INFLAMMATION

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PA 4.1

Acute & Chronic inflammation including stimuli, vascular & cellular events

At the end of the session, IInd MBBS students shall be able to

- Define inflammation
- Enumerate causes & cardinal signs
- Classify inflammation
- Difference between acute & chronic inflammation
- Describe vascular & cellular events

INFLAMMATION

Local response of living mammalian tissue to injury due to any agent.

Goal–

a. to eliminate /prevent spread of injurious agent

b. to remove necrotic cells & tissues

c. to initiate the process of repair

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

Stimuli

Physical agents-heat, cold, mechanical trauma

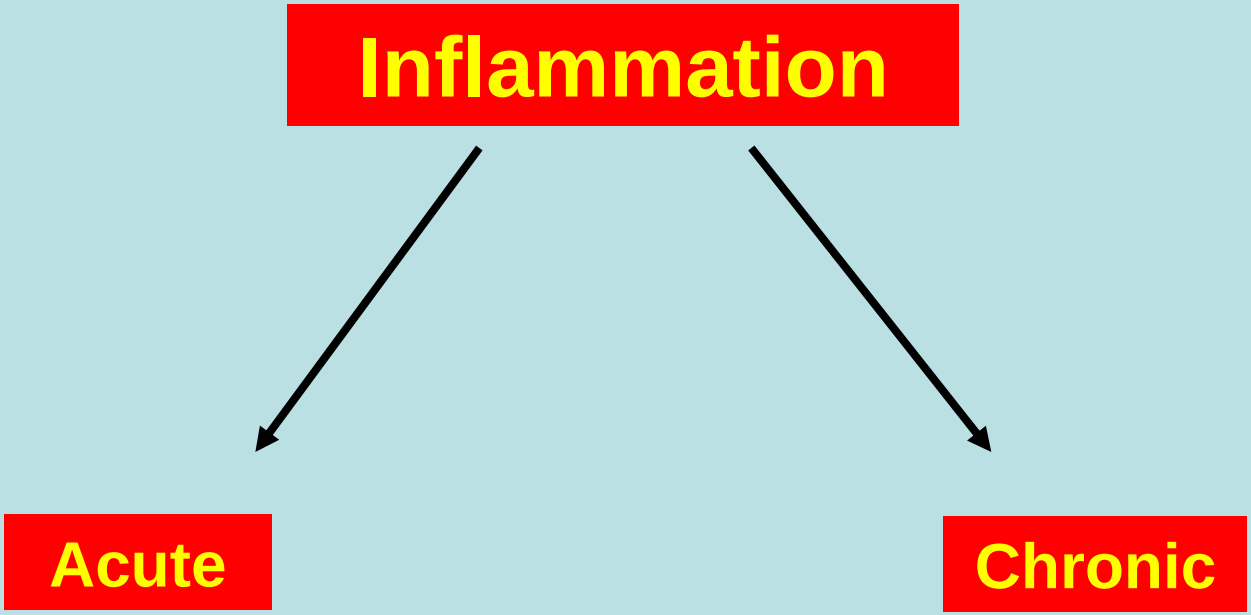
Chemical agents- organic & inorganic poisons

Infective agents- bacteria, viruses, fungi

Immunological agents- CMI,Ag-Ab reactions

Inflammation

- **provoked response to tissue injury**
  - **chemical agents**
  - **cold, heat**
  - **trauma**
  - **invasion of microbes**
- **serves to destroy, dilute or wall off the injurious agent**
- **induces repair**
- ***protective response***
- ***can be potentially harmful***



Acute versus chronic inflammation are distinguished by the duration and the type of infiltrating inflammatory cells

Types

Feature	Acute	Chronic
1.Onset	Rapid – mins to hrs	Insidious- days
2.Cellular Infiltrate	Neutrophils	Lymphocytes,macrophages/ monocytes
3.Tissue injury, Fibrosis	Mild,self limited	Severe ,Progressive
4.Local & systemic signs	Prominent	less
5.Duration	Short(<2 weeks) Resolves quickly	Longer duration

Cellulits = acute skin infection commonly caused by *Streptococcus pyogenes* or *Staphylococcus aureus*

Cardinal signs of (acute) inflammation

- **Rubor = redness**
- **Calor = heat**
- **Dolor = pain**
- **Tumor = swelling**

(described by Celsus 1st. Century AD)

- **Functio laesa = loss of function**

(added by R. Virchow)

The nomenclature used to describe inflammation in different tissues employs the tissue name and the suffix "*-itis*"

e.g

pancreatitis

meningitis

pericarditis

arthritis

Steps of Inflammat0ry Response

- **Recognition of the injurious agent-** by host cells
- **Recruitment of Leukocytes** - from the circulation to the site where the offending agent is located.
- **Removal of agent**-The leukocytes and proteins are activated and work together to destroy and eliminate the offending substance.
- **Regulation of response-**The reaction is controlled and terminated.
- **Repair/Resolution**-The damaged tissue is repaired.

Events in acute inflammation

- Vascular events
  --Haemodynamic changes
  --Altered Vascular permeability
- Cellular events
  --Exudation of leucocytes
  --Phagocytosis

- **Vascular events**

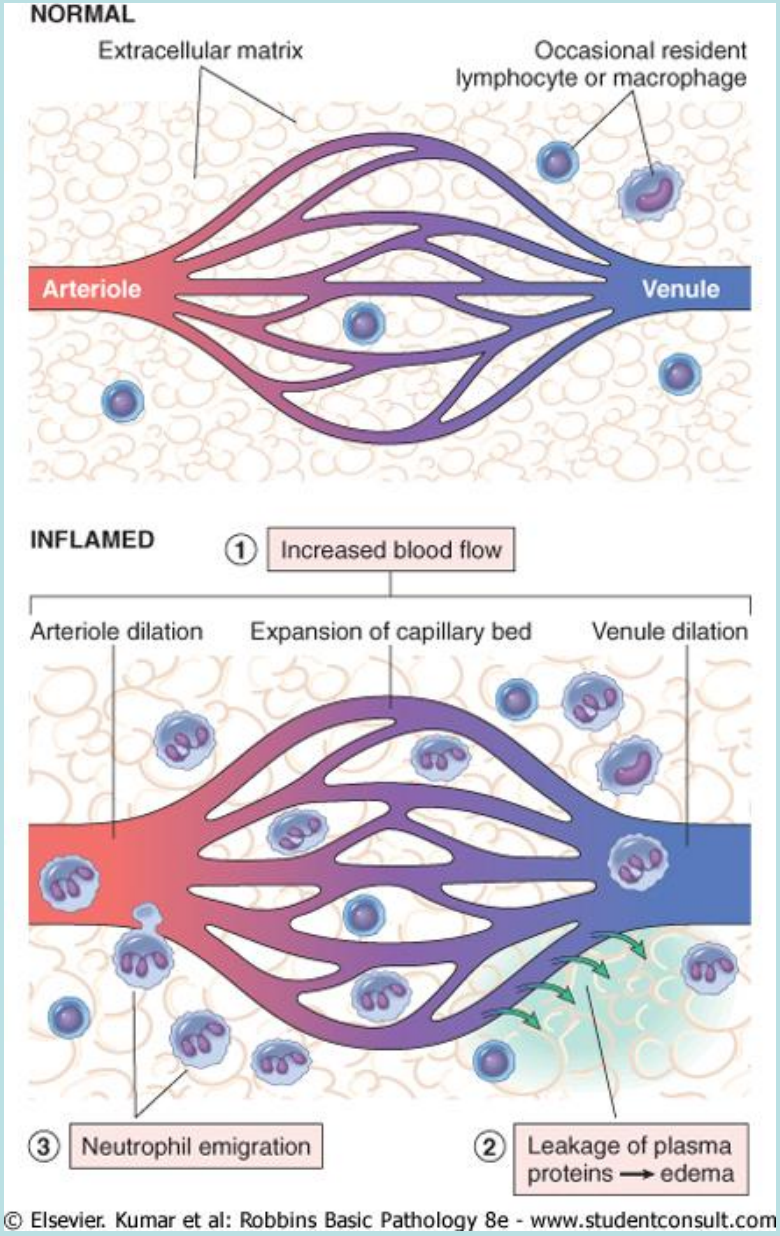
1. **Persistant & progressive vasodilatation**
   (**rubor & calor**)
2. **Increased local hydrostatic pressure →**
   transudation of plasma **(tumor**)
3. **Stasis**
4. **Increased vascular permeability**
   a. Contraction of endothelial cells
   b. Direct injury to endothelial cells
   c. Endothelial injury mediated by leucocytes

Acute inflammation involves:

alteration of vascular caliber
following very brief vasoconstriction (seconds), vasodilation leads to increased blood flow and blood pooling creating redness and warmth (rubor and calor)

changes of microvasculature
increased permeability for plasma proteins and cells creating swelling (tumor). Fluid loss leads to concentration of red blood cells and slowed blood flow (stasis)

emigration of leukocytes from microcirculation
due to stasis and activation leads migration towards offending agent



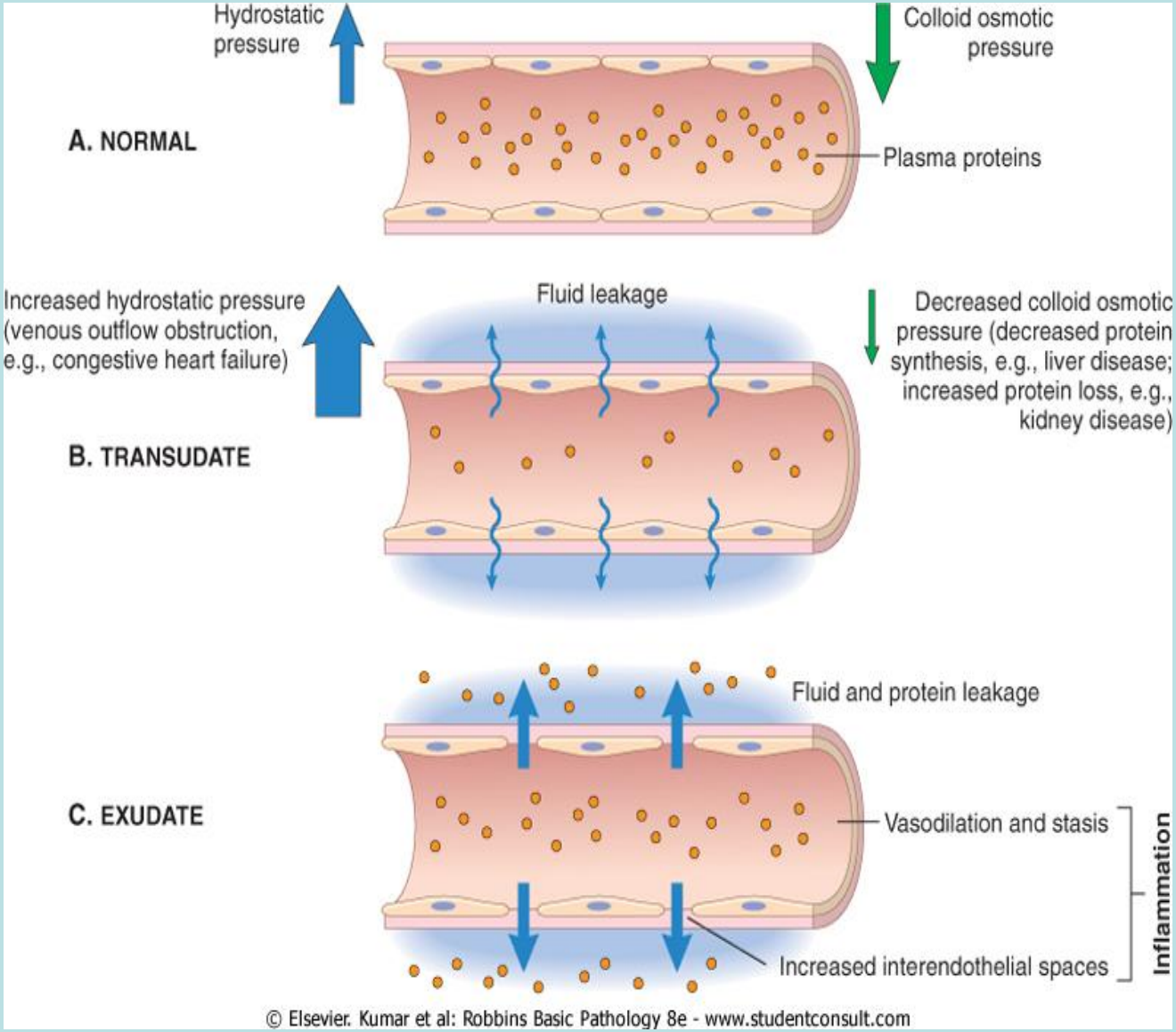
Vascular changes and fluid leakage during acute inflammation lead to *Edema* in a process called *Exudation*

Transudate

- **result of hydrostatic or osmotic imbalance**
- ultrafiltrate of plasma
- Low protein content
- **specific gravity < 1.015**

Exudate

- **result of inflammation**
- vascular permeability ↑
- high protein content
- **specific gravity >1.020**



Increased vascular permeability and edema: a hallmark of acute inflammation

1. Endothelial cell contraction.
2. Direct endothelial injury causing necrotic cell death
3. Leukocyte dependent injury

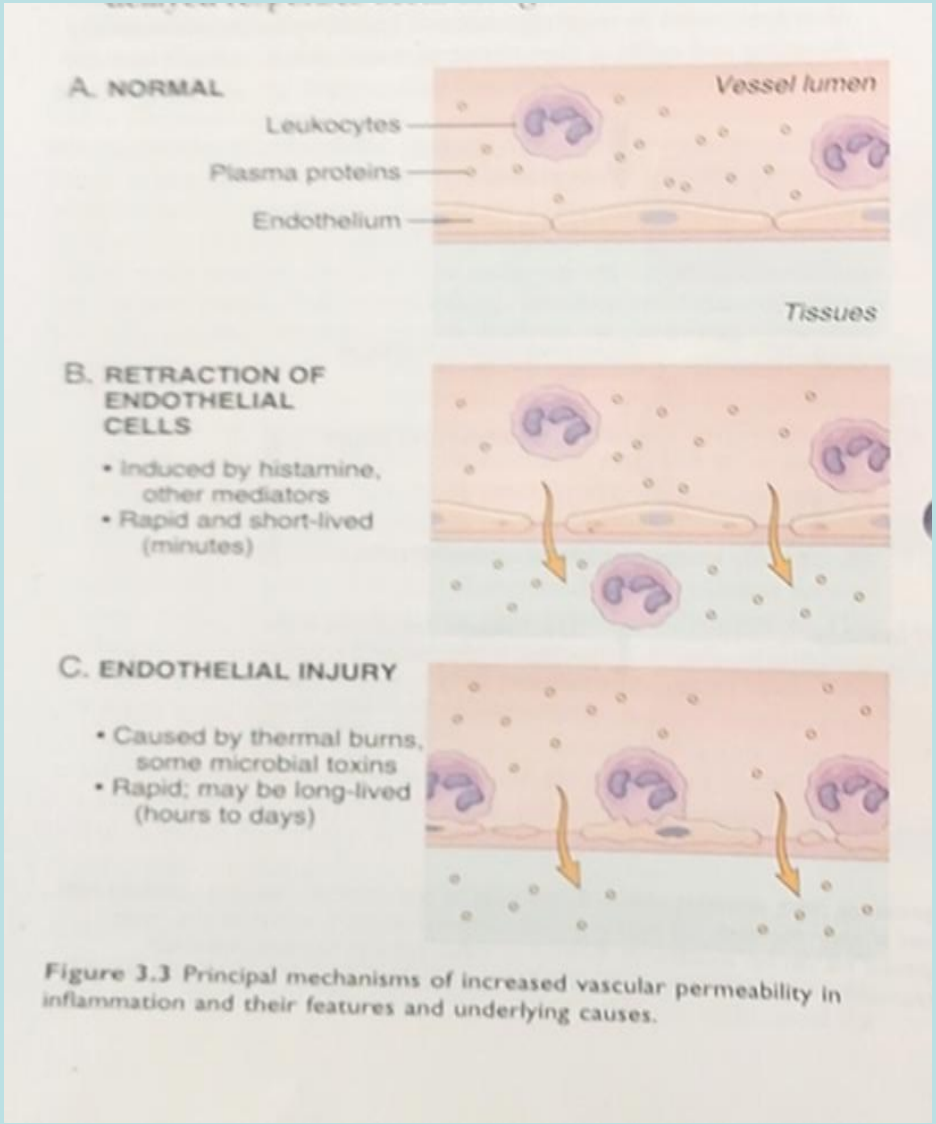


Figure 3.3 Principal mechanisms of increased vascular permeability in inflammation and their features and underlying causes.

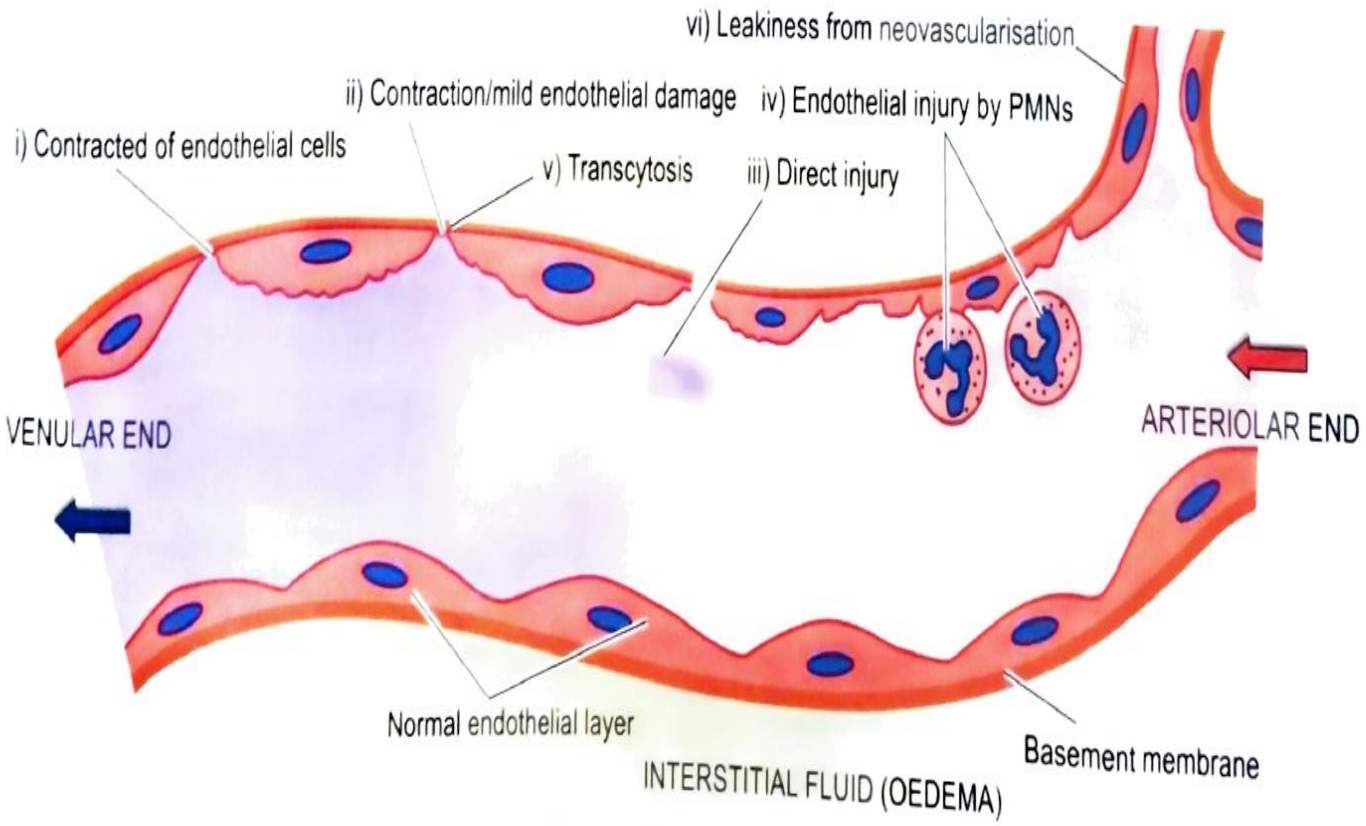


Figure 4.3 Schematic illustration of pathogenesis of increased vascular permeability in acute inflammation. The serial numbers in the figure correspond to six numbers described in the text. (PMNs, polymorphonuclear neutrophils).

Cellular events **-Leucocyte extravasation & Phagocytosis**

1.In the lumen --- **Margination & Pavementing Rolling & Adhesion**

2.Transmigration across the endothelium----- **Emigration & Diapedesis**

3.Migration in interstitial tissues towards a chemotactic stimulus ------ **Chemotaxis**

4. Phagocytosis

Pavementing & Margination

- Normal axial blood flow
- With stasis ,changes in normal axial blood flow
- widening of central stream of cells & narrowing of plasma- margination
- Neutrophils come closer to endothelial cells-pavementing

Rolling & Adhesion

- Neutrophils roll over endothelial cells- **Rolling**
- Transient sticking of neutrophils - **Adhesion**

- **Adhesion molecules**

1.**Selectins**

E-selectin--endothelium

P-selectin—endothelium & platelets

L-selectin– leukocytes

2.Immunoglobulin family

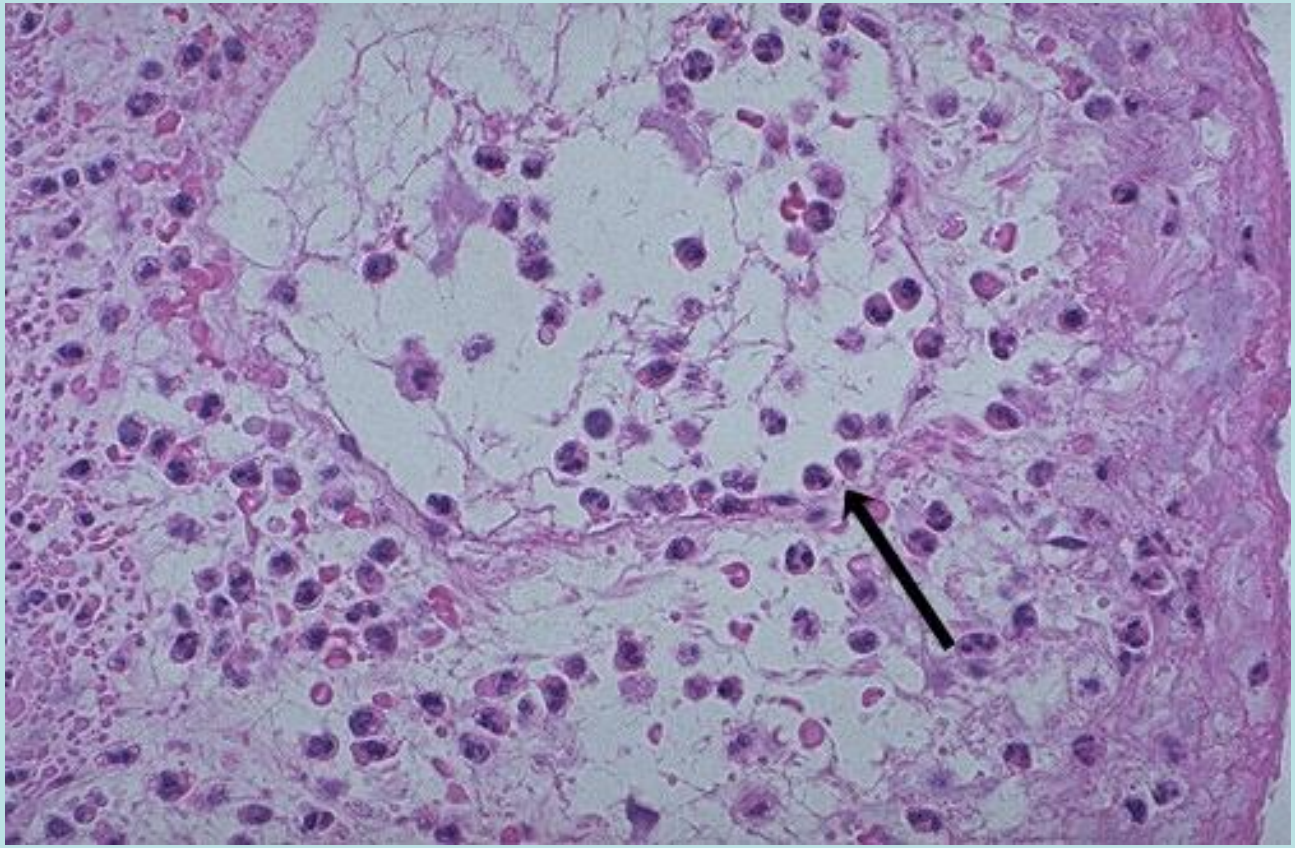
ICAM-1 --endothelium

VCAM-1—endothelium

3.Integrins –Leucocyte surface proteins

4.Mucin like glycoproteins

Acute inflammation: tissue effects



Pavementation and diapedesis

Transmigration

- Process by which motile white cells migrate out of blood vessel.

Emigration

Diapedesis

Crossing several barriers-endothelium, basement membrane,perivascular myofibroblasts & matrix

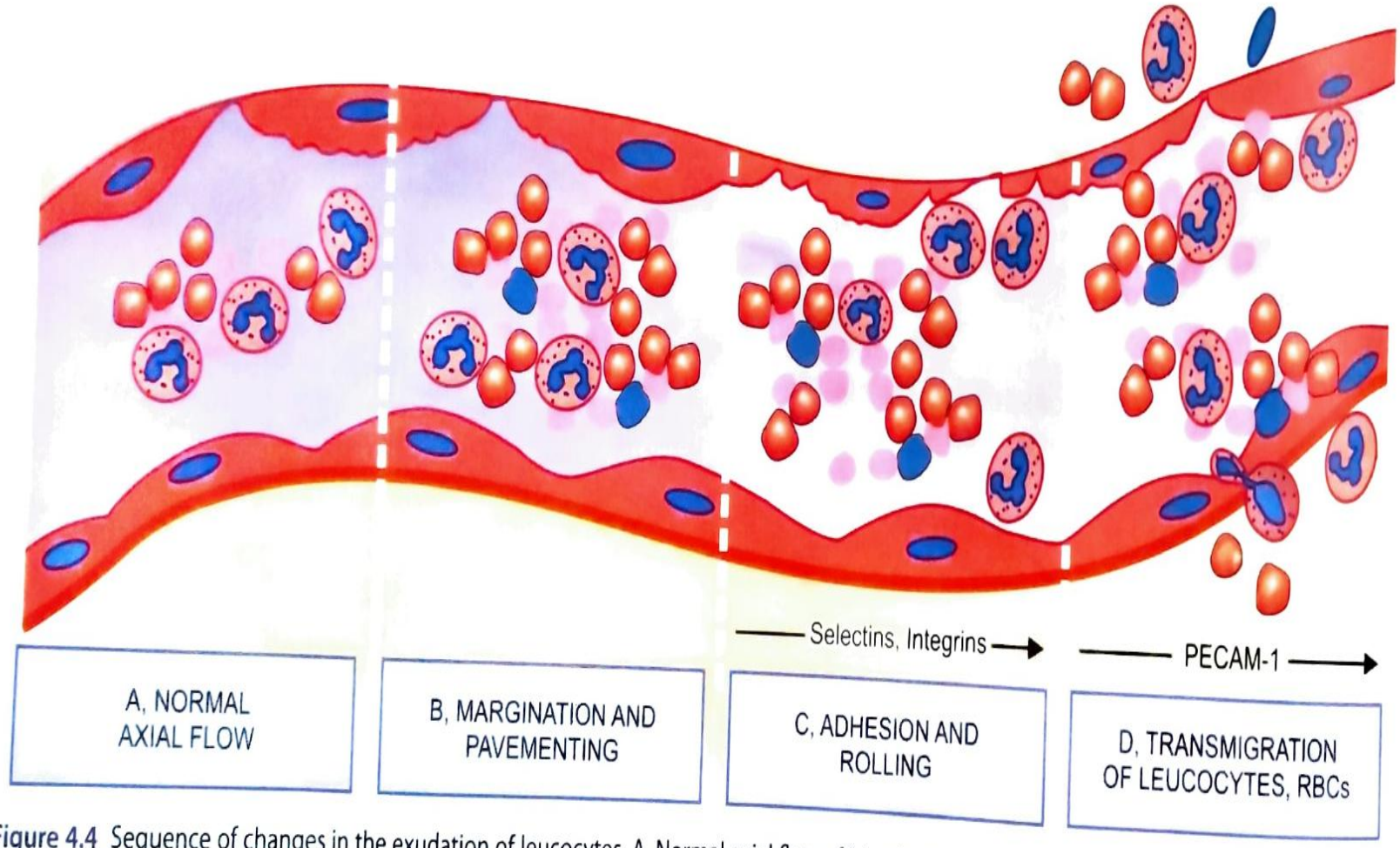


Figure 4.4 Sequence of changes in the exudation of leucocytes. A, Normal axial flow of blood with central column of cells and peripheral zone of cell-free plasma. B, Margination and pavementing of neutrophils with narrow plasmatic zone. C, Adhesion of neutrophils to endothelial cells with pseudopods in the intercellular junctions. D, Emigration of neutrophils and diapedesis with damaged basement membrane.

Chemotaxis

Movement of leucocytes towards direction of chemical molecules /locomotion oriented along chemical gradient (chemo attractants)

- Chemotactic stimuli—
- **Exogenous**– bacterial products

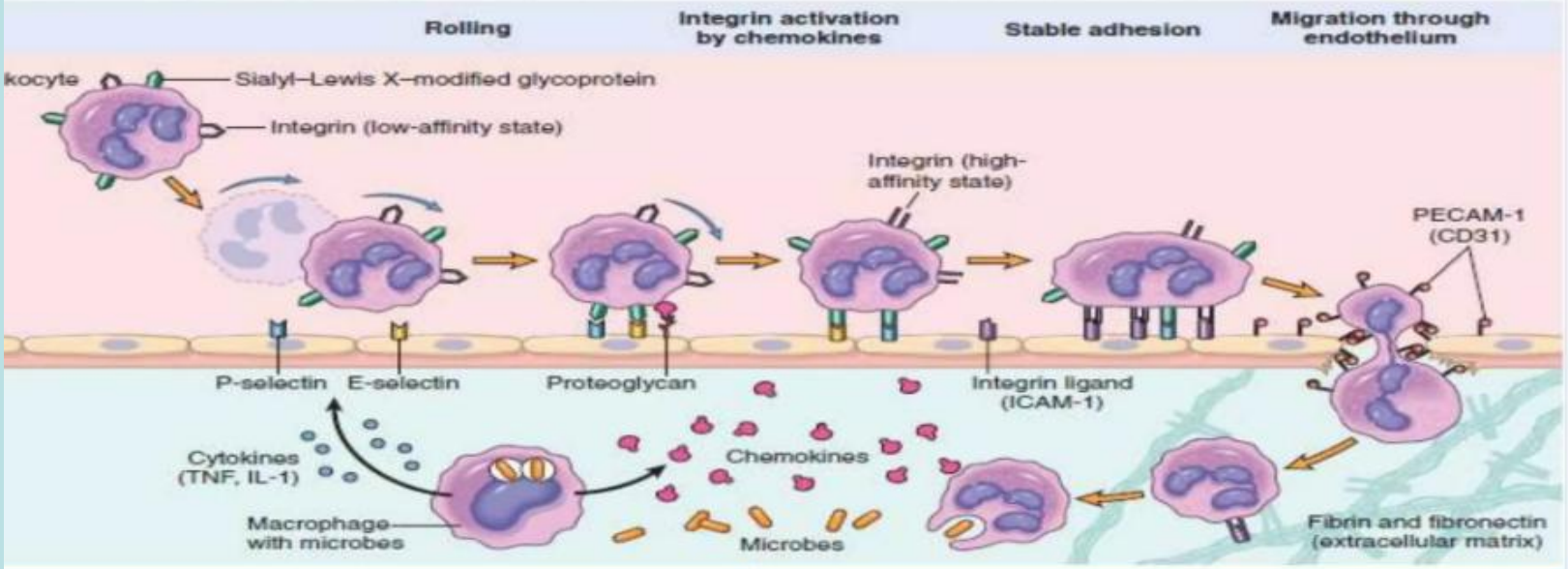
- **Endogenous**–

1.components of compliment system C5a

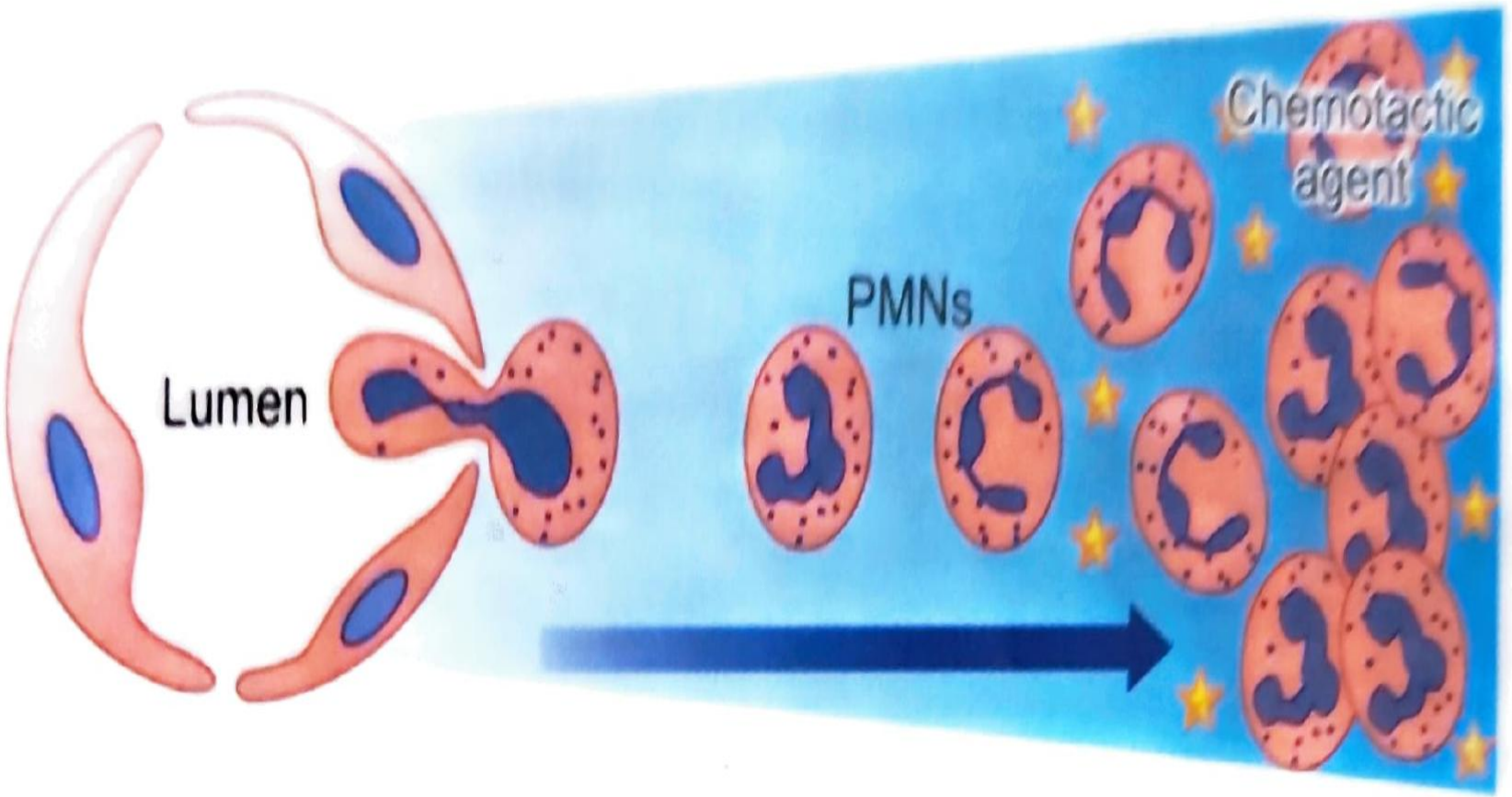
2.products of lipo-oxygenase pathway-LTB4

3.cytokines & chemokines—IL-8

Role of endothelial molecules in acute inflammation



Endothelial molecule	Major role
P-selectin	Rolling
E-selectin	Rolling and Adhesion
ICAM-1 (Integrin – β1)	Adhesion, Arrest & Transmigration
VCAM-1 (Integrin – β2)	Adhesion
PECAM-1 (CD-31)	Diapedesis


Chemotactic agent
PMNs
Lumen

In most of acute inflammation
NEUTROPHILS predominate

--most numerous in blood.

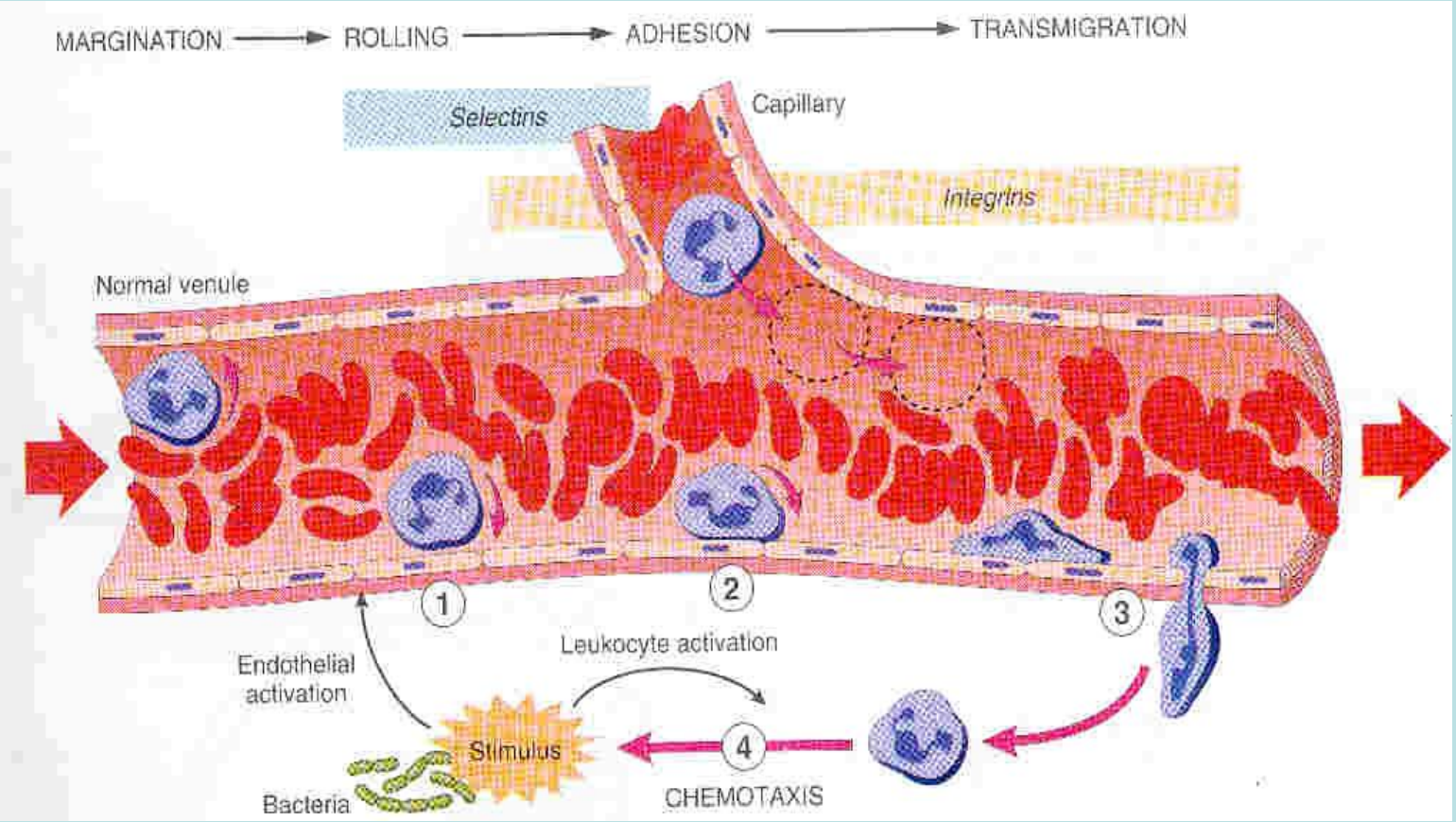
--respond more rapidly to chemokines.

--attach more firmly to adhesion molecules

-- in 24-48 hours.

-- later monocytes/ macrophags which tend to survive longer.

Leukocyte migration in inflammation



MARGINATION

Inflammation

The basis of the five cardinal signs

- Increased blood flow due to vascular dilatation gives **redness** and **heat.**
- Increased vascular permeability gives oedema causing **tissue swelling.**
- Certain chemical mediators stimulate sensory nerve endings giving **pain.** Nerves also stimulated by stretching from oedema.
- Pain and swelling result in loss of **function.**

Cardinal Clinical Signs of Acute Inflammation

Acute inflammation has 5 cardinal signs:

- redness (rubor)
- heat (calor)

→ increased blood flow to the inflamed area

- swelling (tumor) → accumulation of fluid
- pain (dolor) → release of chemicals that stimulate nerve endings

- loss of function → a combination of factors