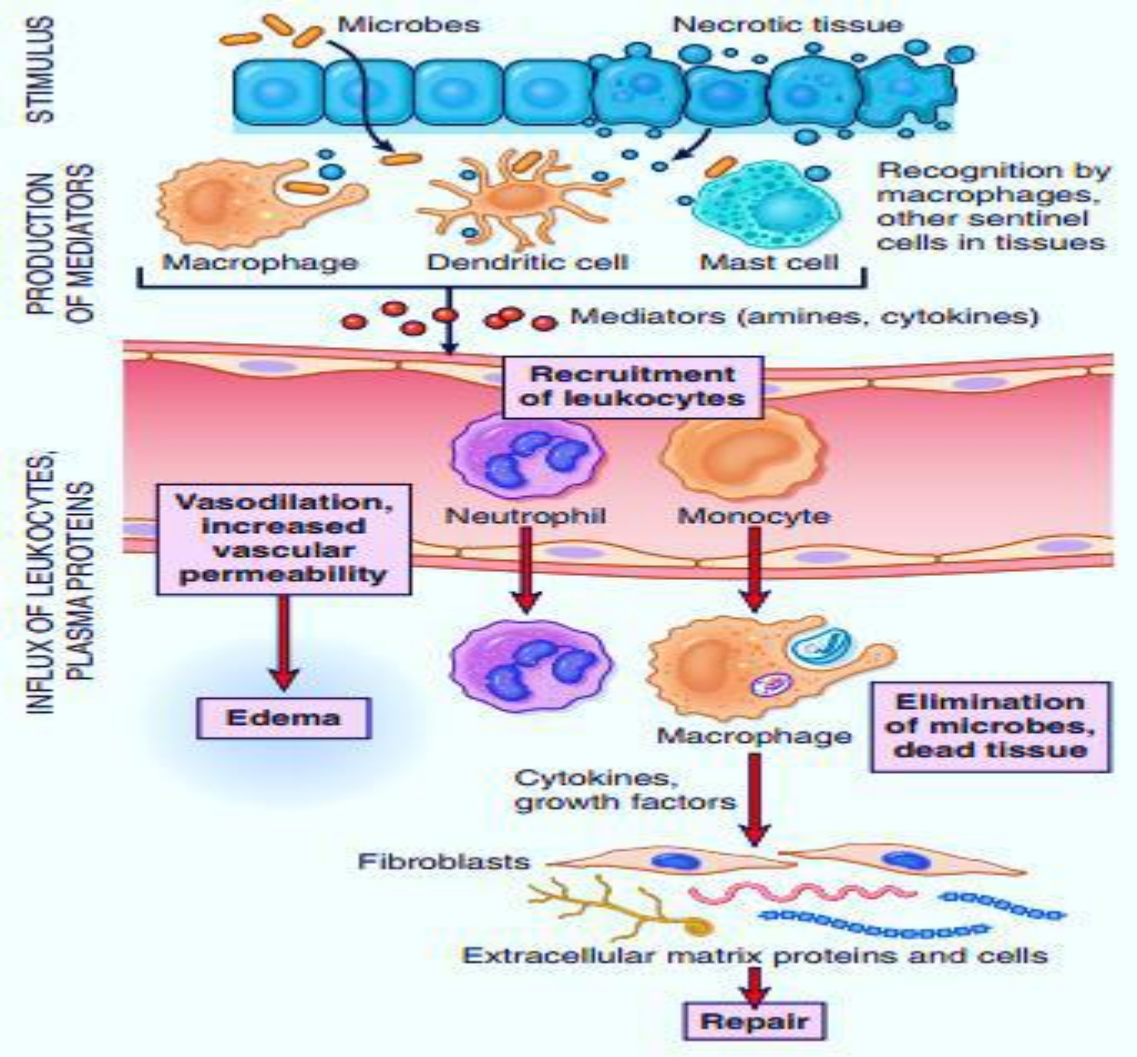
Inflammation

Inflammation is a response of vascularized tissues to infections and tissue damage that brings cells and molecules of host defense from the circulation to the sites where they are needed, to eliminate the offending agents.

The mediators of defense include phagocytic leukocytes, antibodies, and complement proteins.



Causes of Inflammation:

A-Living

1- bacterial 2- viral 3-fungal 4- parasitic.

B- Non living

1-Tissue necrosis (Ischemia).

2- Physical injury (burns or frostbite and irradiation).

3-Chemical injury (toxins, acids and alkalies).

4- Trauma (blunt and penetrating).

5- Foreign bodies (splinters, dirt, sutures and crystal deposits).

C- Immunological reactions (hypersensitivity reactions).

D- genetic/metabolic disorders- examples gout desiese.

The steps of the inflammatory response:

(1) recognition of the injurious agent,
(2) recruitment of leukocytes,
(3) removal or destroy of the agent,
(4) regulation (control) of the response,
(5) The damaged tissue is repaired.

Types of the inflammation:

1- Acute inflammation.
2- Chronic inflammation.

The acute inflammatory

is response rapidly delivers leukocytes and plasma proteins to sites of injury.
The five important signs of acute inflammation are
1. Redness which is due to dilation of small blood vessels.
2. Heat which results from increased blood flow (hyperemia).
3. Swelling which is due to accumulation of fluid in the extravascular space which, in turn, is due to increased vascular permeability.

4. Pain which partly results from destruction of tissues due to inflammatory edema and in part from pus under pressure in, as abscess cavity. Some chemicals of acute inflammation, including bradykinins, prostaglandins and serotonin are also known to induce pain.
5. Loss of function: The inflamed area is inhibited by pain while severe swelling.

Acute inflammation has three major components:

(A) Dilation of small vessels, leading to an increase in blood flow.
(B) Increased permeability of the microvasculature, enabling plasma proteins and leukocytes to leave the circulation.
(C)Emigration of the leukocytes from the microcirculation, their accumulation in the focus of injury, and their activation to eliminate the offending agent.

Mechanism

A- Tissue reaction
B- vascular changes .
C- cellular response.

Tissue reaction:

Inflammation is induced by chemical mediators that are produced by host cells in response to injurious stimuli. When a microbe enters a tissue or the tissue is injured, the presence of the infection or damage is sensed by resident cells, including **macrophages**, **dendritic cells, mast cells**, and other cell types. These cells secrete molecules (cytokines and other mediators) that induce and regulate the subsequent inflammatory response.

Vascular changes :

1- Vasoconstriction in seconds due to neurogenic or chemical stimuli
2-Vasodilation is induced by chemical mediators such as **histamine and prostaglandins** , resulting in locally increased blood flow and engorgement of the down-stream capillary beds. This vascular expansion is the cause of the **redness** (erythema) and **hea**t, This causes the red cells in the flowing blood to become more concentrated, thereby increasing blood viscosity and slowing the circulation. These

changes are reflected microscopically by numerous dilated small vessels packed with red blood cells, called **stasis**.

3- Increased vascular permeability is induced by **histamine**, , **bradykinin, leukotrienes** and other mediators that produce gaps between endothelial cells; by direct or leukocyte-induced endothelial injury; and by increased passage of fluids through the endothelium. This increased permeability allows plasma proteins and leukocytes to enter sites of infection or tissue damage; The resulting **exudat**e .

Exudates must be distinguished from transudates , Fluid accumulation in extravascular spaces, whether from an exudate or a transudate, produces tissue **edema** .

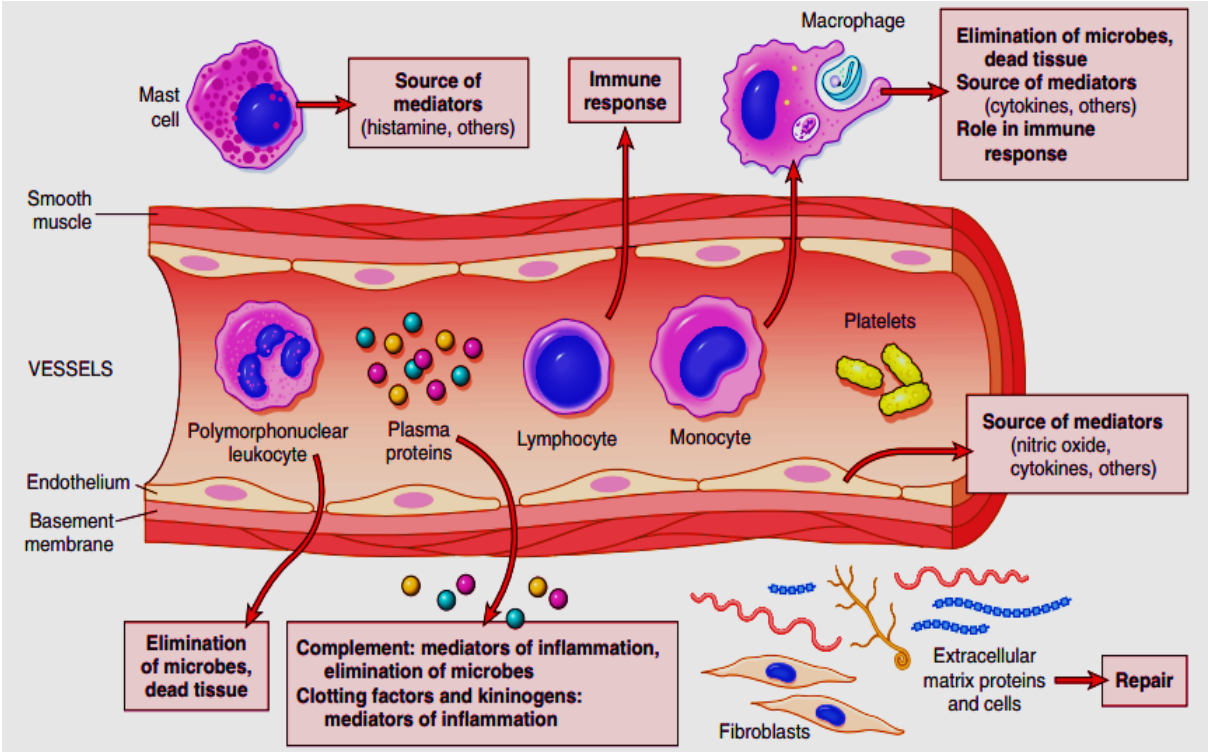


Figure –1: The components of acute and chronic inflammatory responses and their principal functions.

Cellular response:

The cellular response has the following stages:
A. Migration, rolling, adhesion of leukocytes
B. Transmigration of leukocytes
C. Chemotaxis
D. Phagocytosis
Normally blood cells particularly erythrocytes in venules are confined to the central (axial) zone and plasma assumes the peripheral zone. As a result of increased vascular permeability , more and more neutrophils accumulate along the endothelial surfaces (peripheral zone).

A) Migration, rolling, pavementing, and adhesion of leukocytes

Margination is a peripheral positioning of white cells along the endothelial cells. Subsequently, rows of leukocytes tumble slowly along the endothelium in a process known as rolling.
In time, the endothelium can be virtually lined by white cells. This appearance is called ++Thereafter, the binding of leukocytes with endothelial cells is facilitated by cell adhesion molecules such as selectins, immunoglobulins, integrins, etc which result in adhesion of leukocytes with the endothelium.
Neutrophil moving to the site of infection .

B). Transmigration of leukocytes

Leukocytes escape from venules and small veins . The movement of leukocytes by extending pseudopodia through the vascular wall occurs by a process called diapedesis .

C). Chemotaxis:

Chemotaxis is a unidirectional attraction of leukocytes from vascular channels towards the site of inflammation within the tissue space guided by chemical gradients (including bacteria and +cellular debris) .

D) Phagocytosis

Phagocytosis is the process of engulfment and internalization by specialized cells

of particulate material, which includes invading microorganisms,
damaged cells,
and tissue debris. These phagocytic cells include polymorphonuclear leukocytes (particularly neutrophiles), monocytes and tissue macrophages.

Phagocytosis involves three distinct steps.

1). **Recognition and attachment** of the particle to be ingested by the leukocytes:
Phagocytosis is enhanced if the material to be phagocytosed is coated with certain plasma proteins called **opsonins**. These opsonins promote the adhesion between the particulate material and the phagocyte's cell membrane.
2). **Engulfment:** During engulfment, extension of the cytoplasm (pseudopods) flow around the object to be engulfed, eventually resulting in complete enclosure of the particle within the phagosome created by the cytoplasmic membrane of the phagocytic cell and the engulfed particle is exposed to the degradative lysosomal enzymes.
3) **Killing or degradation**
The ultimate step in phagocytosis of bacteria is killing and degradation. There are two forms of bacterial killing.

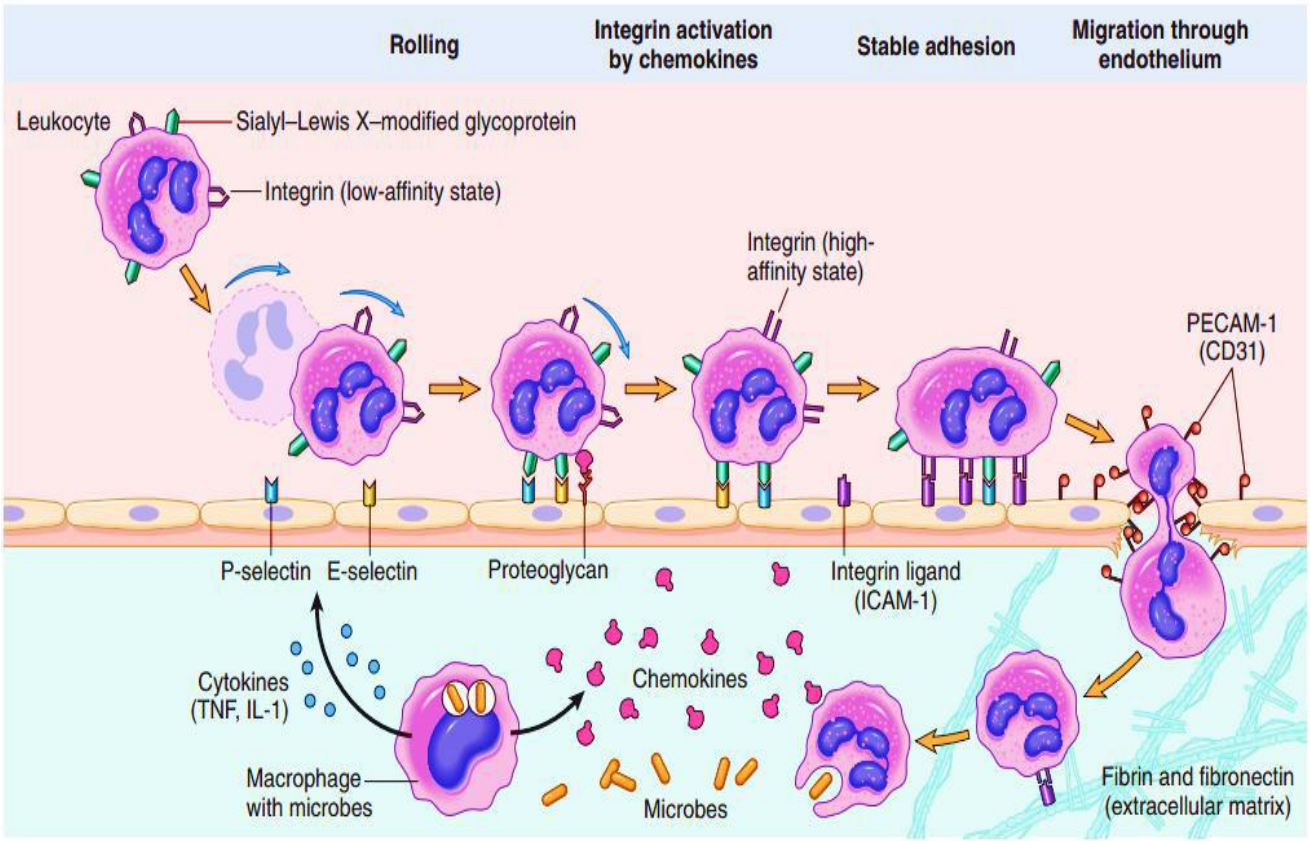


Figure : Mechanisms of leukocyte migration through blood vessels.