INFLAMMATION AND REPAIR
Lecture 1
Definition of inflammation; acute inflammation
Vascular Events in Inflammation

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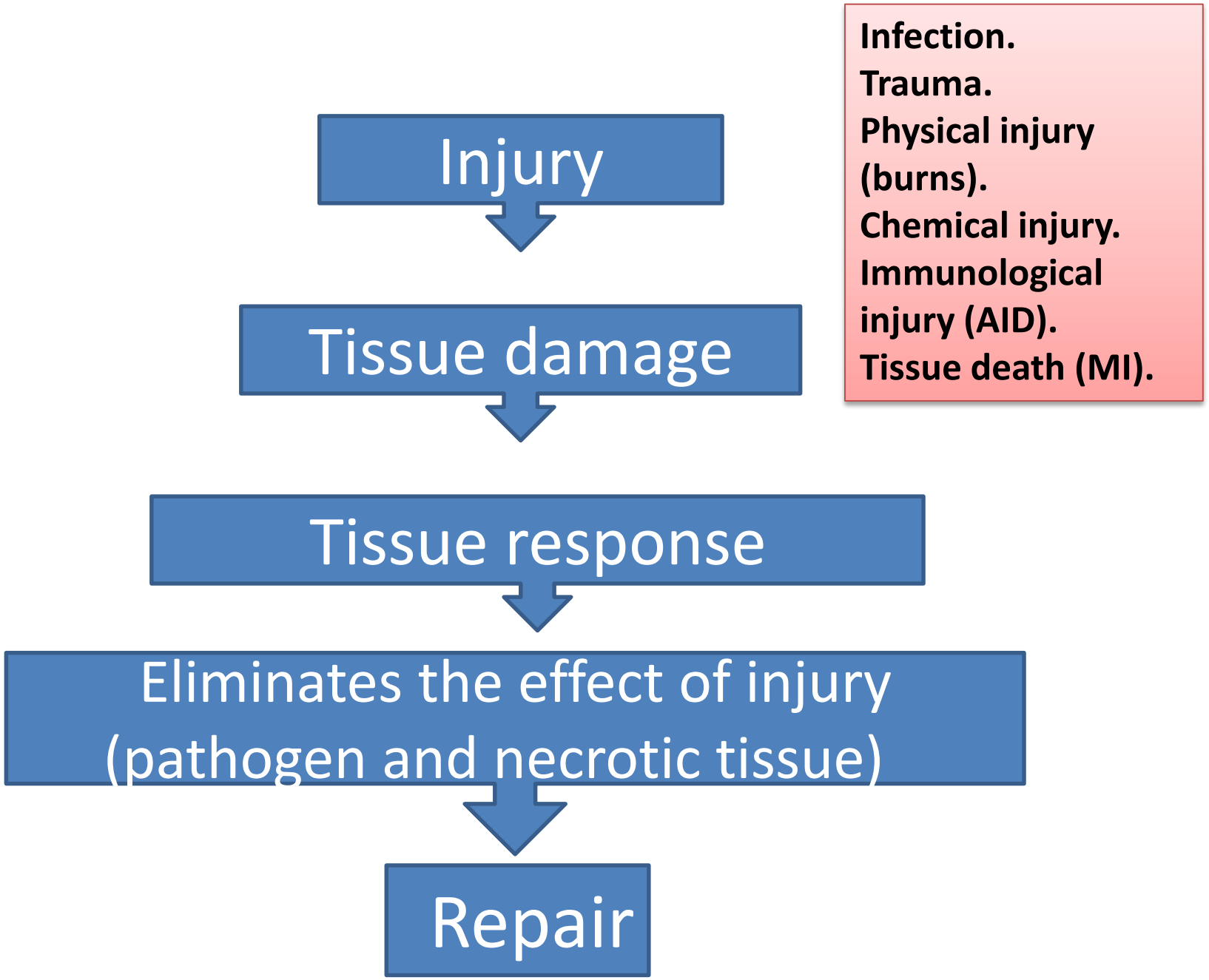
(Foundation Block, Pathology
2015

Learning Objectives:

1. **Define inflammation.**
2. **List cells & molecules that play important roles in inflammation**
3. **Compare between acute and chronic inflammation**
4. **Recognize the cardinal signs of inflammation.**
5. **Describe the sequence of vascular changes in acute inflammation (vasodilation, increased permeability) and their purpose.**
6. **Know the mechanisms of increased vascular permeability.**
7. **Compare normal capillary exchanges with exchange during inflammatory response.**
8. **Define the terms edema, transudate, and exudate.**

Reference book and the relevant page numbers..

- Robbins Basic Pathology 9th edition
- Page: 29 - 34


Injury
Tissue damage
Tissue response
Eliminates the effect of injury (pathogen and necrotic tissue)
Repair
Infection.
Trauma.
Physical injury (burns).
Chemical injury.
Immunological injury (AID).
Tissue death (MI).

What is Inflammation?

- Inflammation is a local response of the vascularized living tissue to infection and damaged tissue that brings cells and molecules of host defense from the circulation to the sites where they are needed

Aim: eliminate the initial cause of cell injury as well as the necrotic cells and tissues resulting from the original insult

- A series of events start which leads as far as possible to the healing and reconstitution of the damaged tissue.

➔ Therefore, Inflammation is part of a broader protective response *(innate immunity)*

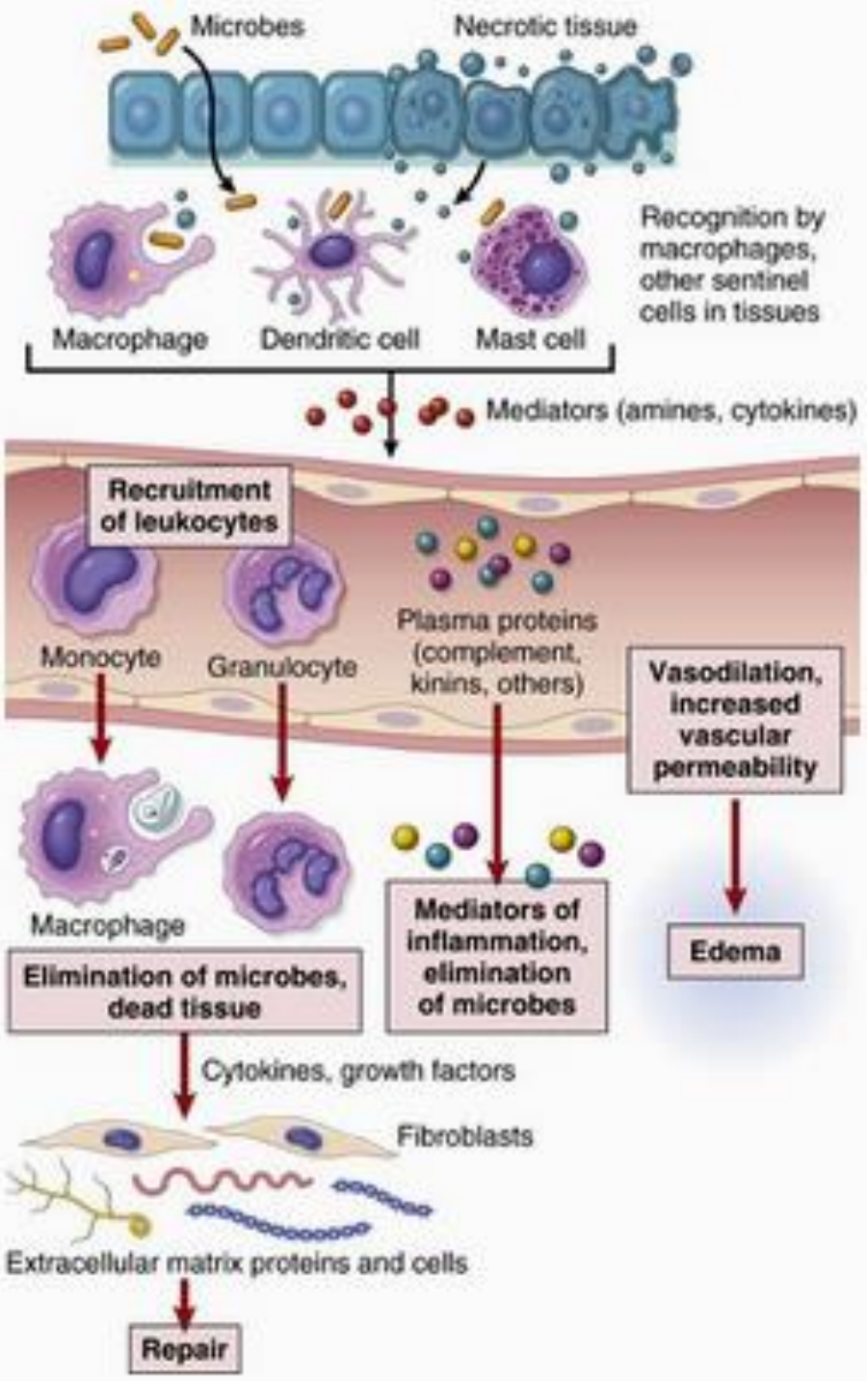
Inflammation

- Although inflammation suggests a harmful reaction symptoms (e.g., pain and functional impairment). Typically, however, these harmful consequences are self-limited and resolve as the inflammation abates, leaving little or no permanent damage.
- It is actually a protective response that is essential for survival. It serves to rid the host of both the initial cause of cell injury (e.g., microbes, toxins) and the consequences of such injury (e.g., necrotic cells and tissues).

Inflammation

- Inflammation is terminated when the offending agent is eliminated and the secreted mediators are broken down or dissipated.

There are active anti-inflammatory mechanisms that serve to control the response and prevent it from causing excessive damage to the host.


Microbes
Necrotic tissue
Recognition by macrophages, other sentinel cells in tissues
Macrophage
Dendritic cell
Mast cell
Mediators (amines, cytokines)
Recruitment of leukocytes
Monocyte
Granulocyte
Plasma proteins (complement, kinins, others)
Vasodilation, increased vascular permeability
Macrophage
Elimination of microbes, dead tissue
Mediators of inflammation, elimination of microbes
Edema
Cytokines, growth factors
Fibroblasts
Extracellular matrix proteins and cells
Repair

Can inflammation be harmful ! ?

- Inflammation can induce harm:

e.g. anaphylactic reaction

rheumatoid arthritis

atherosclerosis

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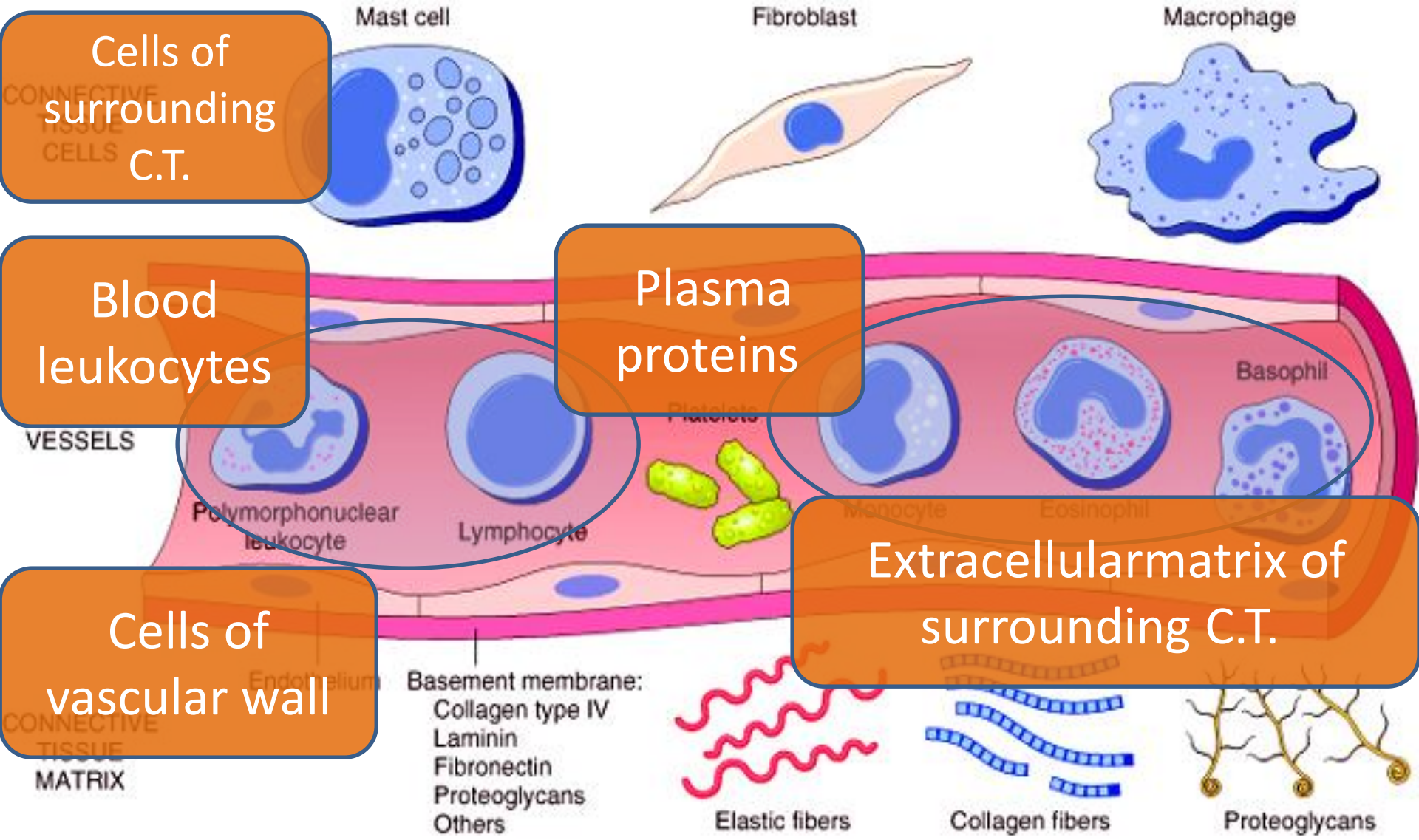
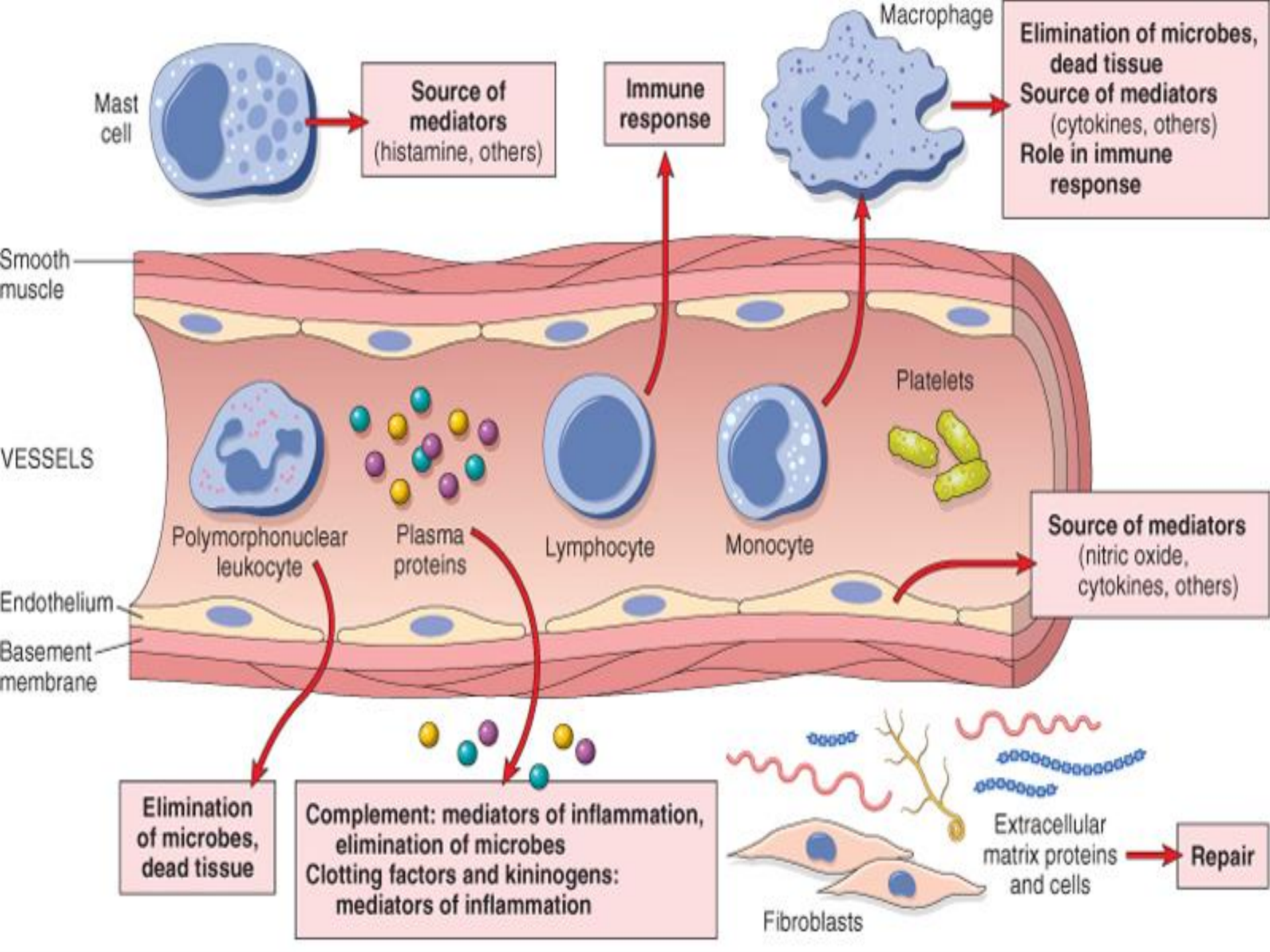
A protective response

Cells & molecules that play important roles in inflammation




Mast cell
Source of mediators (histamine, others)
Immune response
Macrophage
Elimination of microbes, dead tissue
Source of mediators (cytokines, others)
Role in immune response
Smooth muscle
VESSELS
Endothelium
Basement membrane
Polymorphonuclear leukocyte
Plasma proteins
Lymphocyte
Monocyte
Platelets
Source of mediators (nitric oxide, cytokines, others)
Elimination of microbes, dead tissue
Complement: mediators of inflammation, elimination of microbes
Clotting factors and kininogens: mediators of inflammation
Extracellular matrix proteins and cells
Repair
Fibroblasts

Inflammation is mediated by chemical substances called

CHEMICAL MEDIATORS

What is the source of these chemical mediators?

1. Phagocytes and other host cells
Leukocyte
Endothelium
Mast cell

2. Plasma proteins

The typical inflammatory reaction develops through a series of sequential steps:

1. The offending agent, which is located in extravascular tissues, is recognized by host cells and molecules.
2. Leukocytes and plasma proteins are recruited from the circulation to the site where the offending agent is located.
3. The leukocytes and proteins are activated and work together to destroy and eliminate the offending substance.
4. The reaction is controlled and terminated.
5. The damaged tissue is repaired.

The outcome of acute inflammation

is either

- elimination of the noxious stimulus, followed by decline of the reaction and repair of the damaged tissue

or

- persistent injury resulting in chronic inflammation

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TYPES OF INFLAMMATION

Acute inflammation

Chronic Inflammation

Features of acute and chronic inflammation

Feature	Acute	Chronic
Onset		
Cellular infiltrate		
Tissue injury, fibrosis		
Local & systemic signs		

Differences between Acute and Chronic Inflammation

	Acute	Chronic
Duration	Short (days)	Long (weeks to months)
Onset	Acute	Insidious
Specificity	Nonspecific	Specific (where immune response is activated)
Inflammatory cells	Neutrophils, macrophages	Lymphocytes, plasma cells, macrophages, fibroblasts
Vascular changes	Active vasodilation, increased permeability	New vessel formation (granulation tissue) (Chapter 6: Healing & Repair)
Fluid exudation and edema	+	–
Cardinal clinical signs (redness, heat, swelling, pain)	+	–
Tissue necrosis	– (Usually) + (Suppurative and necrotizing inflammation)	+ (ongoing)
Fibrosis (collagen deposition)	–	+
Operative host responses	Plasma factors: complement, immunoglobulins, properdin, etc; neutrophils, nonimmune phagocytosis	Immune response, phagocytosis, repair
Systemic manifestations	Fever, often high	Low–grade fever, weight loss, anemia
Changes in peripheral blood	Neutrophil leukocytosis; lymphocytosis (in viral infections)	Frequently none; variable leukocyte changes, increased plasma immunoglobulin

Acute inflammation

- A rapid response to an injurious agent that serves to deliver mediators of host defense-leukocytes and plasma proteins-to the site of injury.

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Clinical Features

The 5 ancient cardinal signs of inflammation are

Tumor:-swelling

Rubor :– redness

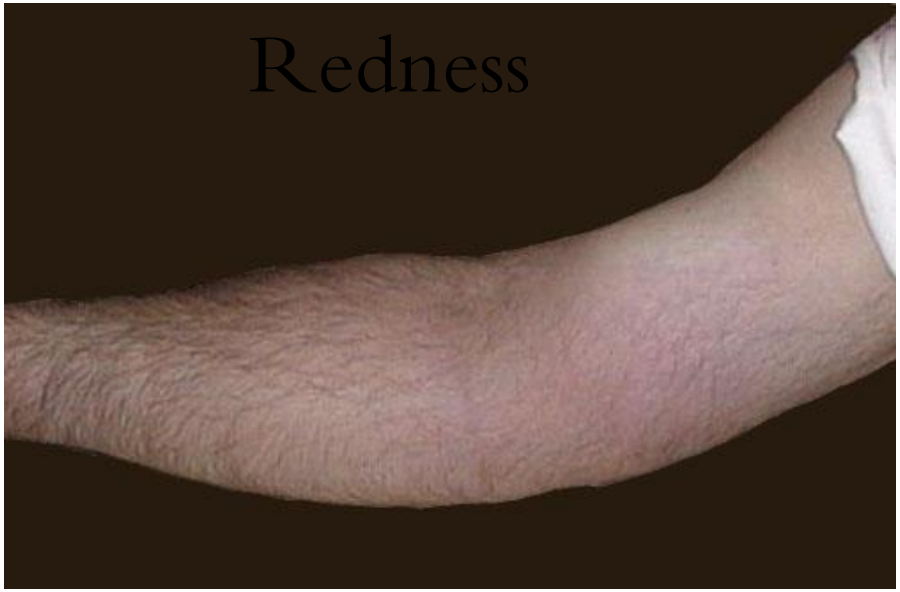
Calor: – warmth

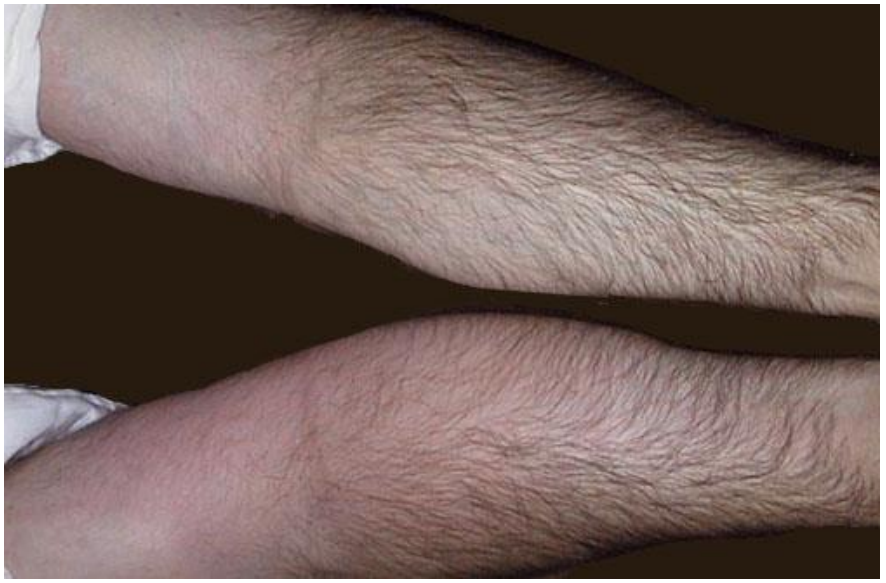
Dolor :– pain

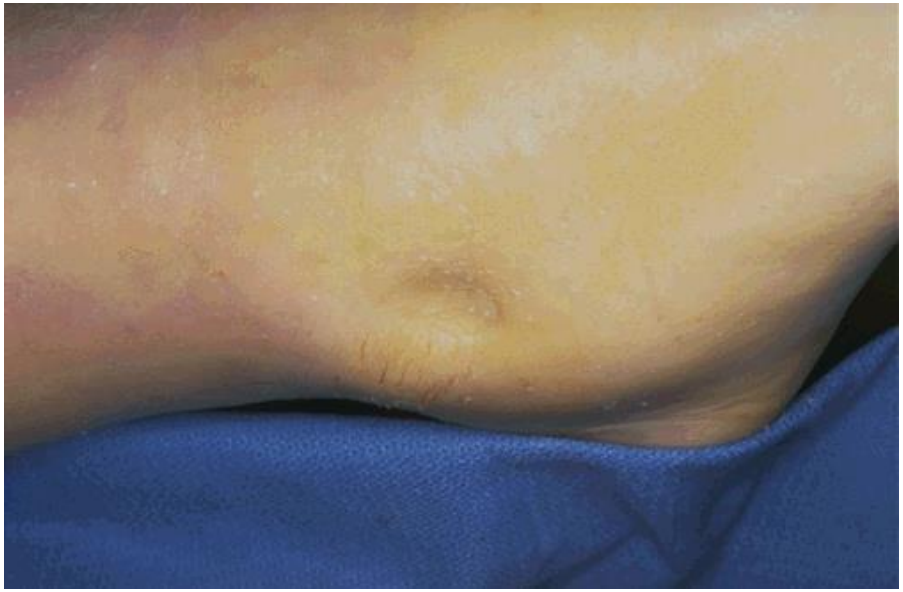
Functio Laesa :– loss of function

The suffix "its" is added to the base word to state the condition as in appendix/appendicitis

Redness







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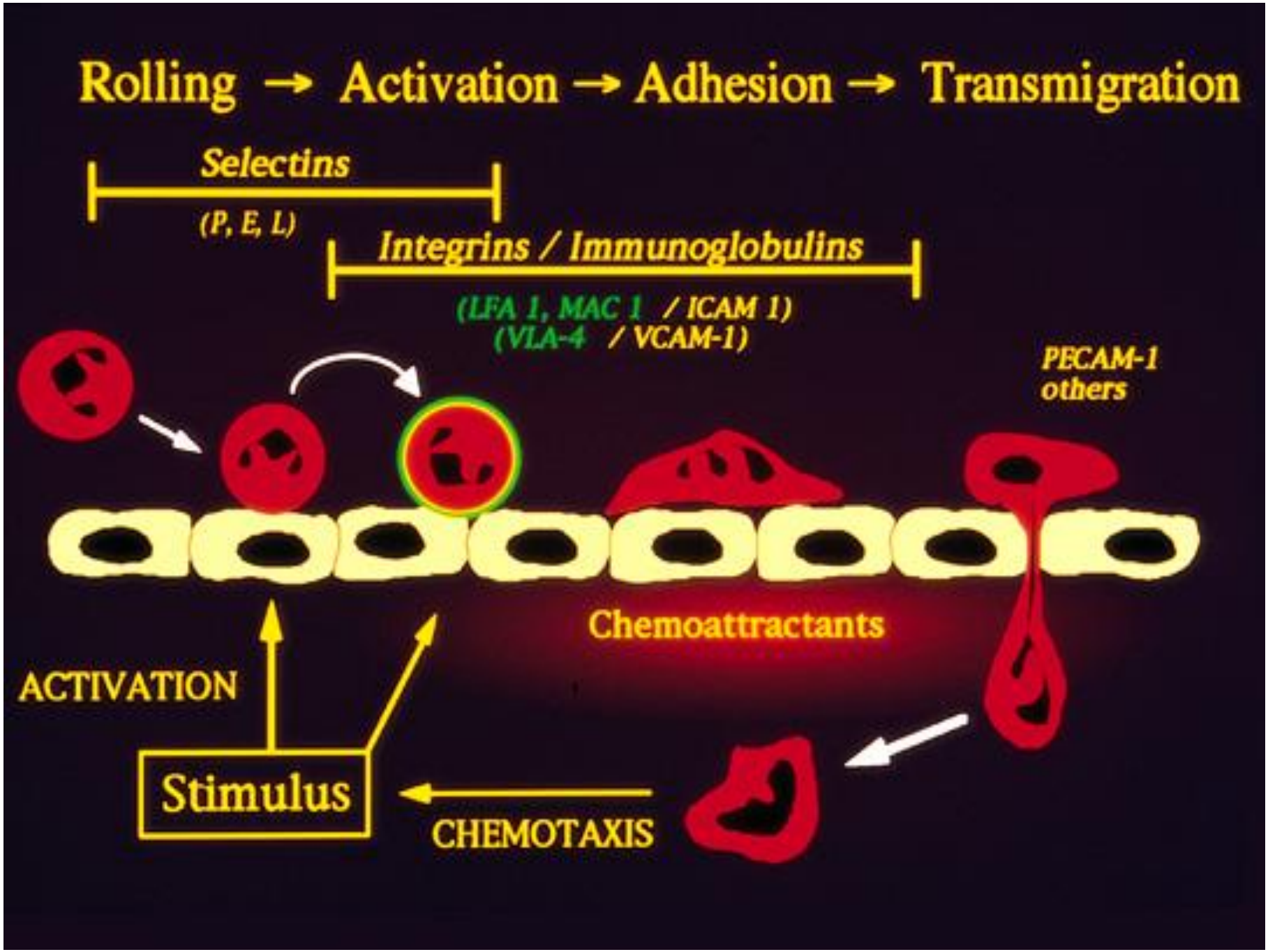

Rolling → Activation → Adhesion → Transmigration
Selectins
(P, E, L)
Integrins / Immunoglobulins
(LFA 1, MAC 1 / ICAM 1)
(VLA-4 / VCAM-1)
PECAM-1
others
Chemoattractants
ACTIVATION
Stimulus
CHEMOTAXIS

Events of acute Inflammation

- Acute inflammation has three main events:

vascular

(1) Hemodynamic changes

(*alterations in vascular caliber that lead to an increase in blood flow)*

(2) Increased vascular permeability

(*structural changes in the microvasculature that permit plasma proteins and leukocytes to leave the circulation)*

cellular

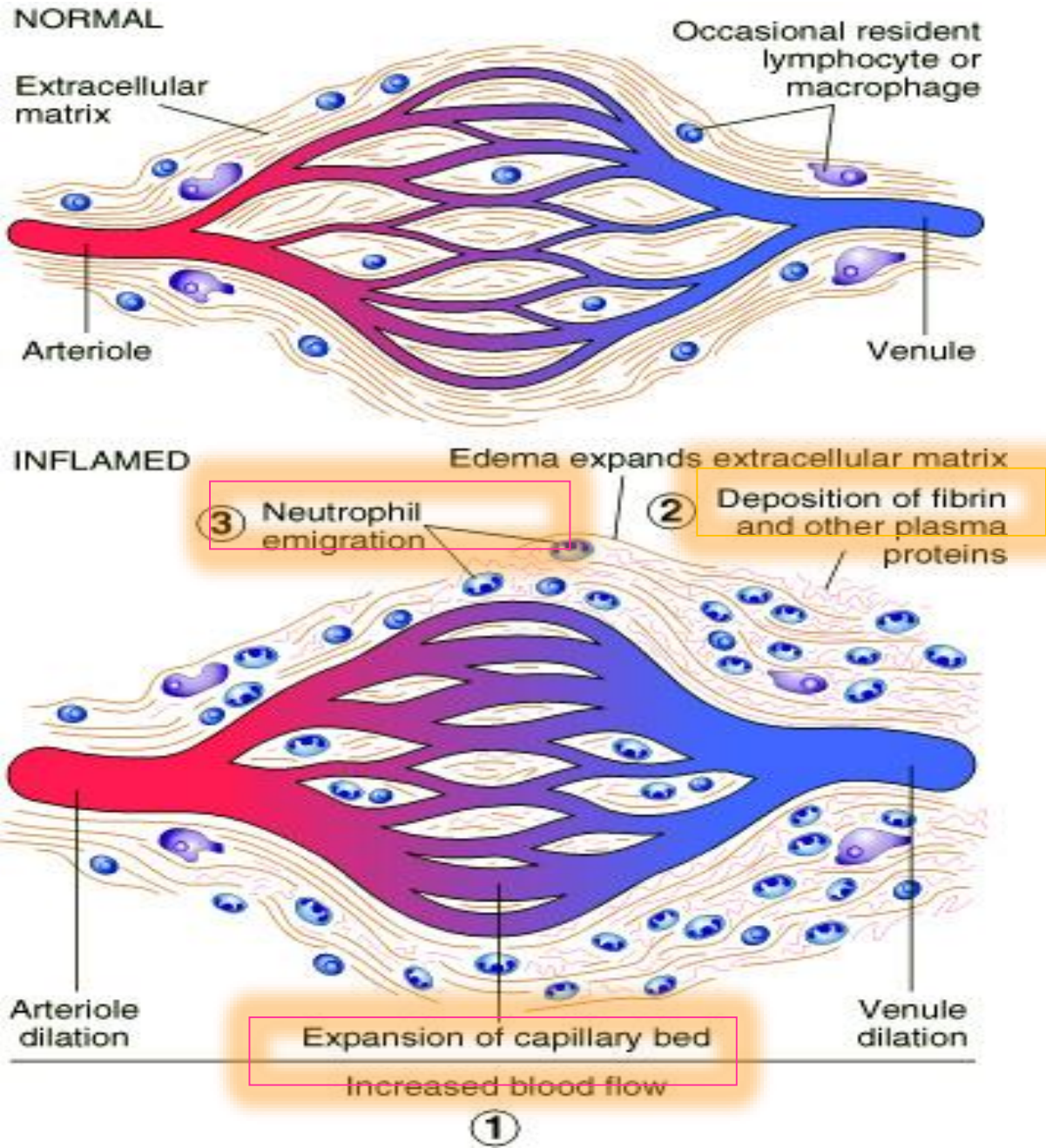
(3) Emigration of the leukocytes from the microcirculation

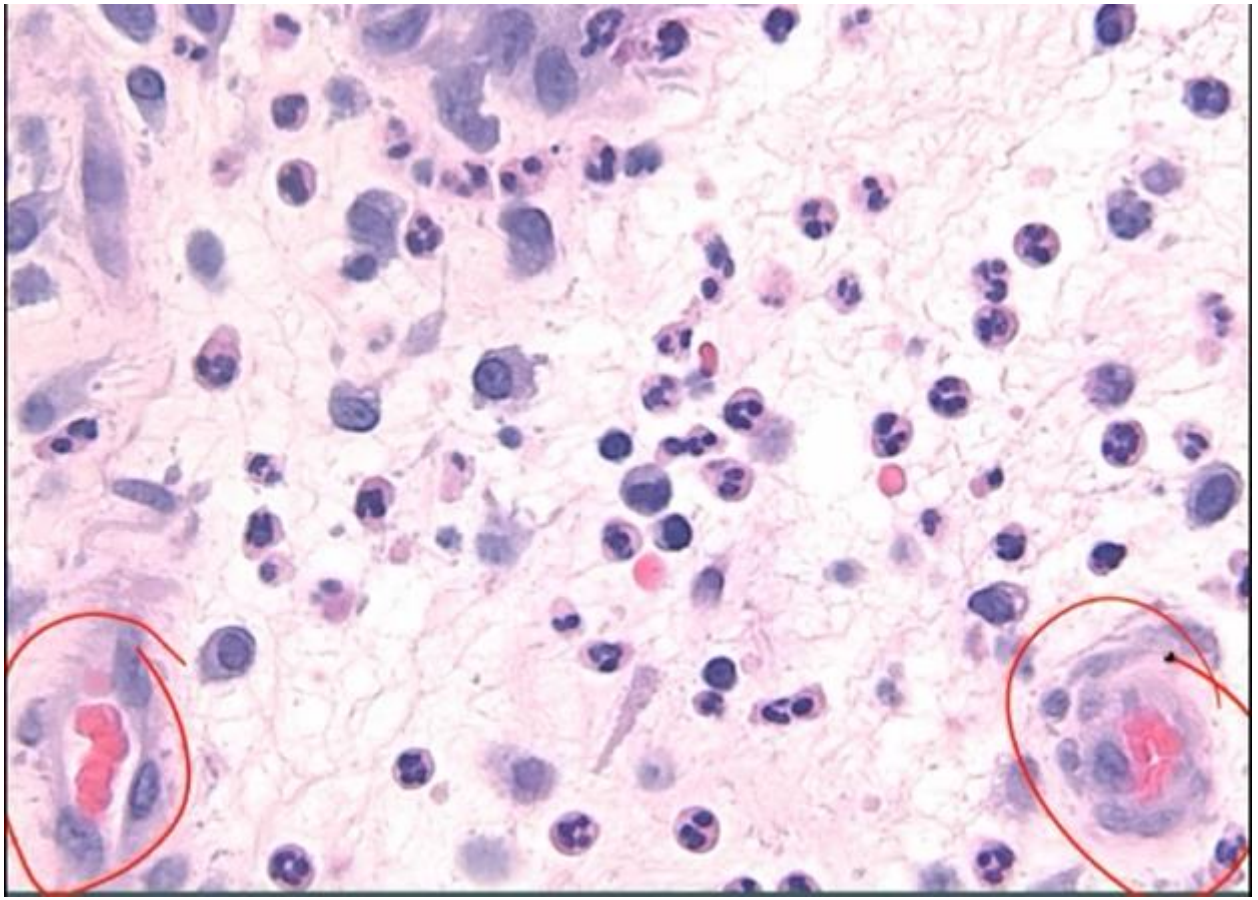
(their accumulation in the focus of injury, *and their activation* to eliminate the offending agent)

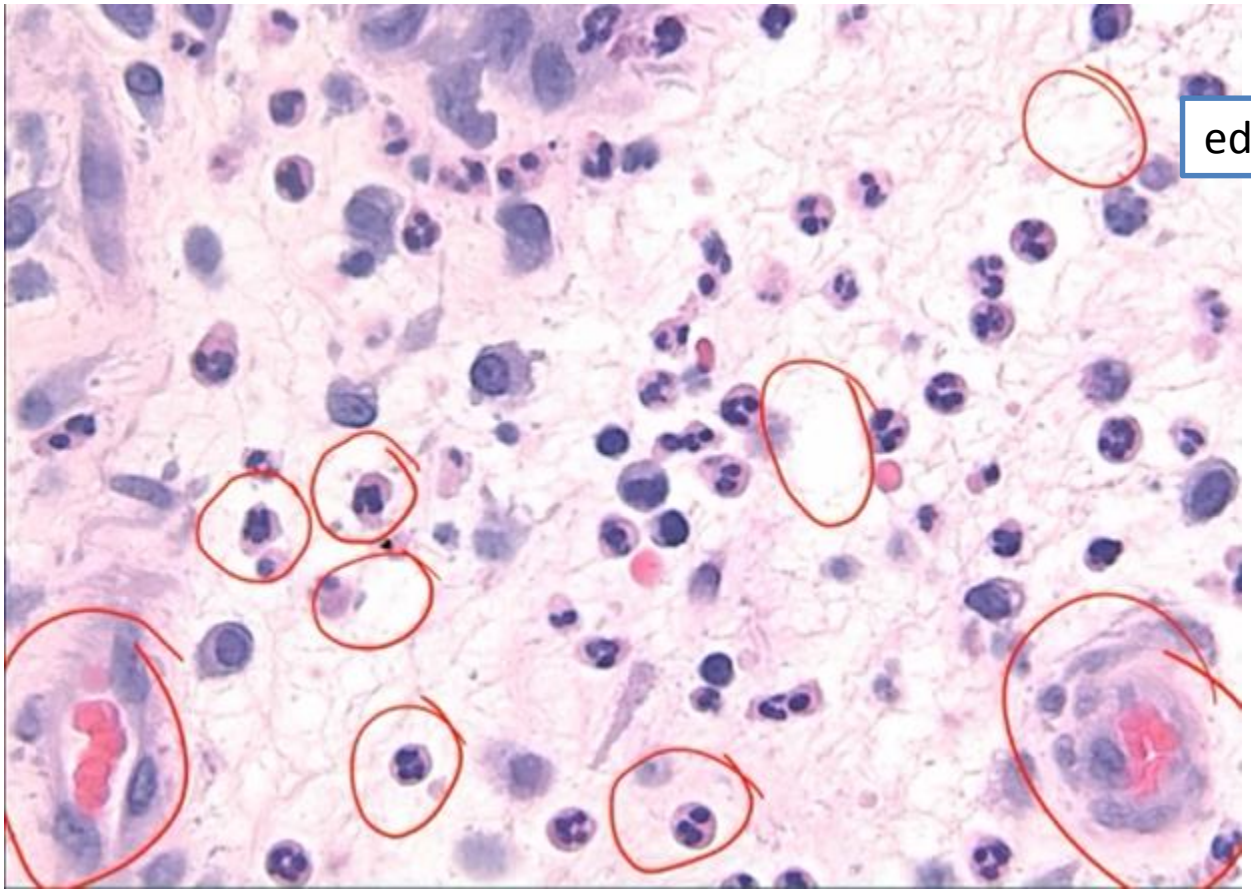
Vascular Events

1. Vasodilatation

Hemodynamic changes






edema

Phases of changes in Vascular Caliber and Flow

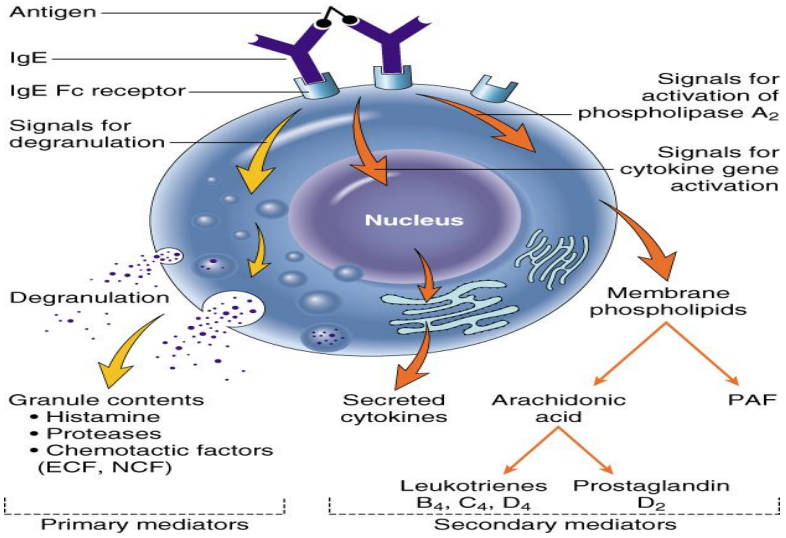
1. Transient vasoconstriction of arterioles

   It disappears within 3-5 seconds in mild injuries

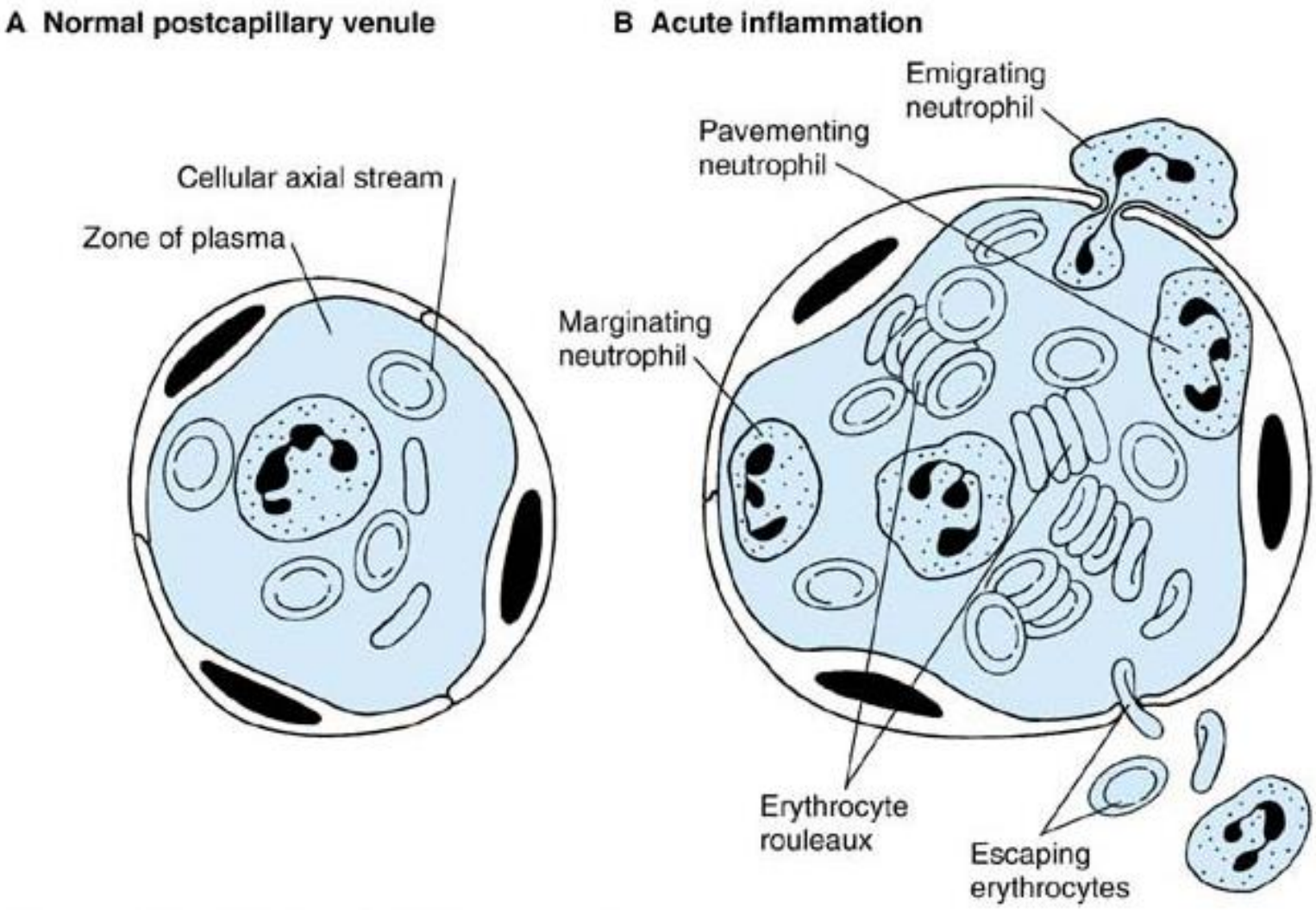
2. Vasodilatation: It involves the **arterioles** results in opening of new microvasculature beds in the area leading to increasing blood flow – Histamine effect

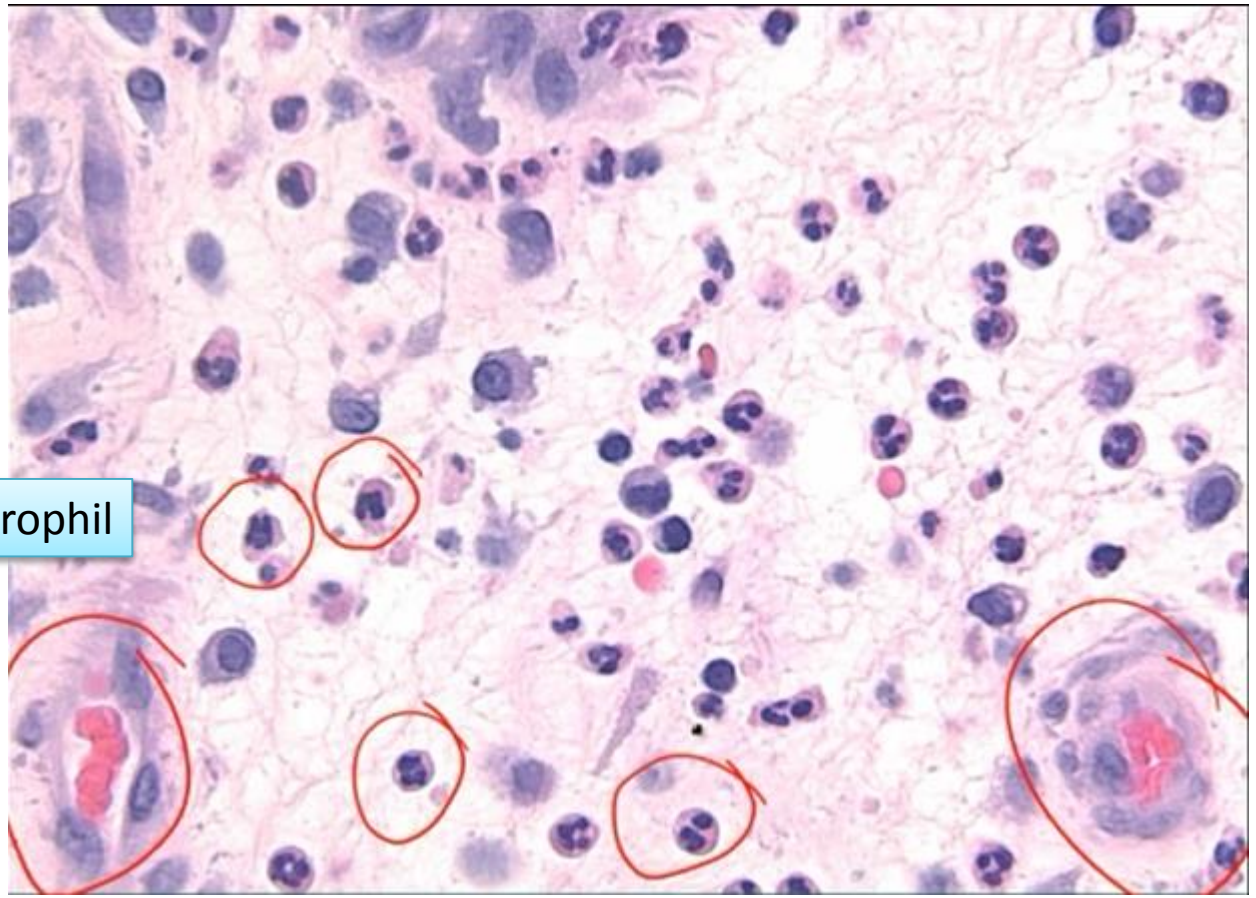
3. Slowing of the circulation due to increased permeability of the microvasculature, this leads to outpouring of protein-rich fluid in the extravascular tissues.

4. Stasis: slow circulation due to dilated small vessels packed with red cells



Slowing of the circulation




neutrophil

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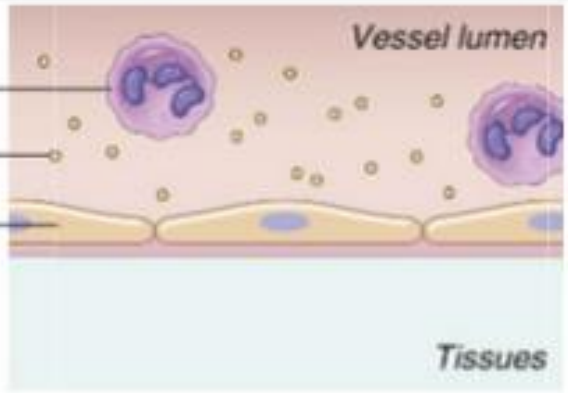
2. Increased Vascular Permeability

- A hallmark of acute inflammation (escape of a protein-rich fluid).
  - induced by histamine, kinins, and other mediators

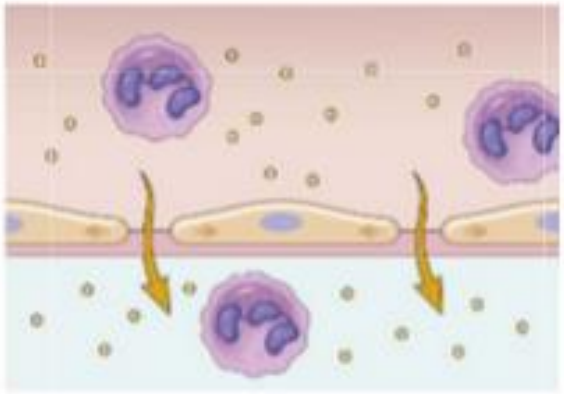
- It affects small & medium size venules, through gaps between endothelial cells

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



B. **RETRACTION OF ENDOTHELIAL CELLS**

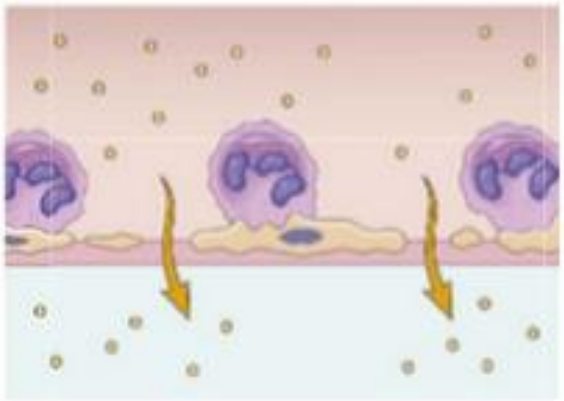
- Induced by histamine, other mediators
- Rapid and short-lived (minutes)



venules

C. **ENDOTHELIAL INJURY**

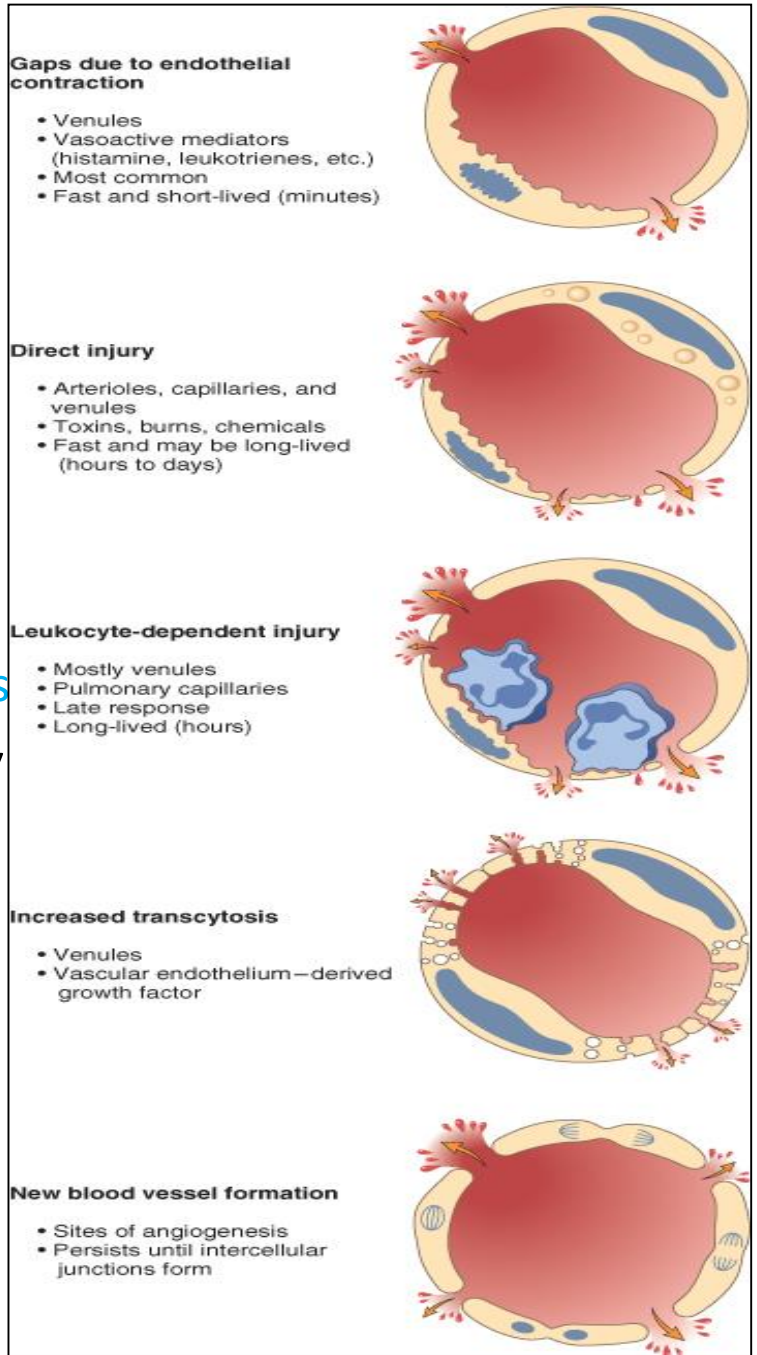
- Caused by burns, some microbial toxins
- Rapid; may be long-lived (hours to days)



Arteriols, capillaries and venules

Mechanisms lead to increased vascular permeability

- *Endothelial cell contraction* 15-30 min
- *Endothelial injury*
  - *immediate sustained response* 6-24 hours
  - *delayed prolonged leakage* *12* hours- days
- *Leukocyte-mediated endothelial injury*
- *Transcytosis (occurs via channels formed by fusion of intracellular vesicles)*
- *Leakage from new blood vessels*



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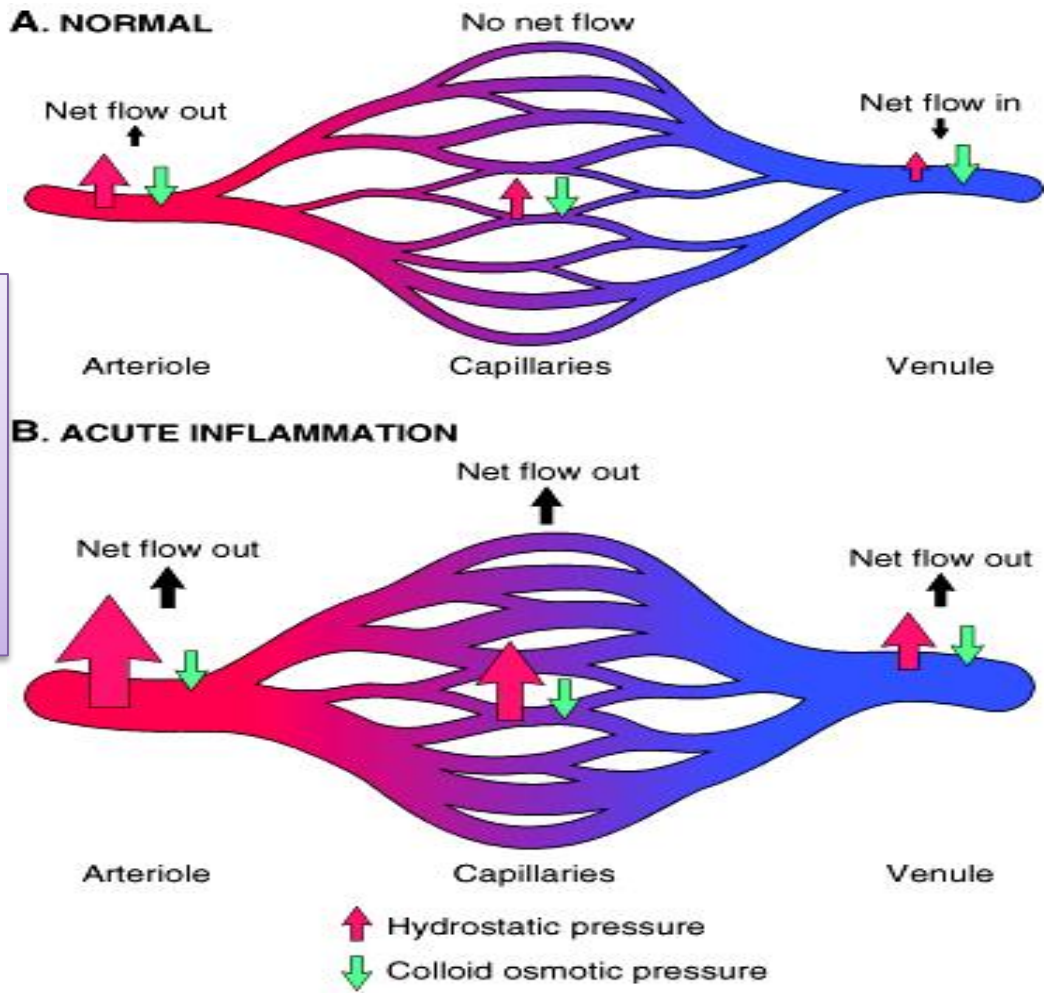
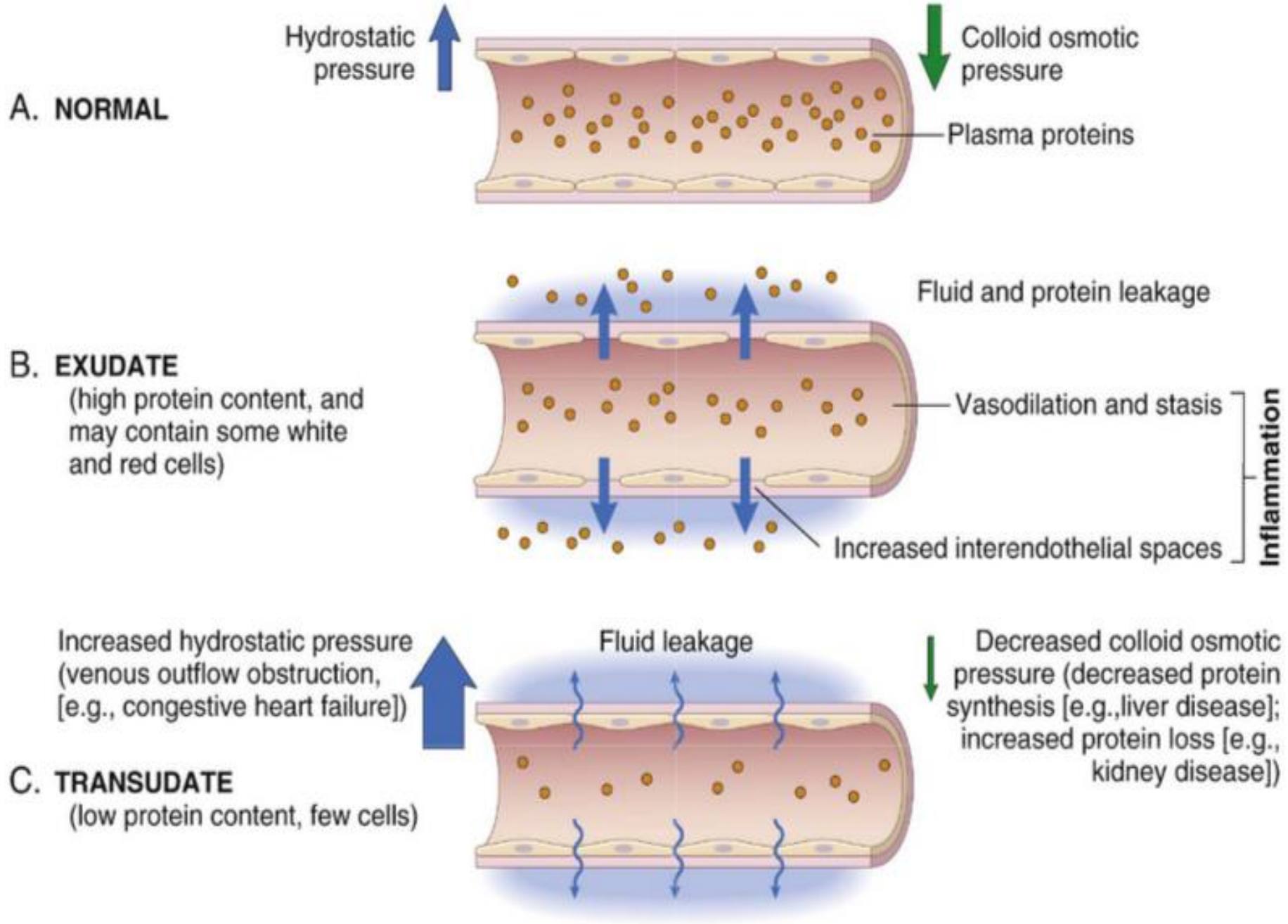
Increased blood volume lead to increased local hydrostatic pressure leading to transudation of protein-poor fluid into the extravascular space.

What is the edema?

denotes an excess of fluid in the interstitial or serous cavities

- It can be either an **exudate or a transudate**




A. NORMAL
Hydrostatic pressure
Colloid osmotic pressure
Plasma proteins
B. EXUDATE
(high protein content, and may contain some white and red cells)
Fluid and protein leakage
Vasodilation and stasis
Increased interendothelial spaces
Inflammation
Increased hydrostatic pressure (venous outflow obstruction, [e.g., congestive heart failure])
Fluid leakage
Decreased colloid osmotic pressure (decreased protein synthesis [e.g.,liver disease]; increased protein loss [e.g., kidney disease])
C. TRANSUDATE
(low protein content, few cells)

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Edema is defined as an excess of fluid in the interstitial space.

What is the difference between transudates and exudates?

Transudate

is a fluid with low protein content and a specific gravity of less than 1.012

It is essentially an ultrafiltrate of blood plasma that results from osmotic or hydrostatic imbalance across the vessel wall

without an increase in vascular permeability

Exudate

An inflammatory extravascular fluid that has a high protein concentration, cellular debris, and a specific gravity above 1.020

It implies significant alteration in the normal permeability of small blood vessels in the area of injury

TAKE HOME MESSAGES

- Inflammation, the local response of the vascularised living tissue to injury.
- Could be acute or chronic.
- Several cells & molecules that play important roles in inflammation.
- Inflammation has vascular and cellular events to eliminate the cause.
- Vascular events include vasodilation and increased permeability to deliver a protein rich fluid to the site of inflammation.