Inflammation:

The inflammatory reaction

Inflammation is the response of a tissue to immune reaction,ischaemic damage and injury . Although painful, the inflammatory reaction is essential for preventing infection of the injured area and elimination of the necrotic cells and damaged tissues as a consequence of injury as well as for initiating the process of healing.

Each inflammatory process starting by injurious stimulus which result in release of certain chemical mediators either from plasma or injured cells which triggers inflammatory response by regulating the subsequent vascular and cellular responces ,such chemical mediators acting together or in sequence to amplify the initial inflammatory response and influence it's evolution .the inflammatory response is terminated when the injurious stimulus is removed and inflammatory mediators have been dissipated ,catabolized or inhibited.

Cells of inflammation:

Many cells and tissue components are involved in inflammatory process ,including endothelial cells(lining of blood vessles),circulating platelets and leukocytes,connective tissue cells(fibroblasts,mast cells and macrophages) with extracellular matrix component.

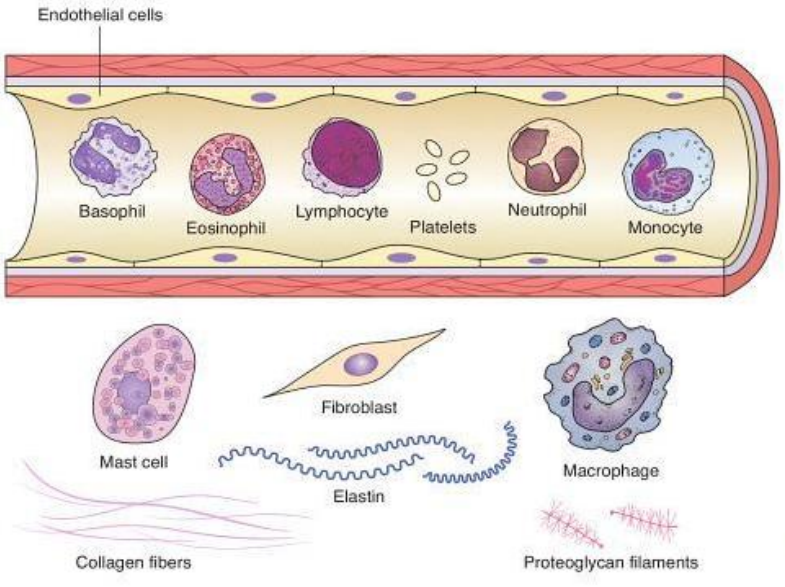


FIGURE 3-1. Cells involved in the inflammatory process.

Inflammation is divided in to:

Acute inflammation:

It is the immediate and early response to noxious stimmuli and other conditions like infections and tissue injury ,with short duration lasting

from few minutes to several days and characterized by fluid and plasma protein exudation with emigration of leukocytes,predominantly neutrophils. A critical function of inflammatory response is to deliver leukocyte to the area of injury to clear invading bacteria (or other infectious agents)as well as degrades necrotic tissues resulting from the damage, unfortunately leukocytes may also prolongs inflammation and induce further tissue damage by releasing enzymes ,chemical mediators and toxic oxygen free radicals.

The clinical manifestation of acute inflammation attributed to immediate vascular responces(vasodilatation and increased capillary permeability),influx of inflammatory cells and release of chemical mediators which produce fever and other signs and symptoms.

Acute inflammation has two stages ;

Vascular response stage and cellular response stage:

Stage of *vascular response* formed by:

1- Short and transient vasoconstriction followed by vasodilatation of the arterioles which lead to local increase in blood flow at the injured area.

2-increased capillary permeability at the injured area with subsequent extravasation of protein rich fluids in to the extravascular tissues leading to swelling and edema. The fluids that enter the injured area are useful for diluting out any bacterial toxins or irritants present in the tissue.

Stage of *Cellular response*

Cellular response or cellular phase formed by leukocyte margination,adhesion and transmigration through the vessel wall.these leukocytes act as a phagocytic cells after their activation and play the phagocytic activity.

Neutrophils are the first white blood cells to arrive in the injured area. Leukocytes are attracted to the injured area by certain bacterial substances as well as by cellular debris and cytokines(*chemotaxis*).

• As fluid leaves the capillaries, the viscosity of blood increases and leukocytes precipitate to the walls of the capillary. This process is called *margination*.

Firm adhesion was maintained through rolling of leukocytes on endothelial cells by specific receptors, Leukocytes undergo a change in shape and squeeze through the now more permeable capillaries into the tissues. The movement of leukocytes through the capillary wall is called *diapedesis or transmigration*.

Once leukocytes at the site of injury phagocytic activity started by debris generated from injured tissue and by foreign microorganisms.Phagocytosis and cell killing obtained by;

opsonization of the microbes or foreign particles by complement factor C3b and immunoglobulin antibody facilitate their recognition by neutrophils through FC and C3b receptors.

• Other white blood cells such as *Eosinophils* and *basophils* also arrive at the injured area and release substances such as *histamine* that enhance the inflammatory reaction. Histamine is a powerful vasodilator that increases capillary permeability. Monocytes will also enter the inflamed tissues where they mature into phagocytic macrophages.

• Cytokines such as interleukin and tumor necrosis factor are released to enhance the inflammatory and immune response.

Prostaglandins are also released by many cells in the injured area and cause fever and vasodilation.

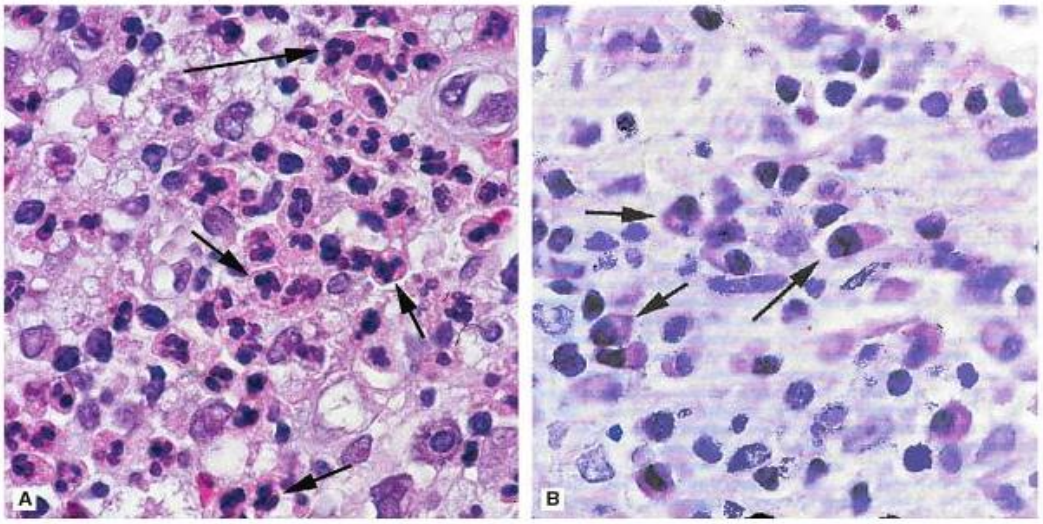
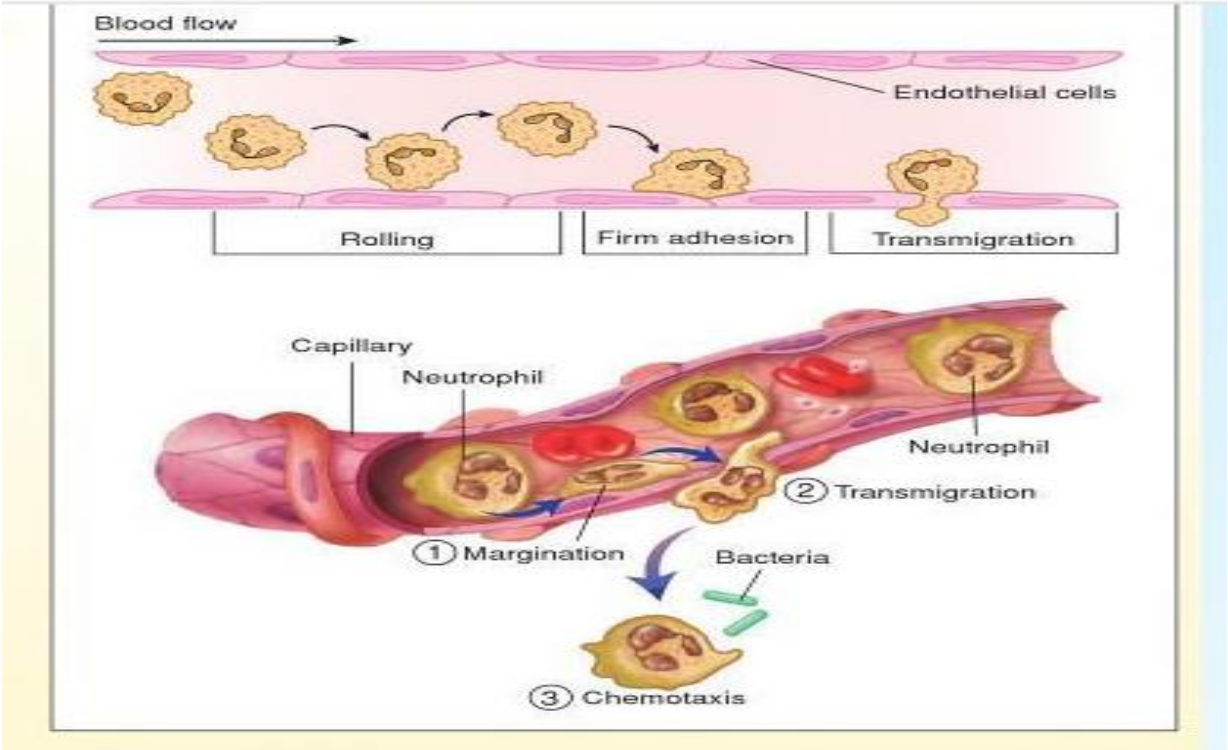
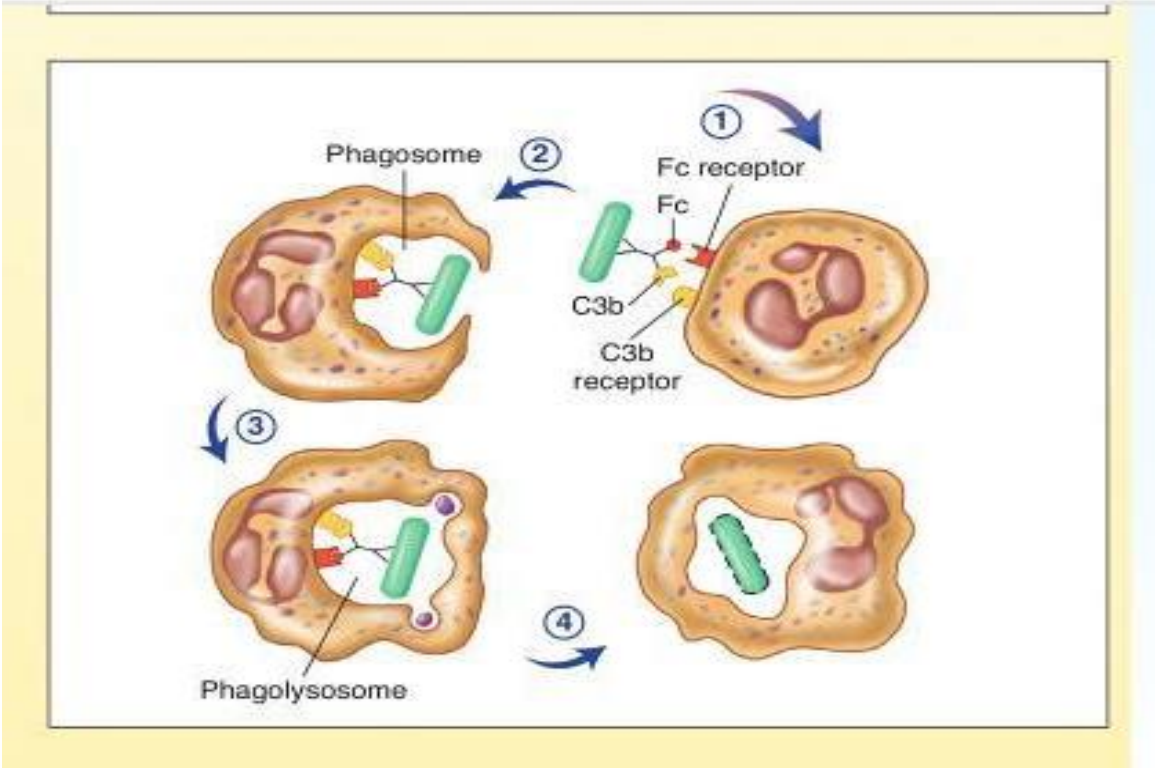


FIGURE 3-2. Inflammatory cells of acute and chronic inflammation. **(A)** Acute inflammation with densely packed polymorphonuclear neutrophils with multilobed nucleus (*arrows*). **(B)** Chronic inflammation with lymphocytes, plasma cells (*arrows*), and a few macrophages. (From Murphy H.S. [2008]. Inflammation. In Rubin R., Strayer D.E. [Eds.], *Rubin's pathology: Clinicopathologic foundations of*


Blood flow
Endothelial cells
Rolling
Firm adhesion
Transmigration
Capillary
Neutrophil
Neutrophil
② Transmigration
① Margination
Bacteria
③ Chemotaxis


①
Phagosome
②
Fc receptor
Fc
C3b
C3b
receptor
③
④
Phagolysosome

There are five **"cardinal signs"** of inflammation:

Redness(Rubor)

The redness that occurs as a result of the increased blood flow to the inflamed area.

Swelling(Tumor)

Swelling of the inflamed tissue as a result of increased capillary permeability and fluid accumulation.

Heat(Calor)

The increase in temperature (heat) that occurs in the inflamed area as a result of increased blood flow.

Pain(Dolor)

Pain that occurs in the inflamed area as a result of stimulation of sensory neurons.

Loss of function(Functio laesa)

Alteration or loss of function in the inflamed tissues.

Outcomes of acute inflammation:

1-complete resolution.

Occurs when the injury is limited or short lived ,little tissue destruction and the affected tissue has the ability to regenerate.

2-scarring and fibrosis.

Occurs after substantial tissue destruction and when the tissue unable to regenerate.

3-abscess formation ,occurs in cases of bacterial or fungal infections(pyogenic or pus forming organisms).

4-progression to chronic inflammation.

Chronic inflammation :

It is of longer duration (days to years) and characterized by influx of lymphocytes,plasma cells,macrophages and fibroblasts ,so , tissue destruction and repair with vascular proliferation and fibrosis is seen.Acute and chronic inflammation may coexist with episodes of acute inflammation being superimposed on chronic inflammation.

Chronic inflammation characterized by:

1-infiltration with mononuclear chronic inflammatory cells (lymphocytes,macrophages,and plasma cells)

2-tissue destruction , induced by inflammatory cells.

3-repair involving new vessele proliferation (angiogenesis) and fibrosis .

Chronic inflammation arises in the following setting:

1-persistent infection.occurs in specific infectious microorganism like TB and syphilitic bacteria.

2-prolonged exposure to potentially toxic agents .(e.g silicosis of the lung)
3-autoimmune diseases.

Tissue repair

Injured or damaged tissues can be repaired in one of two ways, by *regeneration* or *connective tissue replacement*.

The mechanism used for repair will depend upon the type of cells that were injured. Certain cells in the body are fully or partially capable of regenerating after an injury, whereas other cell types are not and can only be replaced with connective tissue(scar).

Types of tissue repair

1. Repair by *regeneration*

• With regeneration, the injured tissue is repaired with the same tissue that was lost. A full return of function occurs with no residual effect of the injury.

• Repair by regeneration can occur only in *labile cells* (cells that continue to divide throughout life) or *stable cells* (cells that have stopped dividing but can be induced to regenerate under appropriate conditions of injury). Examples of labile cells include those of the skin, oral cavity and bone marrow. Examples of stable cells include hepatocytes of the liver. Certain cells such as nerve cells and cardiac muscle cells are *fixed* cells and cannot undergo regeneration under any circumstances. These cell types are capable of repairing injuries through connective tissue replacement.

2. Repair by *connective tissue replacement*

• Involves the replacement of functional tissue with nonfunctional connective tissue (collagen).

• Full function does not return to the injured tissue.

• Scar tissue remains as evidence of the injury.