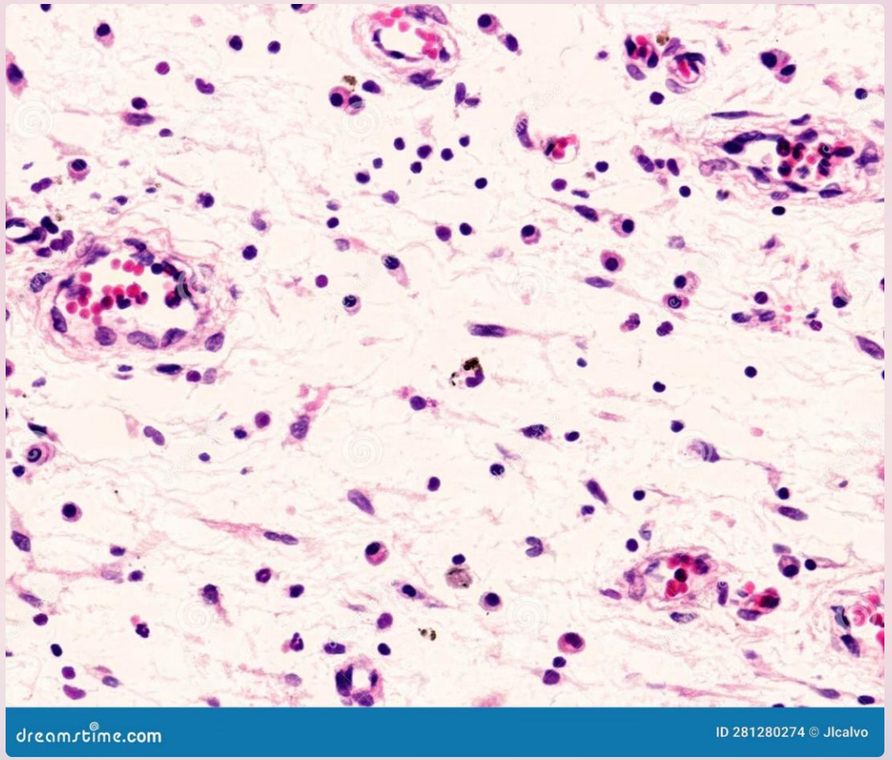
Inflammation

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.

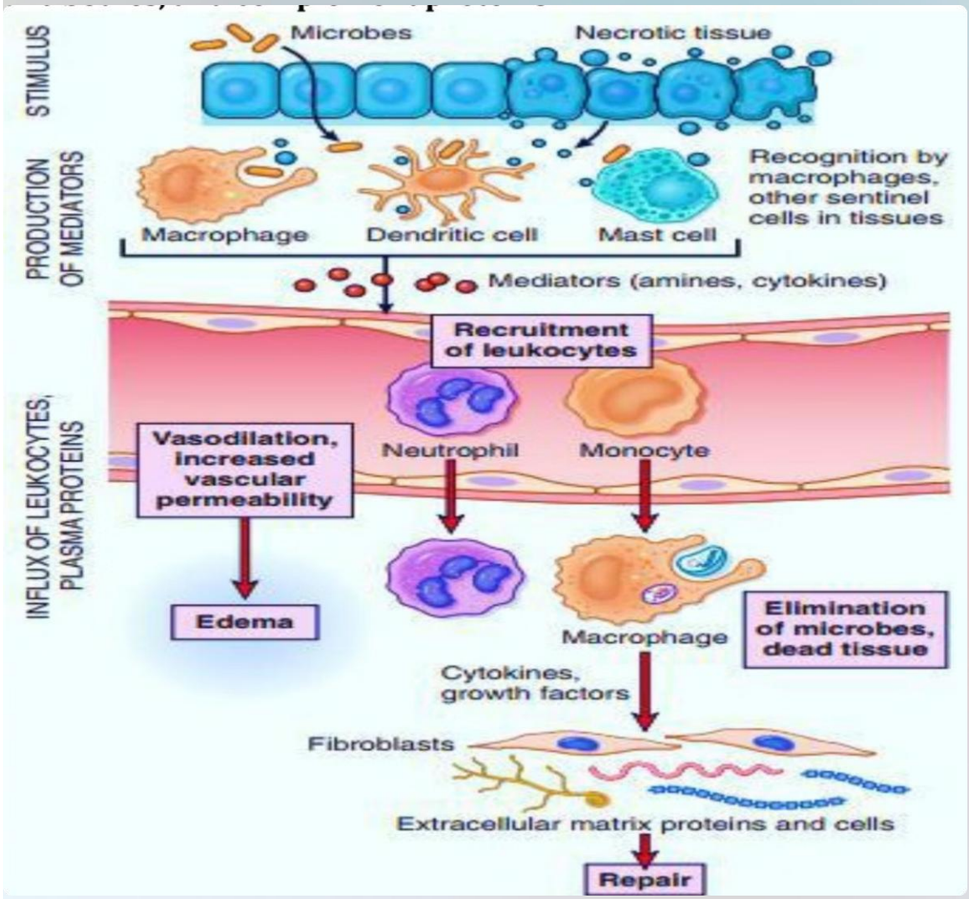
The mediators of defense include phagocytic leukocytes, antibodies, and complement proteins.

Dr. Shaymaa Adil



Understanding Inflammation

Inflammation is a complex biological response that serves as the body's protective mechanism against harmful stimuli. This fundamental process involves the coordinated action of various cellular and molecular components working together to eliminate threats and initiate healing.



Causes of Inflammation

A - Living Causes

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

B - Non Living Causes

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)

Additional Inflammatory Causes

C - Immunological Reactions

Hypersensitivity reactions that trigger inflammatory responses when the immune system overreacts to normally harmless substances.

D - Genetic/Metabolic Disorders

Examples include gout disease, where metabolic dysfunction leads to inflammatory conditions.

The Steps of the Inflammatory Response

01

Recognition of the injurious agent

The body's surveillance system identifies harmful stimuli or tissue damage.

02

Recruitment of leukocytes

White blood cells are mobilized and directed to the site of injury or infection.

03

Removal or destroy of the agent

The offending agents are eliminated through various cellular mechanisms.

04

Regulation (control) of the response

The inflammatory response is carefully controlled to prevent excessive damage.

05

The damaged tissue is repaired

Healing processes restore tissue structure and function.

Types of Inflammation

1 - Acute Inflammation

A rapid response that quickly delivers leukocytes and plasma proteins to sites of injury. This type of inflammation develops within minutes to hours and is characterized by its swift onset and relatively short duration.

2 - Chronic Inflammation

A prolonged inflammatory response that persists for weeks, months, or even years. This type involves different cellular components and can lead to tissue damage and scarring.

The Acute Inflammatory Response

The acute inflammatory response rapidly delivers leukocytes and plasma proteins to sites of injury. This immediate response is crucial for containing damage and eliminating harmful agents before they can spread throughout the body.

The Five Important Signs of Acute Inflammation

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.

Three Major Components of Acute Inflammation

1

(A) Dilation of small vessels

leading to an increase in blood flow.

2

(B) Increased permeability of the microvasculature

enabling plasma proteins and leukocytes to leave the circulation.

3

(C) Emigration of the leukocytes

from the microcirculation, their accumulation in the focus of injury, and their activation to eliminate the offending agent.

Mechanism of Inflammation

A - Tissue reaction

The initial response of tissues to injury or infection.

B - Vascular changes

Modifications in blood vessel structure and function.

C - Cellular response

The mobilization and activation of immune cells.

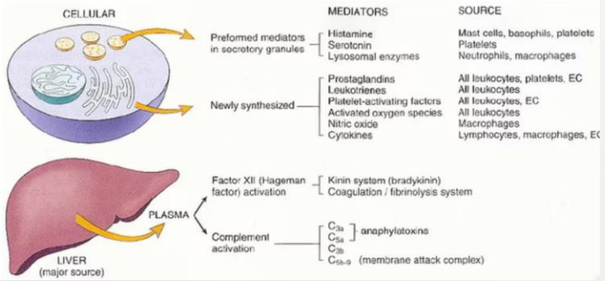
Chemical Mediators of Inflammation

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.

CHEMICAL MEDIATORS OF INFLAMMATION

Definition: Any messenger that acts on blood vessels, inflammatory cells, or other cells to contribute to an inflammatory response. (Pretty much anything...)

- Exogenous
  - Endotoxins
- Endogenous
  - Plasma
  - Leukocytes
  - Endothelial cells
  - Fibroblasts



Vascular Changes in Inflammation

01

Vasoconstriction

in seconds due to neurogenic or chemical stimuli

02

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 **heat**, 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**.

03

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

Components of Inflammatory Responses

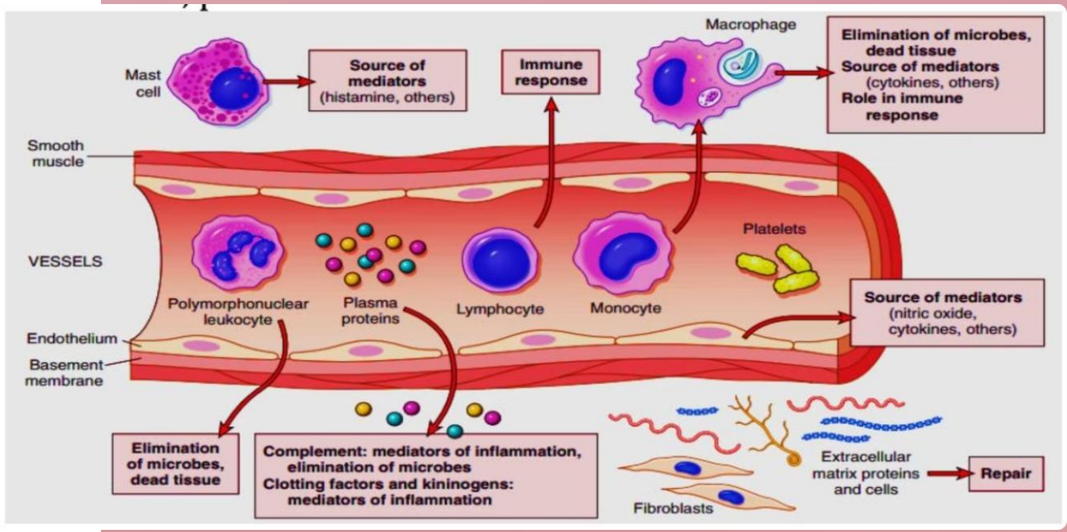


Figure –1: The components of acute and chronic inflammatory responses and their principal functions.

Cellular Response Overview

3 - Cellular response:

The cellular response has the following stages:

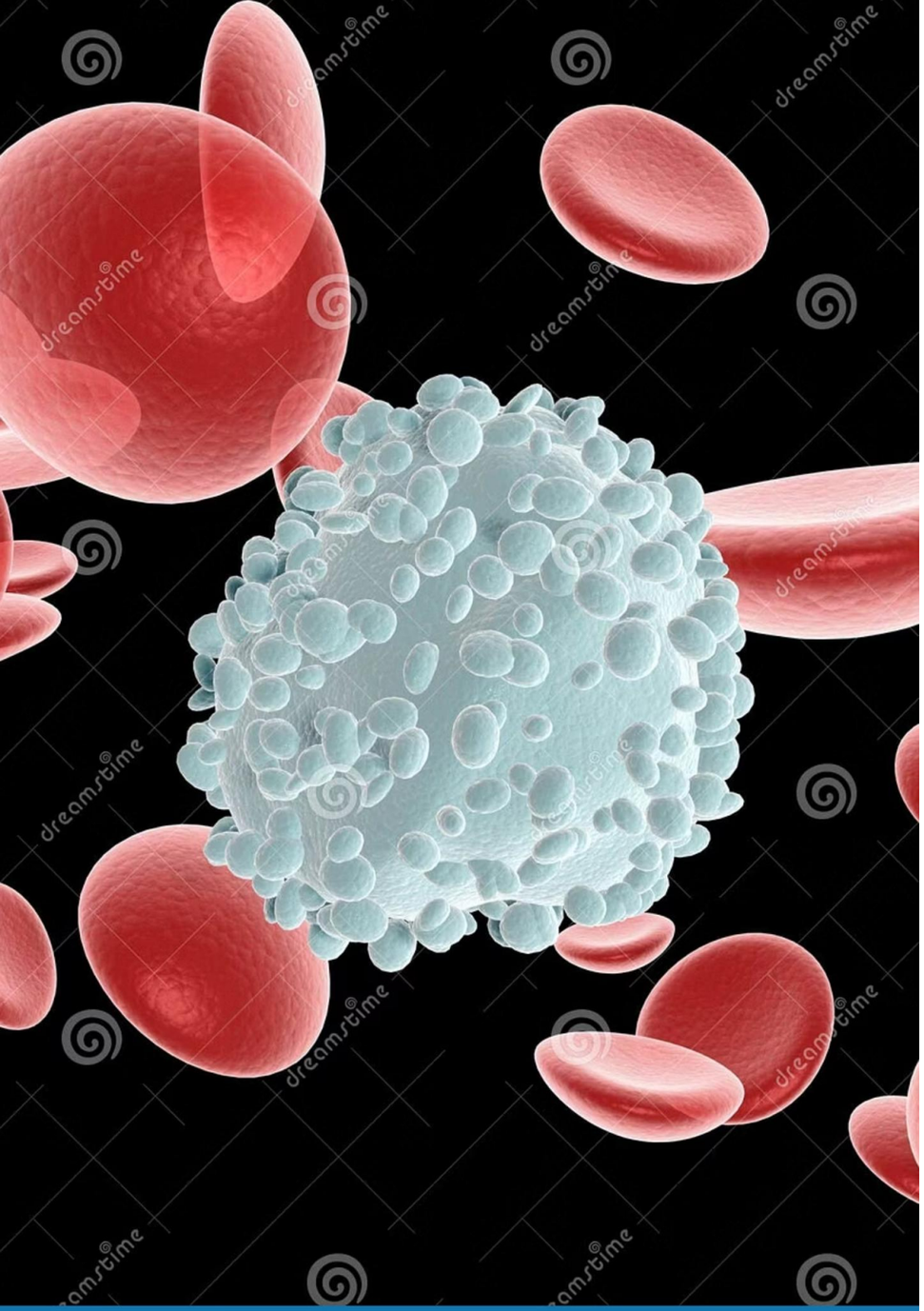
A. Migration, rolling, adhesion of leukocytes

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**.

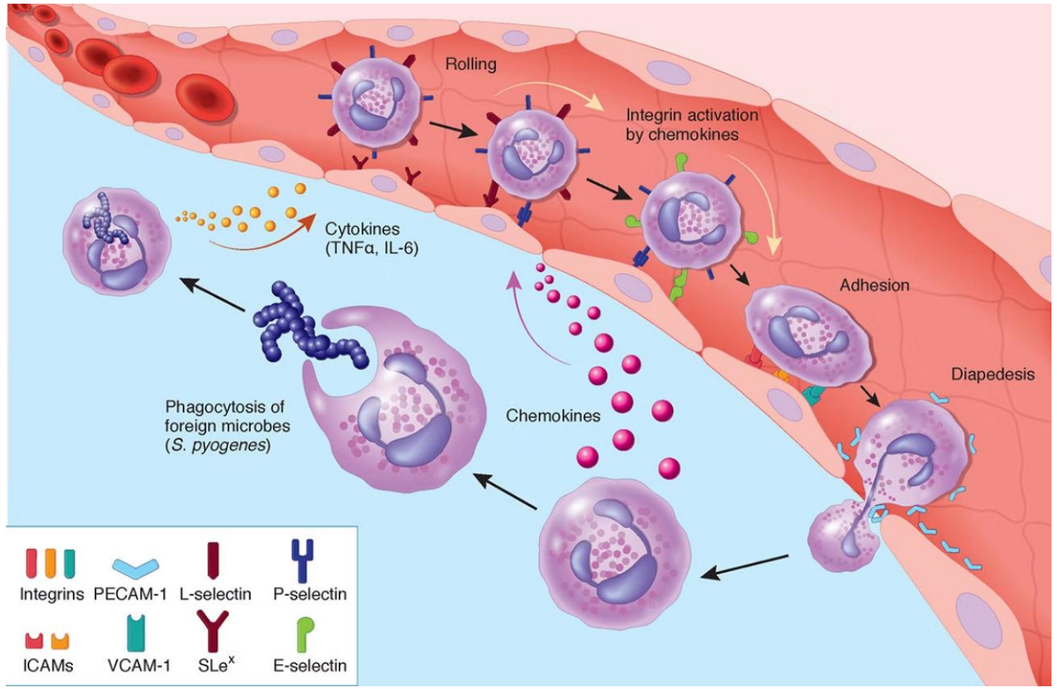
In time, the endothelium can be virtually lined by white cells. This appearance is called ++

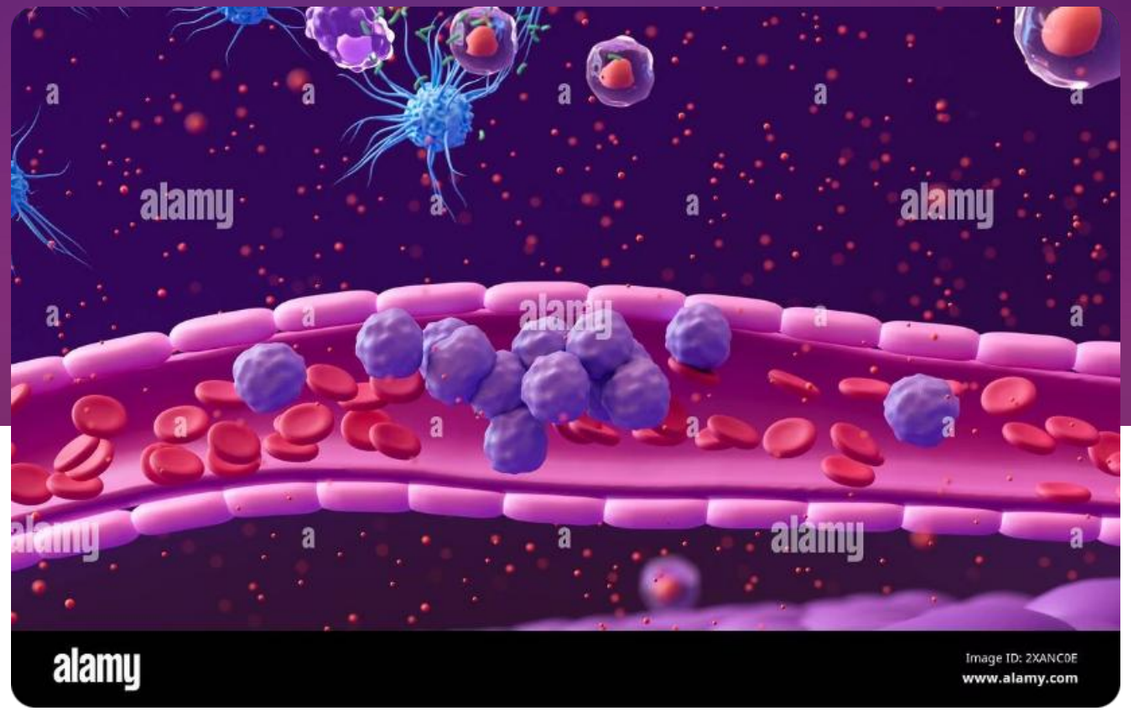
Thereafter, the binding of leukocytes with endothelial cells is facilitated by cell adhesion molecules such as selectins, immunoglobulins, integrins, etc which result in adhesion of leukocytes with the endothelium. Neutrophil moving to the site of infection

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**.

This critical step allows immune cells to leave the bloodstream and enter the tissue where they are needed to combat infection or injury.

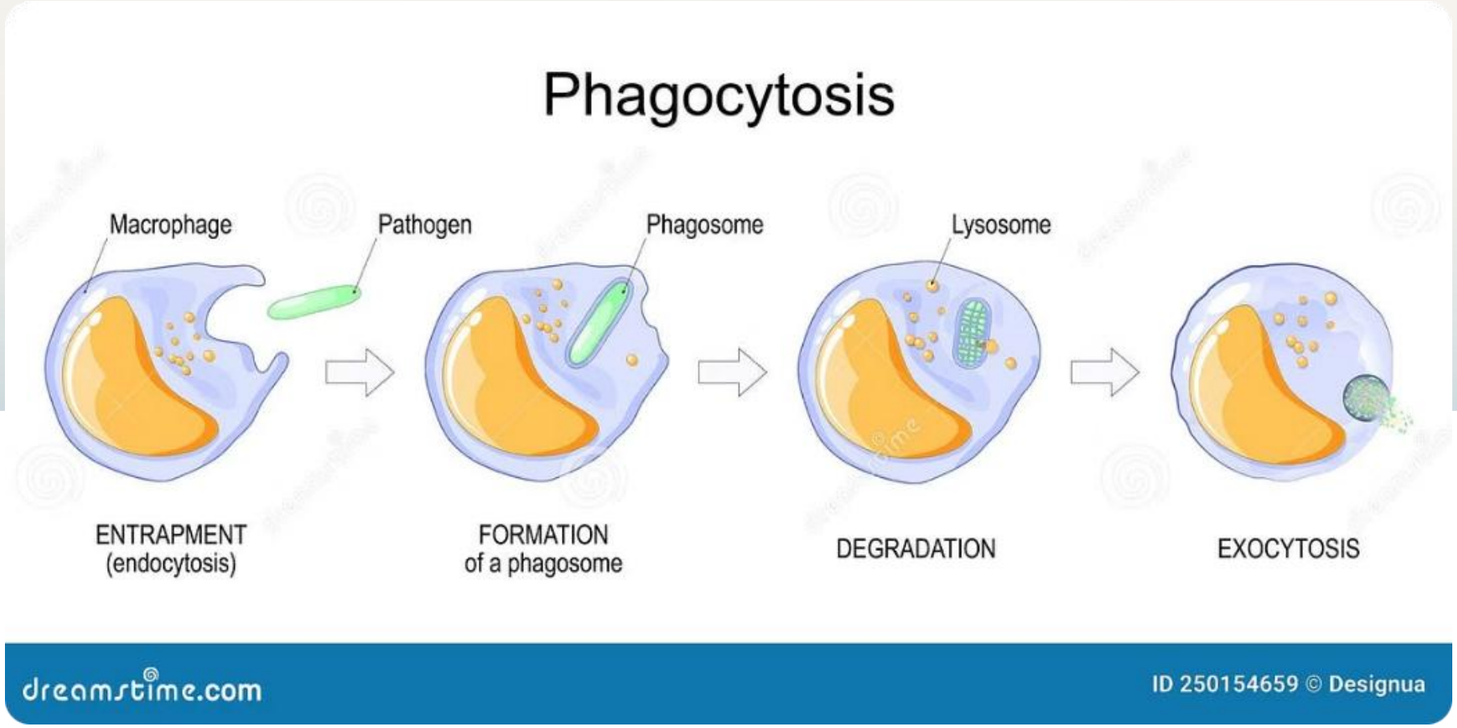




C) Chemotaxis

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).

This process ensures that immune cells are directed precisely to where they are needed most, following molecular signals that indicate the presence of harmful agents or tissue damage.



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 neutrophils), monocytes and tissue macrophages.

Three Distinct Steps of Phagocytosis

1) Recognition and attachment

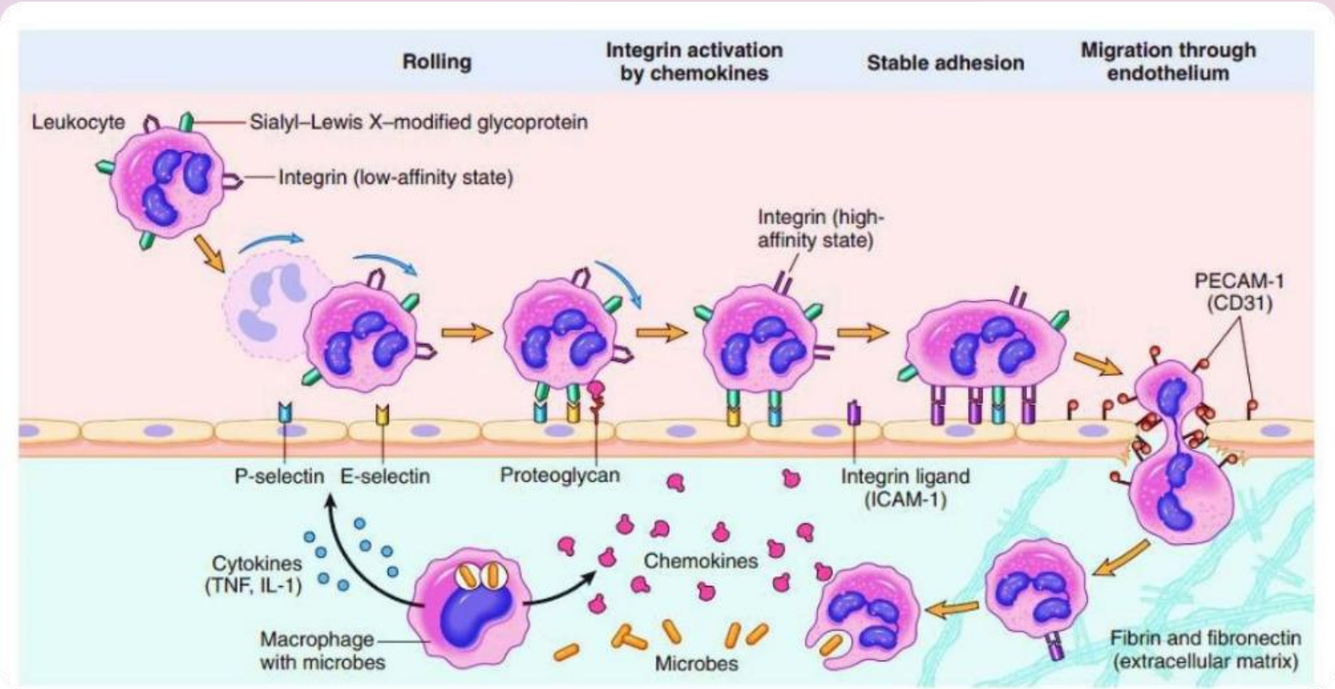
of the particle to be ingested by the leukocytes: Phagocytosis is enhanced if the material to be phagocytosed is coated with certain plasma proteins called **opsonins**. These opsonins promote the adhesion between the particulate material and the phagocyte's cell membrane.

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.



Mechanisms of Leukocyte Migration

Figure: Mechanisms of leukocyte migration through blood vessels.

This comprehensive diagram illustrates the complete process by which leukocytes navigate from the bloodstream to sites of inflammation, demonstrating the coordinated cellular and molecular events that make effective immune responses possible.