SNS COLLEGE OF ALLIED HEALTH SCIENCES

SNS Kalvi Nagar, Coimbatore - 35

Affiliated to Dr MGR Medical University, Chennai

DEPARTMENTOF OPERATION THEATRE AND ANAESTHESIA TECHNOLOGY

COURSE NAME: PATHOLOGY I YEAR

UNIT II: INFLAMMATION

INFLAMMATION

- **Immune system – defence against agents**
- **Inflammation – immune response**
- **injury – damage**
- **Platelets – a cell fragment involved in clotting**
- **Leukocytes – white blood cells for defence mechanism**
- **Lymphocytes – a small leukocytes in lymphatic system**
- **Granulation tissue – formation of new connective tissue and tiny blood vessels for healing**

Inflammation

- **Inflammation** is a process by which the body's white blood cells protect the body from infection from outside invaders, such as bacteria and viruses.

- It is a body **defense reaction** in order to eliminate or limit the spread of injurious agent.

Inflammation

- Ultimate goal is get rid of initial cause of cell injury (microbes, toxins)
- Consequences of such injury causes necrosis
- Without inflammation wounds go unchecked and it will never heal

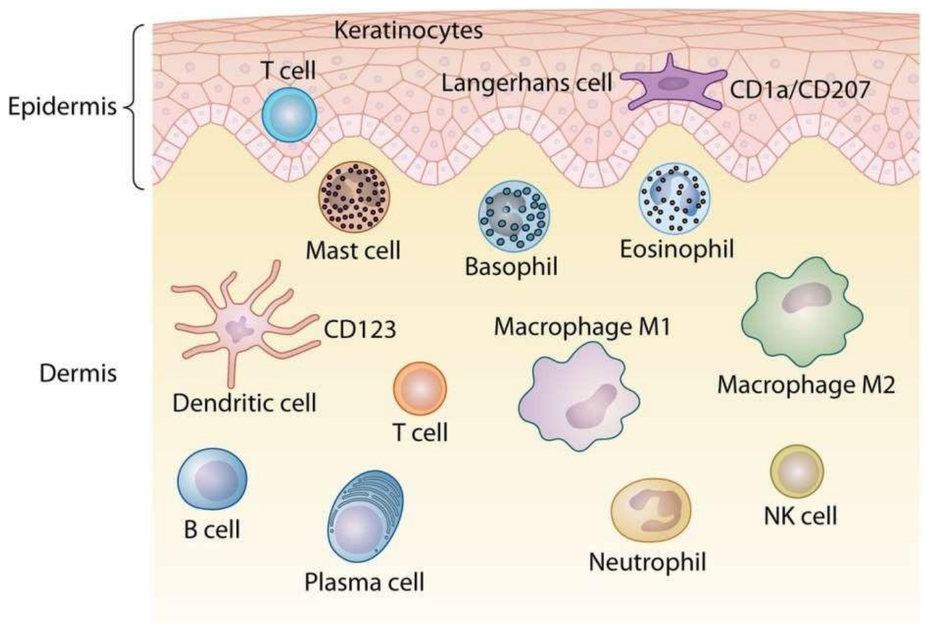
Inflammatory Agents

***Infective agents* like,**

- Bacteria
- viruses and their toxins
- fungi
- Parasites

***Immunological agents* like,**

- cell-mediated
- antigen antibody reactions



Inflammatory agents

***Physical agents* like,**

- Heat
- Cold
- Radiation
- Mechanical trauma.

***Chemical agents* like,**

- organic
- inorganic poisons.

***Inert materials* such as foreign bodies**

Signs of Inflammation

Types of Inflammation

•Depending upon the defense capacity of the host and duration of response, Inflammation can be classified as **acute and chronic.**

Acute Inflammation:

- Short duration
- Represents early body reaction – followed by healing.

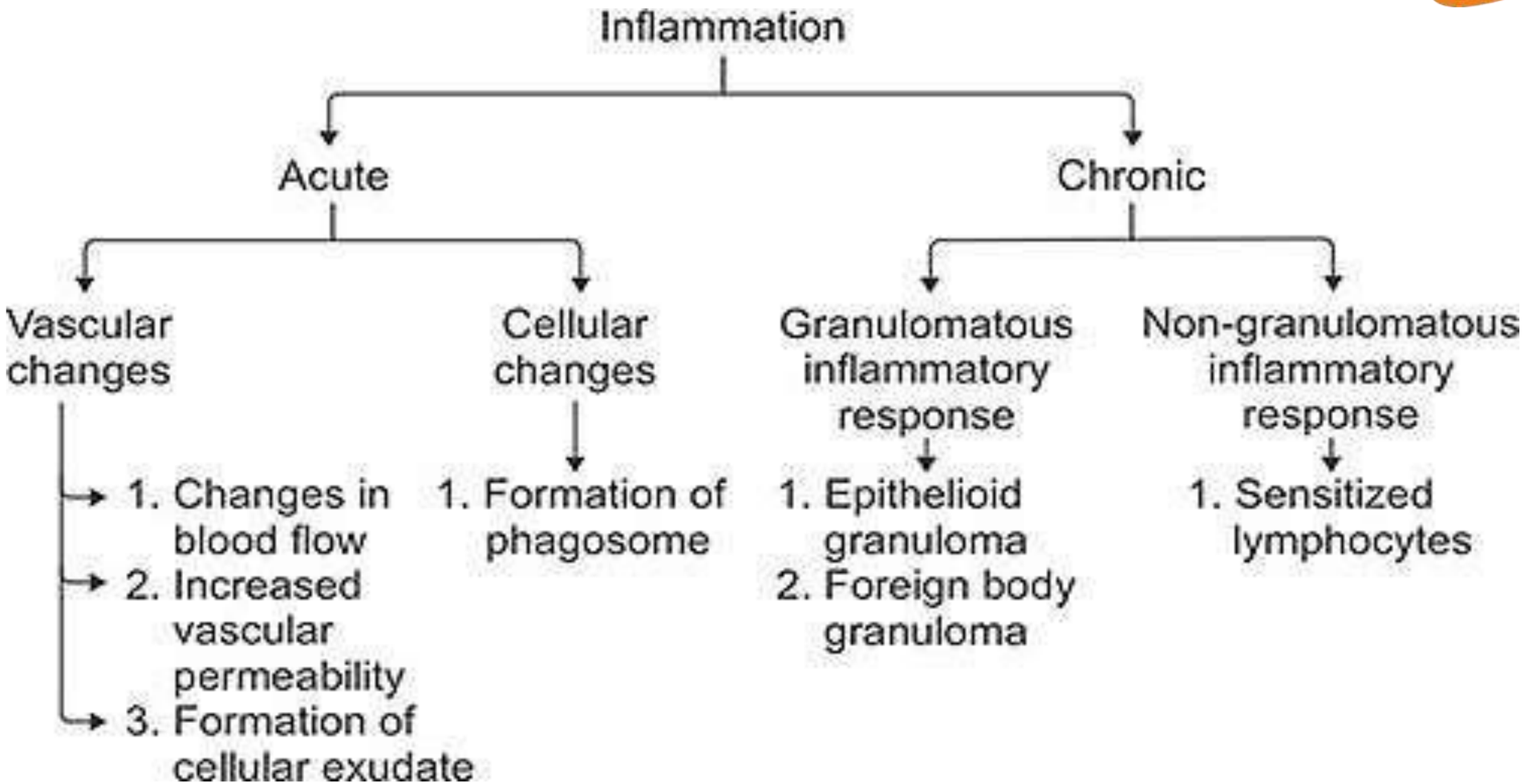
Chronic Inflammation:

- Long duration
- Causative agent of acute inflammation lasts for a long time .

Features of Acute inflammation

- Accumulation of fluid and plasma at the affected site
- Intravascular activation of platelets
- Polymorphonuclear neutrophils as inflammatory cells.

ACUTE INFLAMMATION



Acute inflammation

Acute inflammation is divided into,

Vascular event

Cellular event

Vascular event is further divided into,

Haemodynamic changes

Changes in vascular permeability

VASCULAR EVENT

- Hemodynamic change – ***change in blood flow and calibre of small vessel in injured tissue***

Sequence of events:

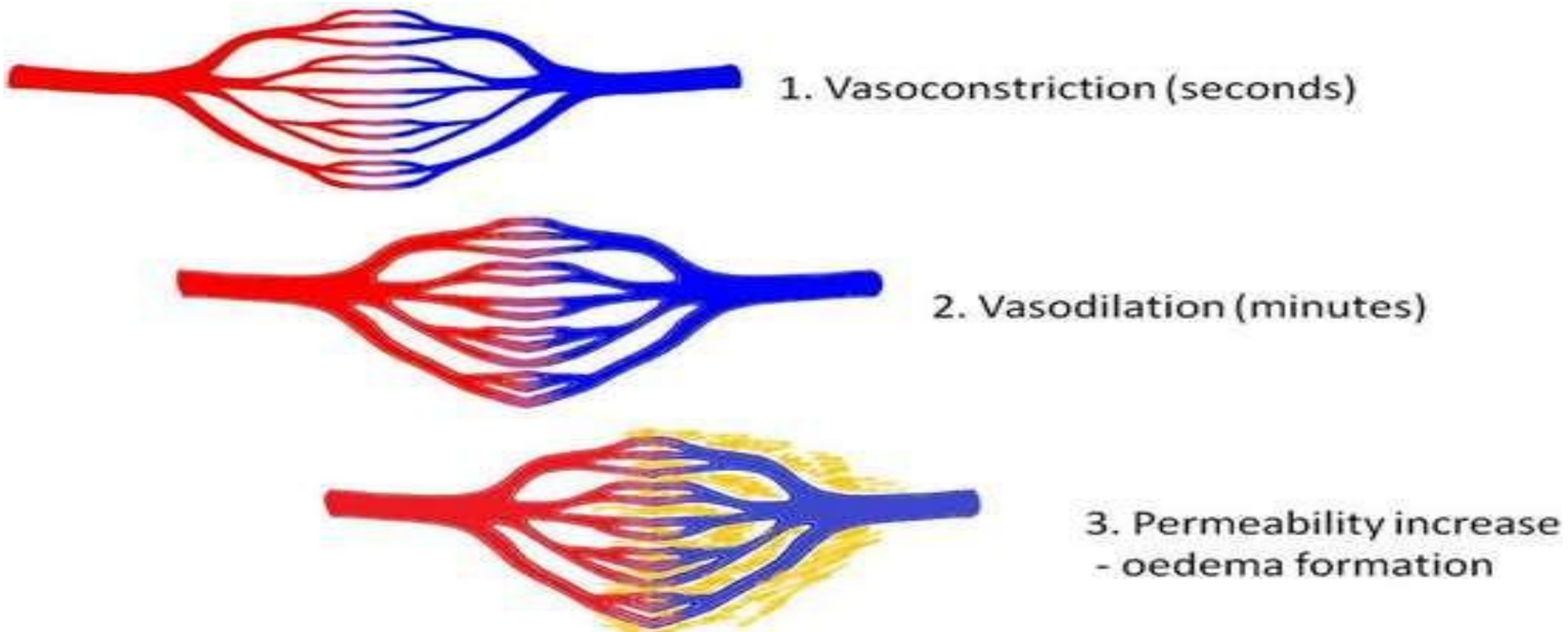
- **Transient vasoconstriction** of arterioles (mild – blood flow established in 3 – 5 seconds, severe – 5 minutes).

- **Persistent progressive vasodilatation** in arterioles, increases microvascular circulation ---causes **redness and warmth** at the site of acute inflammation. It occurs within half an hour of injury.

- **Elevated Local hydrostatic pressure** resulting in transudation of fluid into the extracellular space. This is responsible for **swelling** at the local site of acute inflammation.

Hemodynamic changes

- **Slowing or stasis** of microcirculation causes increased concentration of red cells and raised blood viscosity
- **Leucocytic margination.**

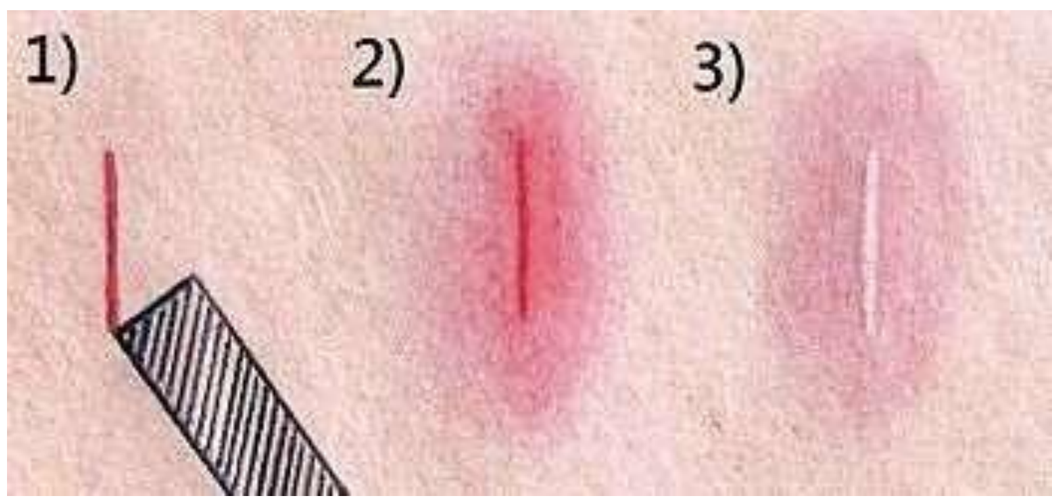


Lewis experiment

Lewis induced the changes in the skin of inner aspect of forearm by firm stroking with a blunt point

It is called as ***triple response*** **or** ***red line response***

The response are ***redline , flare and wheal***



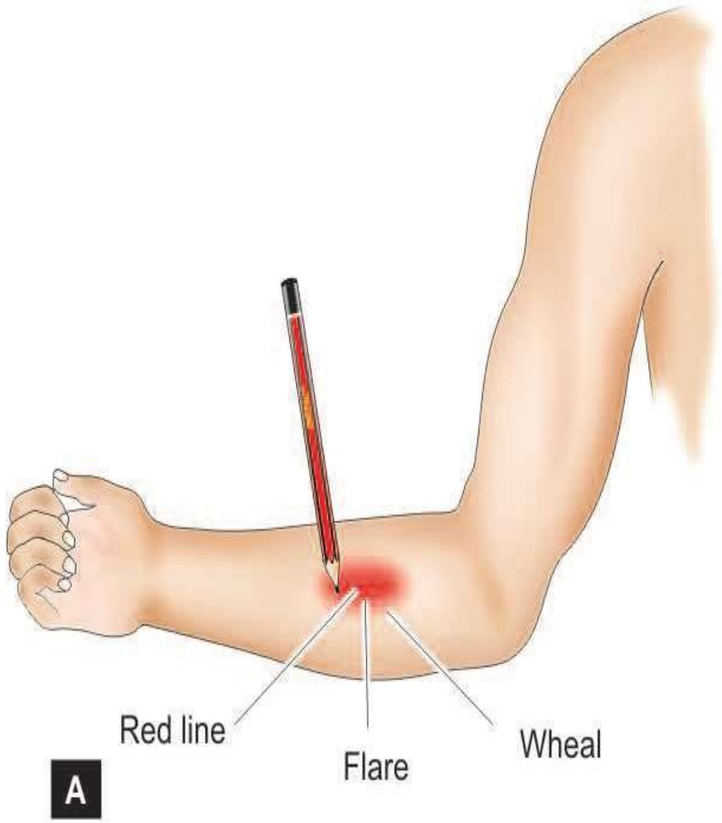
Lewis experiment

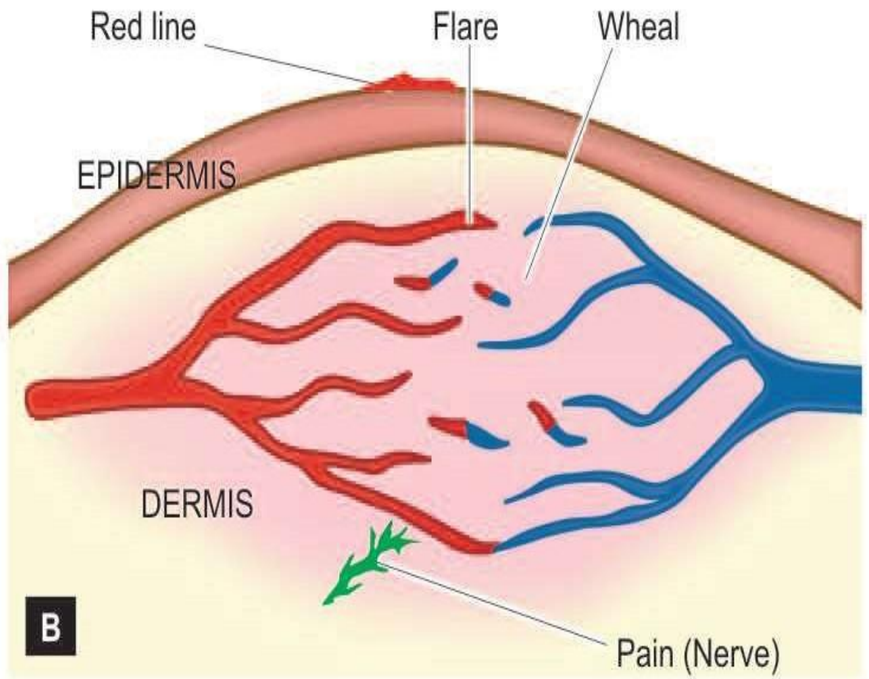
- ***Red line*** appears within a few seconds following stroking and is due to local **vasodilatation** of capillaries and venules.

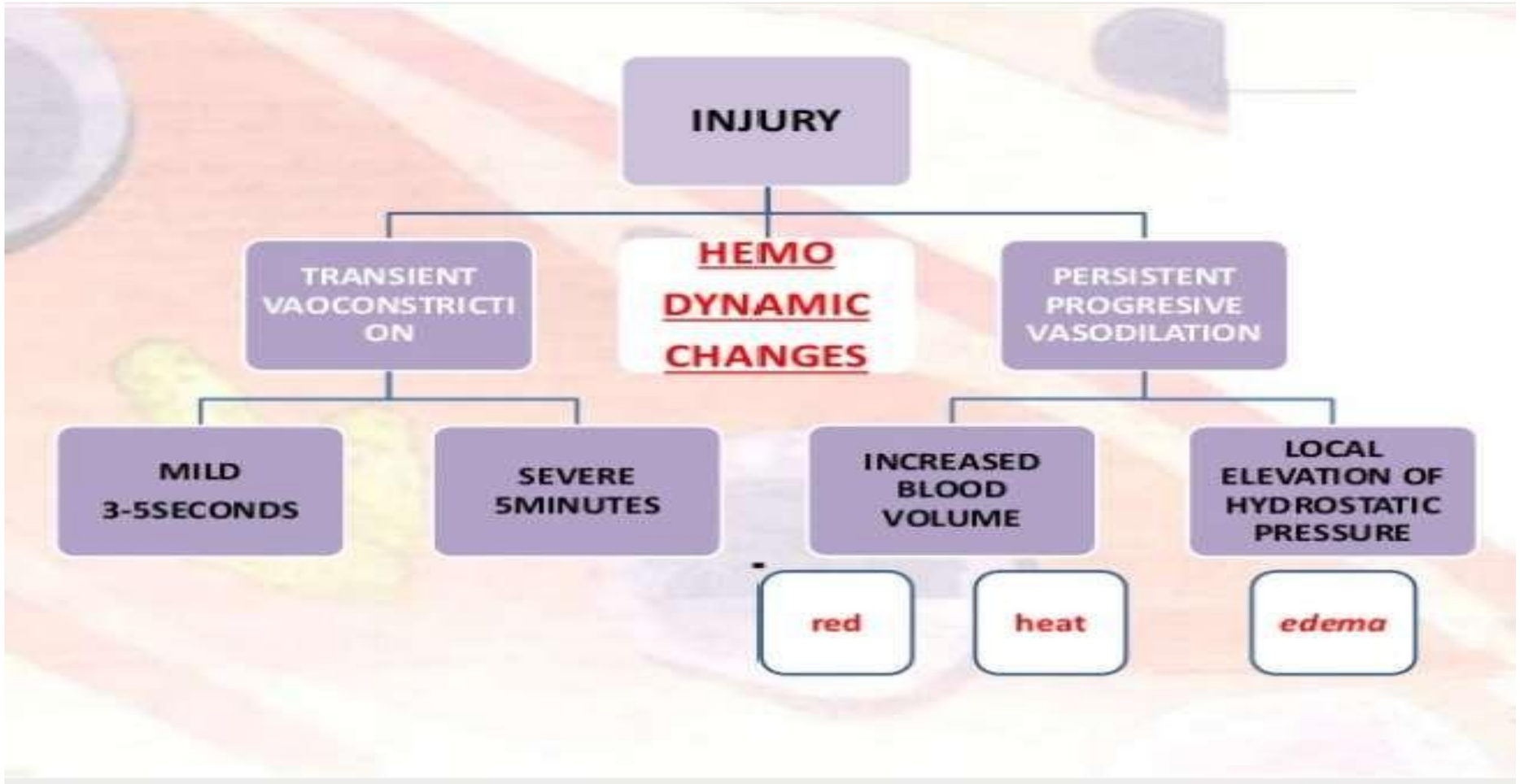
- ***Flare*** is the bright reddish appearance or flush surrounding the red line and results from vasodilatation of the adjacent arterioles.

- ***Wheal*** is the swelling or oedema of the surrounding skin occurring due to **transudation of fluid** into the extravascular space

Lewis experiment






INJURY
HEMO DYNAMIC CHANGES
TRANSIENT VAOCONSTRICTION
PERSISTENT PROGRESIVE VASODILATION
MILD 3-5SECONDS
SEVERE 5MINUTES
INCREASED BLOOD VOLUME
LOCAL ELEVATION OF HYDROSTATIC PRESSURE
red
heat
edema

Changes in vascular permeability

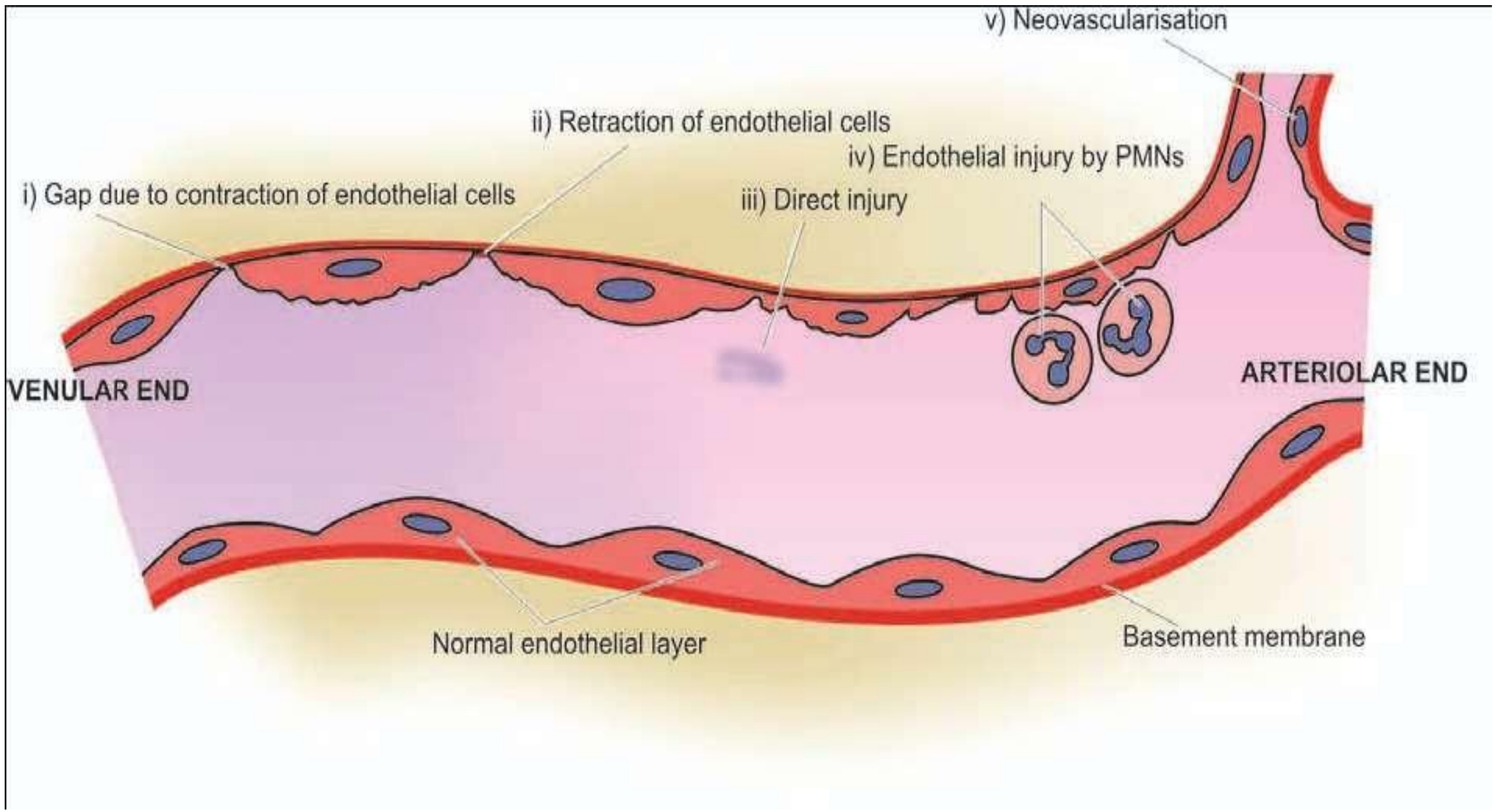
- The inflammatory oedema occurs because of increased vascular permeability, which is explained by **Starling's hypothesis.**

It states that,

- Forces that cause **outward movement** of fluid from microcirculation are *intravascular hydrostatic pressure* and *colloid osmotic pressure of interstitial fluid*.

- Forces that cause **inward movement** of interstitial fluid into circulation are *intravascular colloid osmotic pressure* and *hydrostatic pressure of interstitial fluid*.

Mechanism of vascular permeability



Mechanism of vascular permeability

- **Contraction of endothelial cells** – creates a gap between the endothelial cell that leads to vascular leakiness

- It is mediated by the release of **histamine, bradykinin and other chemical mediators.**

- The response begins immediately after injury, is usually reversible, and is for short duration (15-30 minutes).

Mechanism of vascular permeability

- **Retraction of endothelial cells -** structural re-organisation of the cytoskeleton of endothelial cells causes reversible retraction

- It is mediated by cytokines such as i**nterleukin-1 (IL-1) and tumour necrosis factor (TNF)-α.**

- The onset of response takes 4-6 hours after injury and lasts for 2-4 hours

Mechanism of vascular permeability

- **Direct injury to endothelial cells -** causes cell necrosis and appearance of physical gaps at the sites of detached endothelial cells.

- The permeability will be immediate or delayed and lasts for 2 – 12 hours or even days

Mechanism of vascular permeability

Endothelial injury mediated by leucocytes

Adherence of leukocytes to the endothelium

↓

Activation of leucocytes

↓

Release proteolytic enzymes and toxin

↓

Endothelial injury

↓

Vascular leakiness

Mechanism of vascular permeability

- **Leakiness in neovascularisation** the newly formed capillaries under the influence of **vascular endothelial growth factor (VEGF)** during the process of repair and in tumours are excessively leaky.

Cellular events

The cellular phase of inflammation consists of 2 processes:

- **Exudation of leucocytes**
- **Phagocytosis**

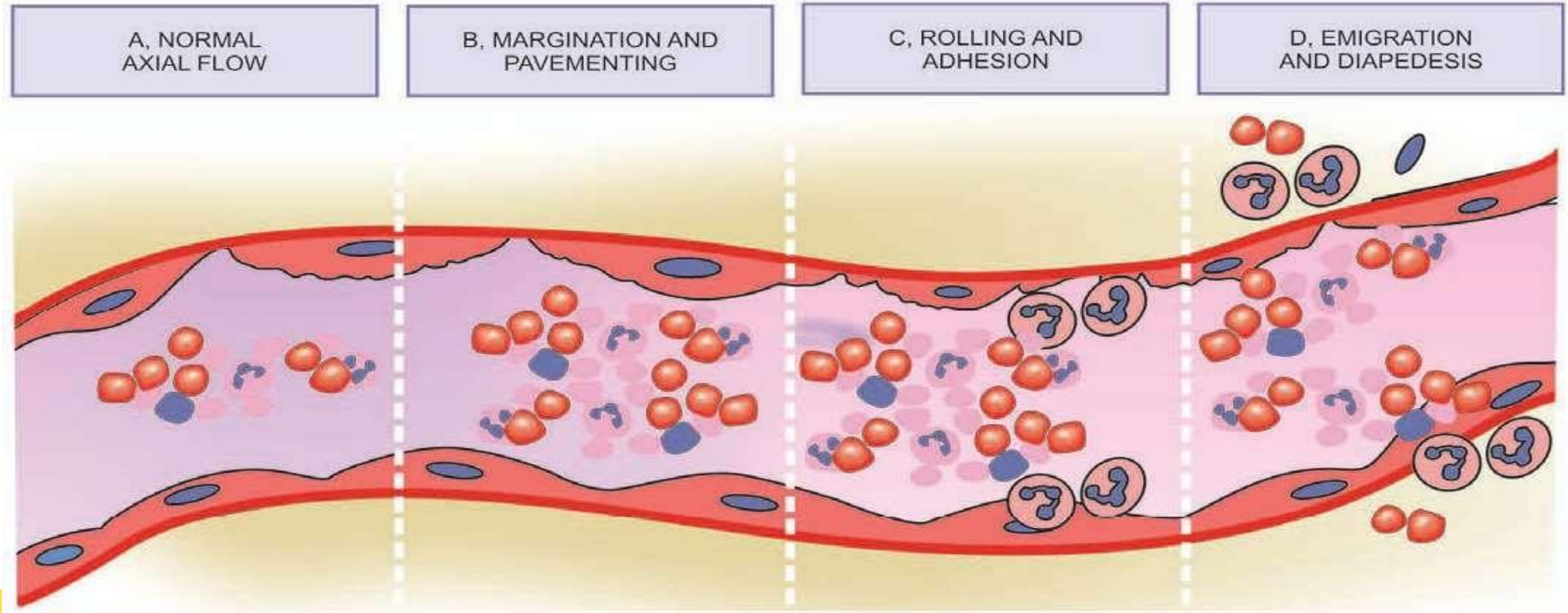
Exudation of Leukocytes

- The escape of fluid , proteins and the blood cells from the vascular system into the interstitial tissue or body cavity

The changes leads to this migration are,

- **Changes in formed elements**
- **Rolling and adhesion**
- **Emigration**
- **Chemotaxis**

Exudation of Leukocytes



Changes in formed elements

- **Normal axial flow**
  - cells at centre
  - plasma at periphery
- **Changes in normal axial flow**
  - narrowing of plasma due to exudation (known as **margination**)
  - Neutrophils come to vessel wall called **Pavementing.**

Rolling and Adhesion

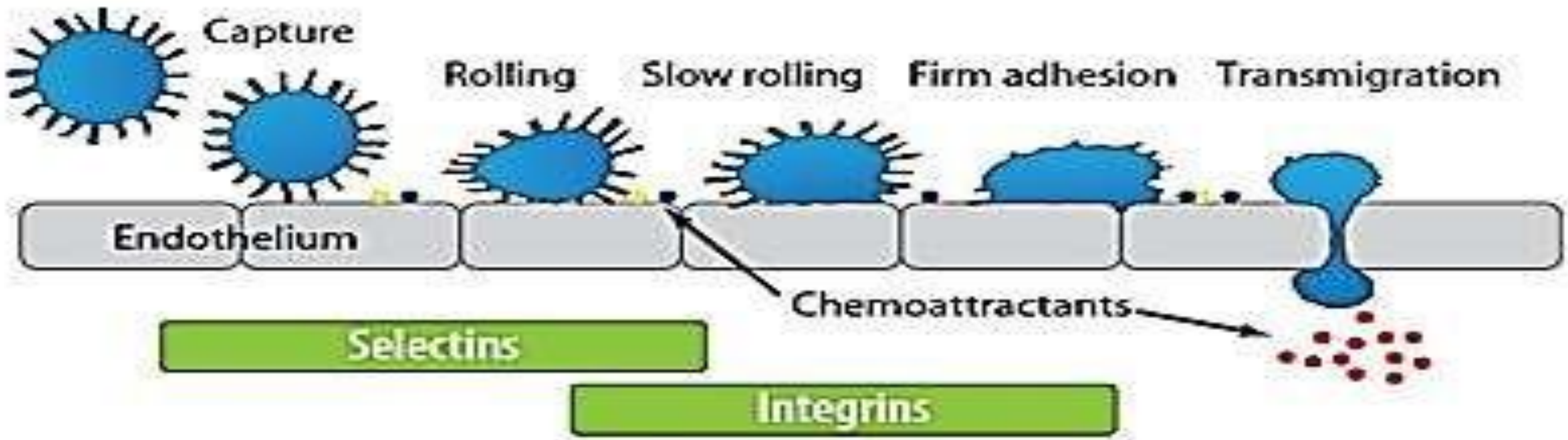
- **Rolling phase** – the Pavemented neutrophils slowly roll over the endothelial cells lining vessel wall
- Transient bond between the leucocytes and endothelial cells becoming firmer **(adhesion phase)**
- **The molecules helps in rolling and adhesion are, selectins, integrins and Immunoglobulin gene superfamily adhesion molecule**

Rolling and Adhesion

- **Selectins** on the surface of activated endothelial cells
- Recognize the carbohydrates on neutrophils **(s-Lewis X molecule)**
- homing of circulating lymphocytes to the endothelial cells

Rolling and Adhesion

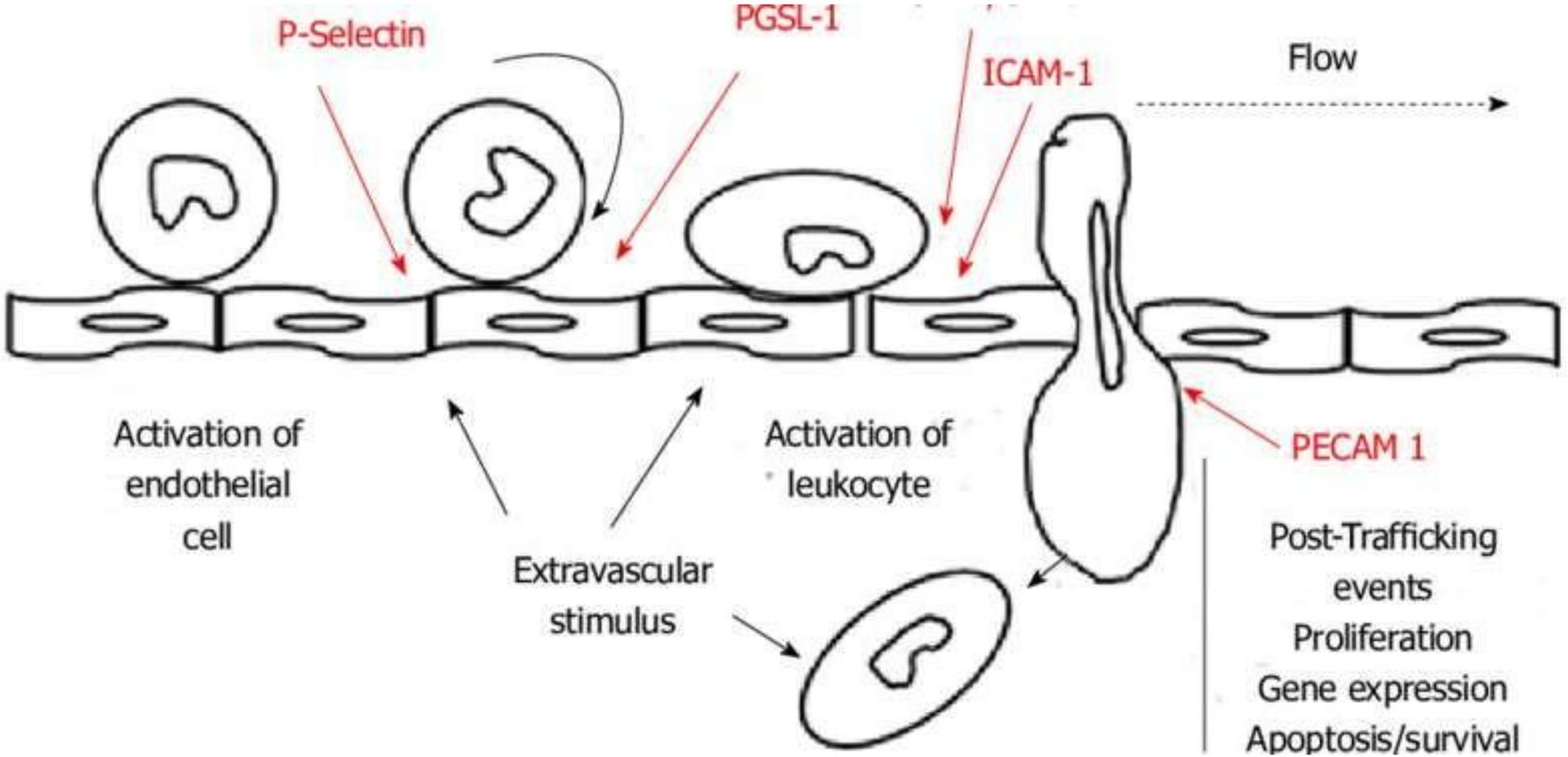
- **Integrins** on the endothelial cell surface are activated during the process of loose and transient adhesions between endothelial cells and leucocytes.



Rolling and Adhesion

- **Immunoglobulin gene superfamily adhesion molecule** such as **intercellular adhesion molecule-1 (ICAM-1)** and **vascular cell adhesion molecule-1 (VCAM-1)** allow a tighter adhesion

- **Platelet-endothelial cell adhesion molecule- 1 (PECAM-1)** may also be involved in leucocyte migration from the endothelial surface.


P-Selectin
PGSL-1
ICAM-1
Flow
Activation of endothelial cell
Activation of leukocyte
PECAM 1
Extravascular stimulus
Post-Trafficking events
Proliferation
Gene expression
Apoptosis/survival

EMIGRATION

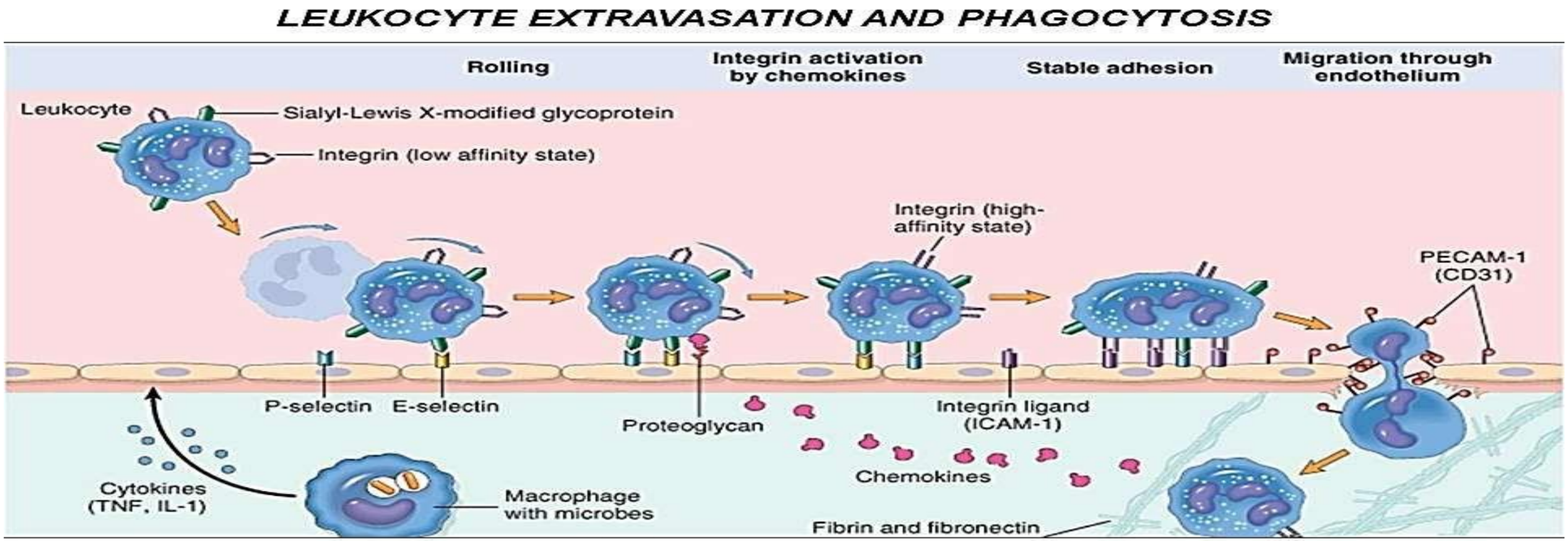
- After sticking of neutrophils to endothelium,
- The former move along the endothelial surface till a suitable site between the endothelial cells is found where the neutrophils throw out cytoplasmic pseudopods.
- Cross the basement membrane by damaging it locally – collagenases and escape out into the extravascular space - ***emigration***

chemotaxis

- After extravasating from the blood, Leukocytes **migrate toward sites of infection or injury** along a chemical gradient by a process called **chemotaxis**

- They have to cross several barriers - endothelium, basement membrane, perivascular myofibroblasts and matrix.

Summary


LEUKOCYTE EXTRAVASATION AND PHAGOCYTOSIS
Rolling
Integrin activation by chemokines
Stable adhesion
Migration through endothelium
Leukocyte
Sialyl-Lewis X-modified glycoprotein
Integrin (low affinity state)
Integrin (high-affinity state)
PECAM-1 (CD31)
P-selectin
E-selectin
Proteoglycan
Integrin ligand (ICAM-1)
Chemokines
Cytokines (TNF, IL-1)
Macrophage with microbes
Fibrin and fibronectin

Phagocytosis

- Phagocytosis is defined as the process of engulfment of solid particulate material by the cells (**cell-eating**).

- The two main phagocytic cells are,
  - Polymorphonuclear neutrophils (PMNs)
  - Macrophages

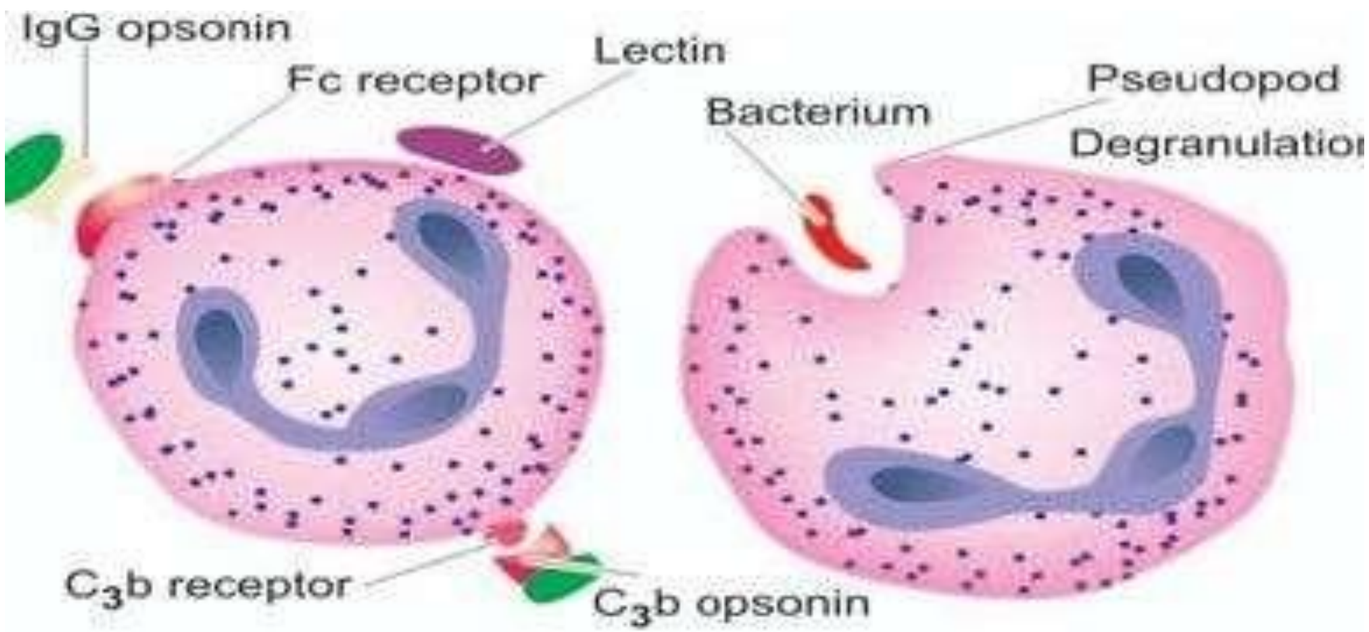
Process of phagocytosis

The microbe undergoes the process of phagocytosis in following 3 steps : –

- **Recognition and attachment**
- **Engulfment**
- **Killing and degradation**

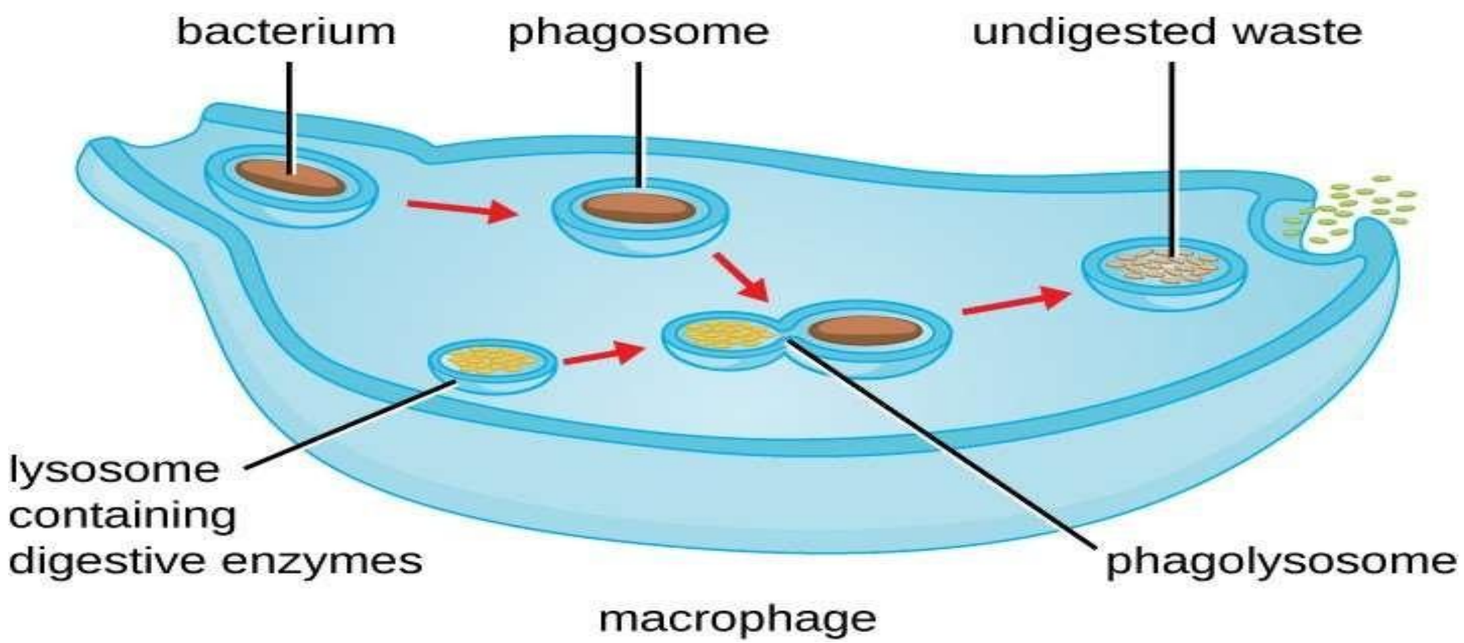
Engulfment

- The opsonised particle bound to the surface of phagocyte is ready to be engulfed. This is accomplished by formation of cytoplasmic pseudopods



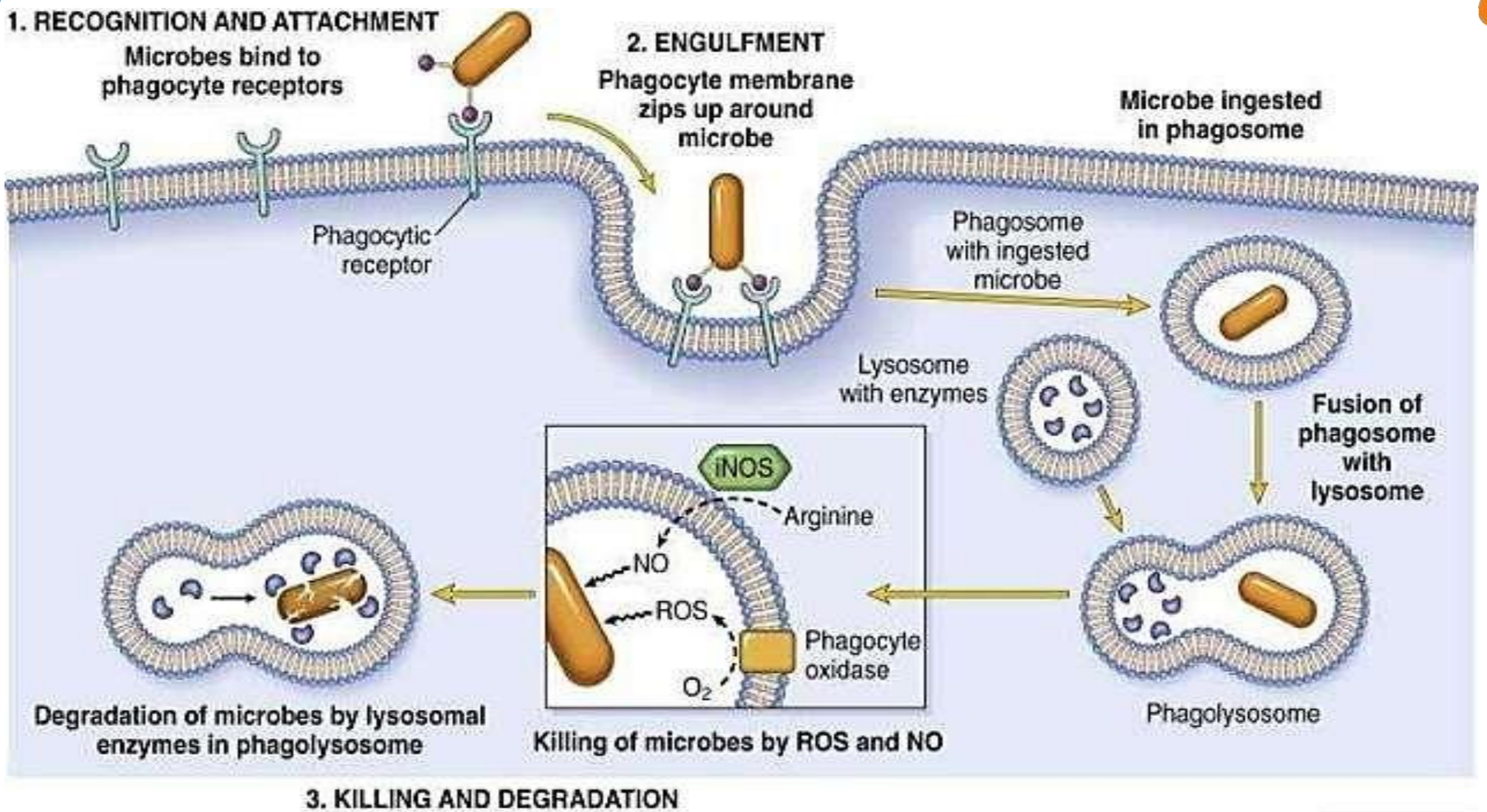
Killing and Degradation

- The cells act as scavenger cells
- The microorganisms after being killed by antibacterial substances are degraded by hydrolytic enzymes.



Disposal of microorganisms

- **Intracellular mechanisms**
  - Oxidative bactericidal mechanism by **oxygen free radicals**
    - MPO-dependent
    - MPO-independent
  - Oxidative bactericidal mechanism by **lysosomal granules**
  - Non-oxidative bactericidal mechanism
- **Extracellular mechanisms**
  - Granules
  - Immune mechanisms


1. RECOGNITION AND ATTACHMENT
Microbes bind to phagocyte receptors
Phagocytic receptor
2. ENGULFMENT
Phagocyte membrane zips up around microbe
Microbe ingested in phagosome
Phagosome with ingested microbe
Lysosome with enzymes
Fusion of phagosome with lysosome
iNOS
Arginine
NO
ROS
O_2
Phagocyte oxidase
Degradation of microbes by lysosomal enzymes in phagolysosome
Killing of microbes by ROS and NO
Phagolysosome
3. KILLING AND DEGRADATION

Outcomes of Acute Inflammation

- **Resolution** – restoration to normal - Limited injury

  Chemical substances neutralization

  Normalization of vascular permeability

  Apoptosis of Inflammatory cells

  Lymphatic drainage

- **Suppuration -** When the pyogenic bacteria causing acute inflammation result in severe tissue necrosis, the process progresses to suppuration. (Abscess formation) and (Calcification)

- **Healing by scar**

- **Progression into chronic inflammation**

Summary of Acute Inflammation

- Acute inflammation - **short duration**
- Divided into **vascular and cellular events**
- Vascular events - **hemodynamic changes** and vascular permeability
- Hemodynamic changes - vasoconstriction and vasodilatation - Lewis experiment
- **Vascular permeability** - inflammatory cells
- Cellular events - **exudation of leukocytes and phagocytosis.**