isincomplete and is accompanied by scarring.

2- **Repair by connective tissue:**

Repair occurs by replacement of the nonregenerated cells with connective tissue, or by a combination of regeneration of some cells and scar formation:

1- If tissue injury is severe or chronic, and results in damage to parenchymal cells and epithelia as well as the stromal framework.

2 -If nondividing cells are injured, repair cannot be accomplished by regeneration alone.

**Aberrations of cell growth and ECM production**

This may occur even in what begins as normal wound healing.

1**. Keloid**: refers to the accumulation of exuberant amounts of collagen that give rise to prominent, raised scars. There appears to be a heritable predisposition to keloid formation, and the condition is more common in blacks.

2. **Exuberant granulation**: healing wounds may also generate excessive granulation tissue that protrudes above the level of the surrounding skin and hinders re-epithelialization. The restoration of epithelial continuity requires cautery or surgical resection of the granulation tissue.

3. **Disabling fibrosis** associated with chronic inflammatory diseases such as rheumatoid arthritis, pulmonary fibrosis, and cirrhosis have many similarities to those involved in normal wound healing. In these diseases, however, persistent stimulation of fibrogenesis results from chronic immune reactions that sustain the synthesis and secretion of growth factors, fibrogenic cytokines, and proteases.

***Delay healing:***

**Factors causes delay healing**:

1- **Infection** is the single most important cause of delay in healing; it prolongs the Inflammatory phase of the process and increases the local tissue injury.

2- **Nutritional deficiency** like vitamin C deficiency, inhibits collagen synthesis

and retards healing.

3- **Glucocorticoids** (steroids) have well-documented anti-inflammatory effects,

and their administration may result in poor wound strength due to diminished

fibrosis.

4- **Mechanical injuries** such as increased local pressure or torsion may cause

wounds to pull apart, or opened.

5- **Diminished blood supply**, due either to arteriosclerosis and diabetes or to

obstructed venous drainage (e.g. in varicose veins).

6- **Foreign bodies** such as fragments of steel, glass, or fractured bone.



**G0: quiescent stage , G1: growth presynthetic, S: DNA synthesis G2: growth premitotic, M: mitotic**

**The G1 and S stages generally constitute the majority of the timeof the cell cycle; the mitotic (M) phase is typically brief. Note the G1 restriction point, and the G1/S and G2/M**

**checkpoints.**

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***HEALING OF BONE FRACTURE***

Bone fracture is caused by physical trauma, leading to discontinuity of the bone. The separation of fractured ends may be complete or incomplete. The latter is common in young children and called greenstick fracture. The fracture may be a closed one i.e. with an intact overlying skin or open i.e. the overlying skin is also injured so that the fractured bone is exposed through a gaping wound. A comminated fracture is the one in which the bone is divided into multiple fragments.

**Fracture healing**

Due to tearing of blood vessels in the medullary cavity, cortex and periosteum, **a hematoma** forms at the site of fracture. The periosteum is stripped off form the bone surfaces. The bone with haemopoietic marrow around the fracture site undergoes **ischemic** **necrosis**. Bone death is recognized histologically by loss of

osteocytes from lacunae (empty lacunae).

Organization of the hematoma is associated with a local inflammatory response, with hyperaemia, exudation of protein rich fluid, & migration of neutrophils & macrophages. These cells phagocytose the hematoma & necrotic debris. This is followed by in-growth of capillaries & fibroblasts, producing fibrovascular granulation tissue.

**At the end of the 1st week,** osteoblasts derived from osteoprogenitor cells of the inner layer of the periosteum will migrate into the granulation tissue and proceed to deposit larger quantities of osteoid in a haphazard way, producing a **woven bone** pattern. **External** **callus** is thus formed by the periosteum and tends to immobilize the bone fracture site. The two enlarging cuffs of callus advance towards each other until finally unite to bridge the fracture gap outside externally.

If there is a significant gap between the bone ends, it may induce cartilage formation.

The **internal callus derived from endosteal osteoprogenitor cells** bridges the fracture from within the medullary cavity, and rarely contains cartilage due to better vascularization.

The cartilaginous component of callus is converted to bone by endochondral ossification.

 Callus is usually formed by the 3rd week after the incident of fracture, but the **initial bony union is by woven bone, which is** **mechanically weak.**

The amount of periosteal callus formed (external callus) depends on the site of fracture & the degree of immobilization. It tends to be abundant in poorly immobilized fracture e.g. clavicle & ribs.

**Remodelling** of callus occurs once the defect between the two bone ends is bridged by bony callus, so the newly laid down bone is reconstructed to restore full mechanical strength. The newly formed woven bone is resorbed and gradually replaced by **lamellar bone**(compact).

The cortex is re-formed across the fracture gap & gradually the medullary callus is removed with restoration of the marrow cavity. Remodelling is done by the osteoblasts & osteoclasts.

The whole reparative process may take about a year, although the time varies from site to site. It is also more rapid and more complete in children.

***Factors Affecting Fracture Healing***

These are basically similar to those of affecting healing in general. However, mobility of fracture ends and mal-alignment play a detrimental role in interfering fracture healing. Vitamin D deficiency leads to abundant callus, which fails to calcify & remains soft.

**Complications of fractures**

1. **Delayed union,** after fibrous union, bony conversion is slow.

2. **Non-union,** in which the fractured bone ends do not join by bone. This occurs if the fibrous tissue becomes very dense. The latter is then is converted to fibrocartilage.

3. **Fat embolism,** which may follow damage to the bone marrow. In such cases globules of fat embolize to such sites as the lungs, brain, and kidneys with the ultimate result of ischemic necrosis (infarction).

4. **Osteonecrosis;** this refers to local bone necrosis after fracture. It may occur depending on local peculiarities of the blood supply, e.g. fracture of femoral neck is often followed by osteonecrosis of the femoral head.

5. **Osteoarthritis (osteoarthosis)**; this degenerative joint disease may occur when the fracture line has involved the articular surface that result in the production of an incontinuity of the articular cartilage.

**Pathological Fracture**

For fracture of normal bone to occur, the causative trauma has to be severe enough.In contrast, trivial trauma may cause fracture when the underlying bone is abnormal e.g**. presence of osteoporosis** (reduced bone mass) that occurs in the elderly may be associated with pathological fractures particularly in the femur & vertebral column. **Osteomalacia** (vitamin D deficiency led to inadequate bone mineralization→ soft weak bone**), Primary or metastatic** **tumors** (from carcinoma of breast bronchus, thyroid & kidney) may be associated with pathological fractures.