Inflammation

Topic covered

- Definition
- Clinical sign and types of Inflammation
- Mechanism of Inflammation

What is Inflammation?

- **Definition:-** Inflammation is defined as the local response of living tissues to injury due to any agent.

It is a body defense reaction in order to eliminate or limit the spread of injurious agent as well as to remove the consequent necrosed cells and tissue

- Celsus, listed four cardinal signs of acute inflammation:
  - *Rubor* (erythema [redness]): vasodilatation, increased blood flow
    - *Tumor* (swelling): extravascular accumulation of fluid
    - *Calor* (heat): vasodilatation, increased blood flow
    - *Dolor* (pain)

These signs are mainly due to the vascular events of vasodilation (increased blood flow) and increased vascular permeability (movement of plasma fluids, proteins and inflammatory cells from the lumen of the vascular system out into the tissues).

Types of Inflammation

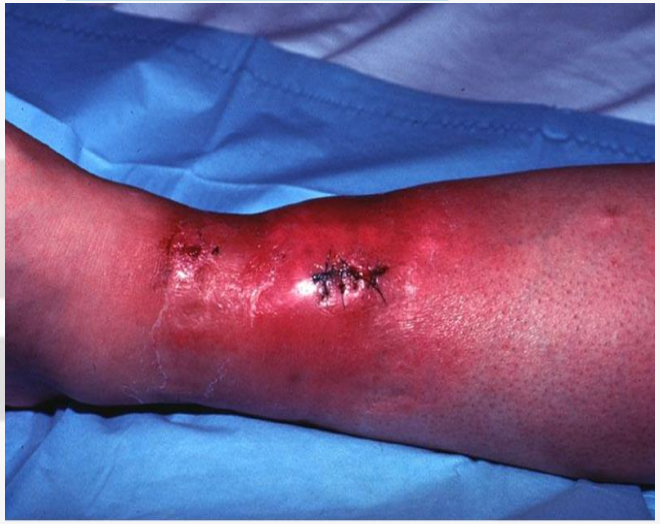
- Acute inflammation
  - Short duration
  - Edema
  - Mainly neutrophils
- Granulomatous inflammation
  - Distinctive pattern of chronic inflammation
  - Activated macrophages (epithelioid cells) predominate
  - +/- Multinucleated giant cells
- Chronic inflammation
  - Longer duration
  - Lymphocytes & macrophages predominate
  - Fibrosis
  - New blood vessels (angiogenesis)

Acute inflammation

- It is a type of inflammation characterized by….

1. Sudden onset
2. Short duration
3. Caused by strong irritant
4. Exudative in nature
5. Followed by repair

Redness
Hotness
Swelling
Pain
Loss of function



Acute Inflammation

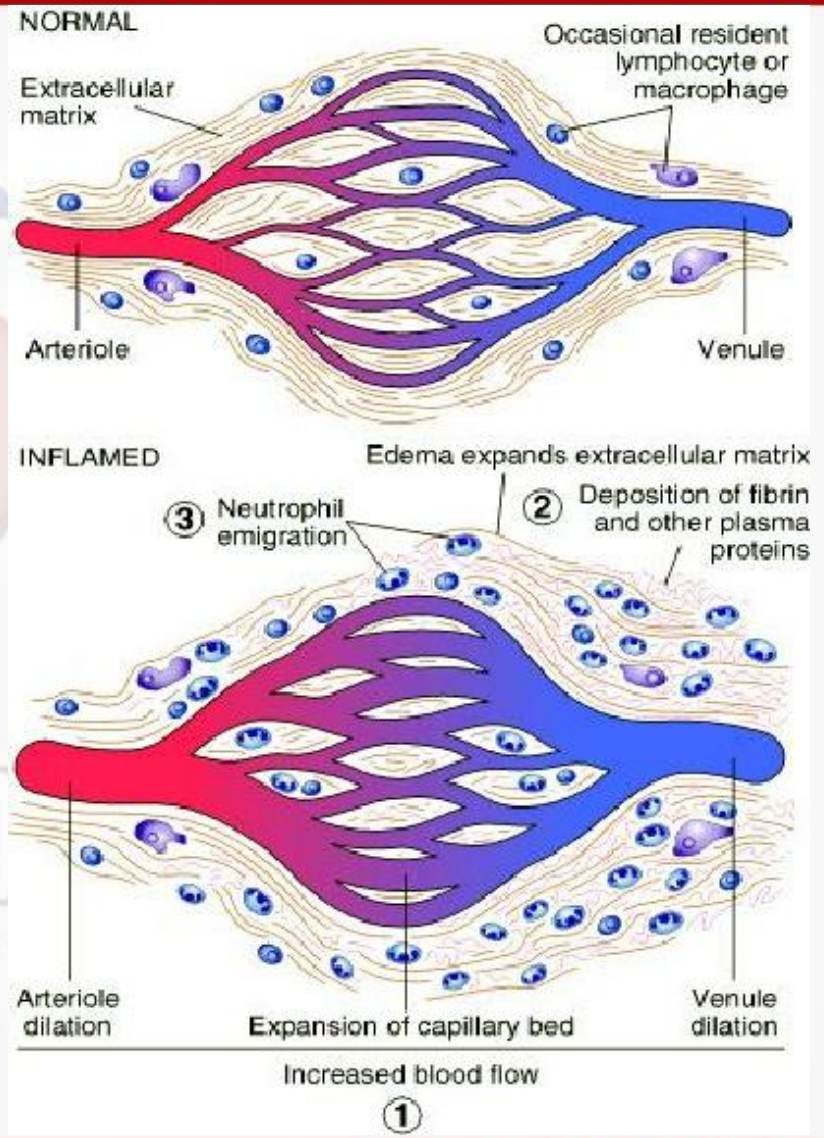
- Two major events:
- 1. Vascular events
- Transient Vasoconstriction
  - Edema results from increased hydrostatic pressure (vasodilation) and lowered intravascular osmotic pressure (protein leakage)
    - Increase in blood flow (redness & warmth)

2. Cellular events
  - Leukocytes extravasation from microcirculation and accumulate in the focus of injury
- Stimuli: infections, trauma, physical or chemical agents, foreign bodies, immune reactions

Acute inflammation

Vascular changes

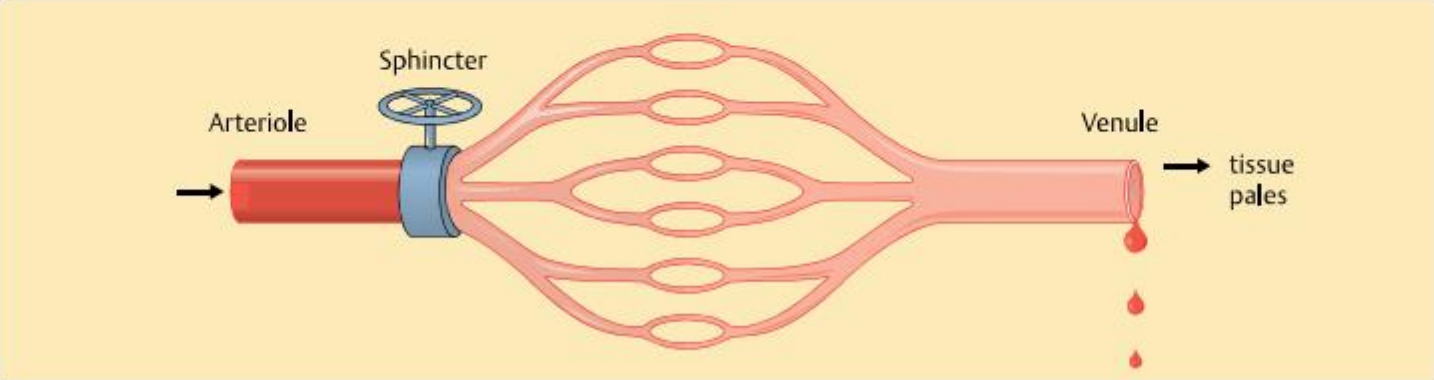
- Initial (seconds-5 min.) arteriolar vasoconstriction.
- After that there's precapillary arteriolar vasodilatation resulting in greater blood flow to the area. This lasts as long as the acute inflammation persists (redness and hotness)
- Also, there's increased vascular permeability (exudate &swelling)



Changes in Microcirculation

1st phase: transient arteriolar vasoconstriction (sec-min). NOT detectable in every inflammatory reaction.

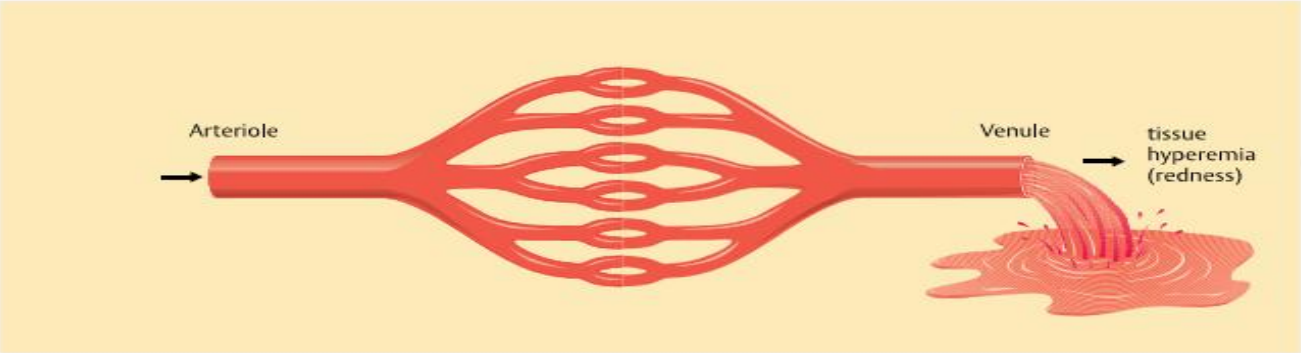
- The noxious agent ENTERS the tissue. The "faucet" is turned off by means of arteriolar vasoconstriction, preventing further spread of the noxious agent.
- Result: Brief paling of the inflamed area.



Changes in Microcirculation

2nd phase: vasodilatation of the arterioles, capillaries, and postcapillary venules. This causes exudation of blood serum that leads to inflammatory tissue swelling with stimulation of the pain nerves.

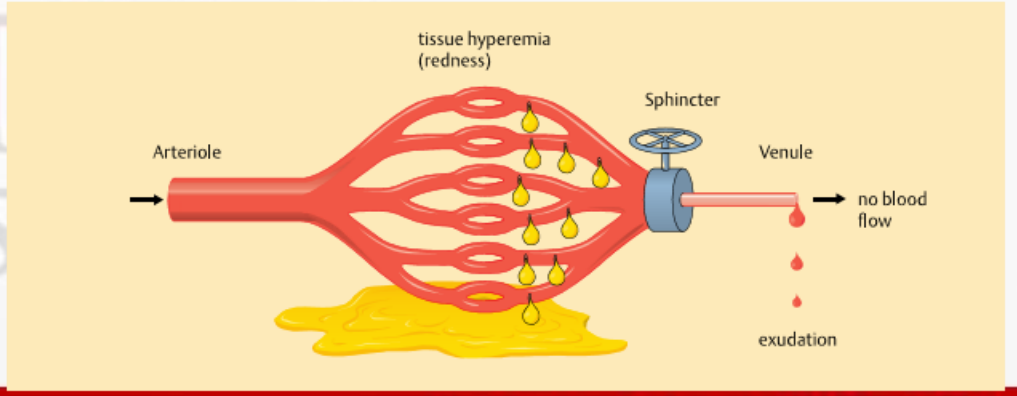
- The agent IS IN the tissue. All “faucets” are turned on by means of vasodilatation of the arterioles, capillaries, and venules to thoroughly flush out the noxious agent.
- Result: Erythema, swelling, and pain in the inflamed area.



Changes in Microcirculation

3rd phase: vaso*dilatation* of the capillaries and arterioles and vaso*constriction* of the venules. This slows the circulation, elevates filtration pressure, and increases vascular permeability in the inflamed area

- The noxious agent REMAINS in the tissue. All "faucets" are turned and sealed off by means of vasoconstriction of the venules and formation of microthrombi.
- The area damaged by the noxious agent is sealed off, paving the way for the "strike force" of leukocytes.



Changes in permeability

Biologic purpose of exudation:

— Contaminants are diluted by the protein-rich exudate.

— Contaminants are neutralized by the rapid introduction of counteractive substances such as antibodies.

— Contaminants are fixed and damage is controlled. The coagulated fibrin in the tissue demarcates the inflammatory damage and fixes the pathogens.

Leukocyte Transmigration

Biologic purpose:

The leucocytes traveling into the inflamed regions, exit the blood via the vascular wall, must construct a temporary and efficient "defensive system".

SEQUENCE OF EVENTS:

- Leukocyte margination and rolling
- Leukocyte adhesion
- Leukocyte transmigration (chemotaxis)
- Leukocytes ingest offending agents (phagocytosis), kill microbes, and degrade necrotic tissue and foreign antigens

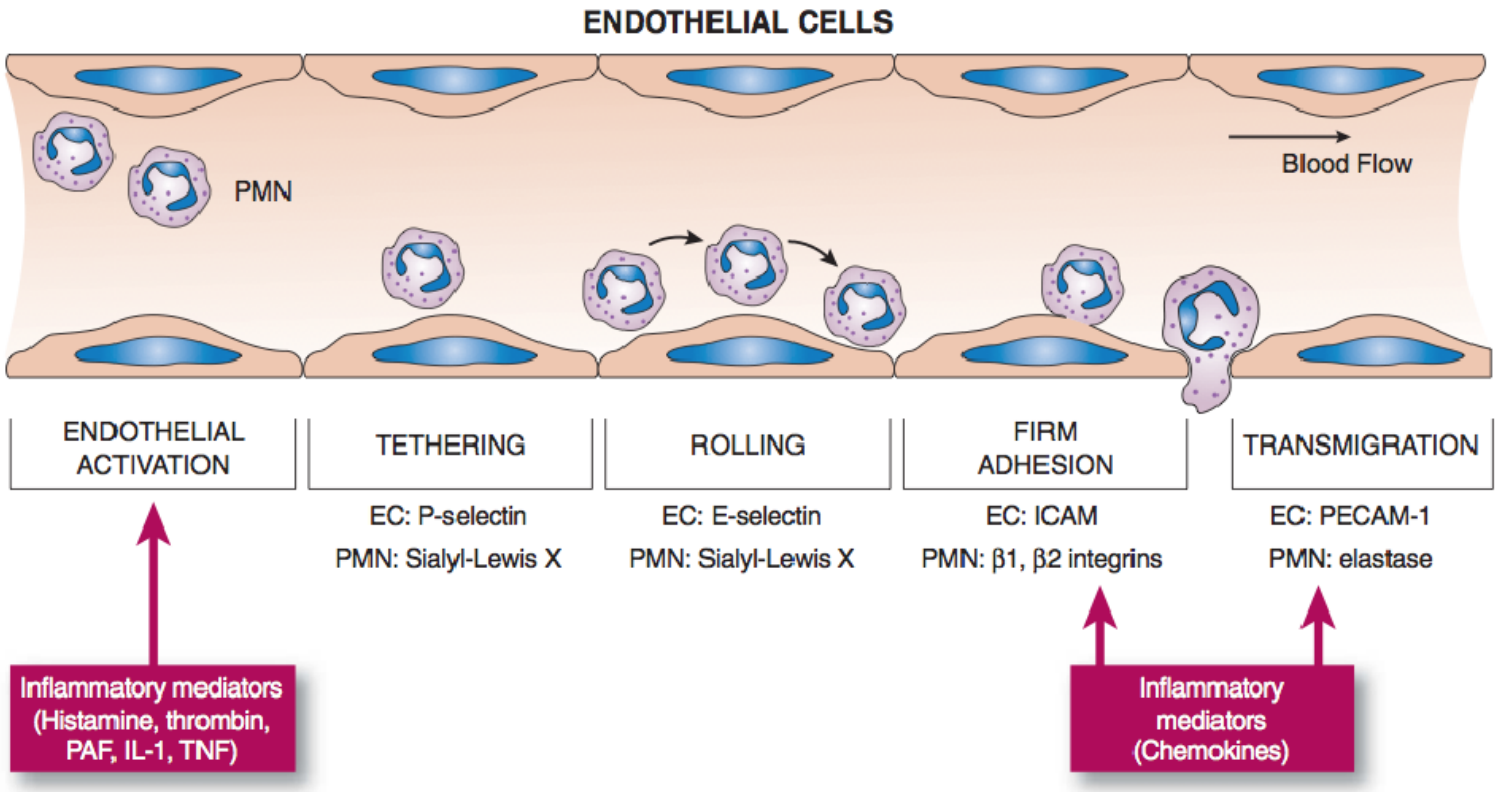
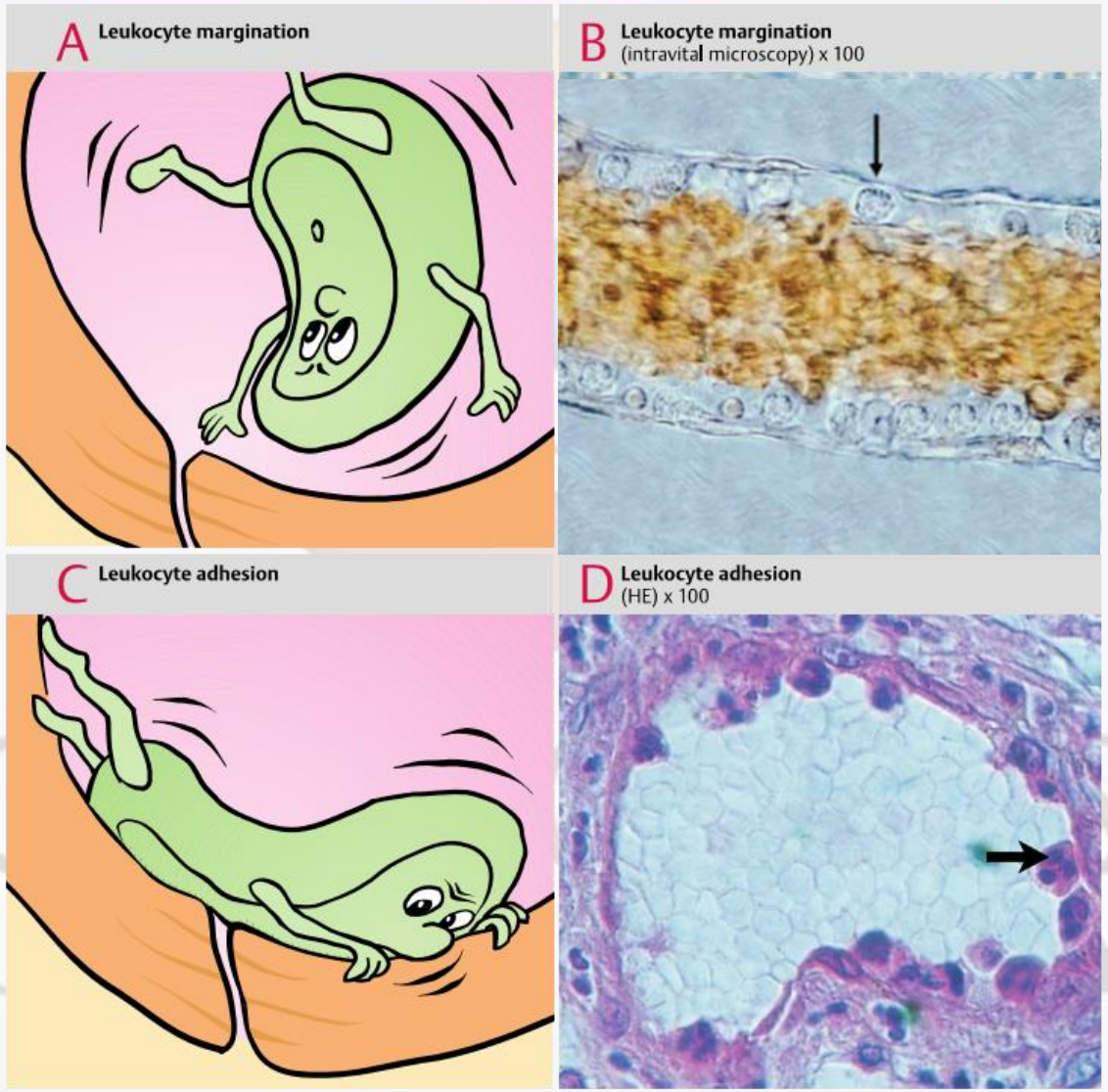
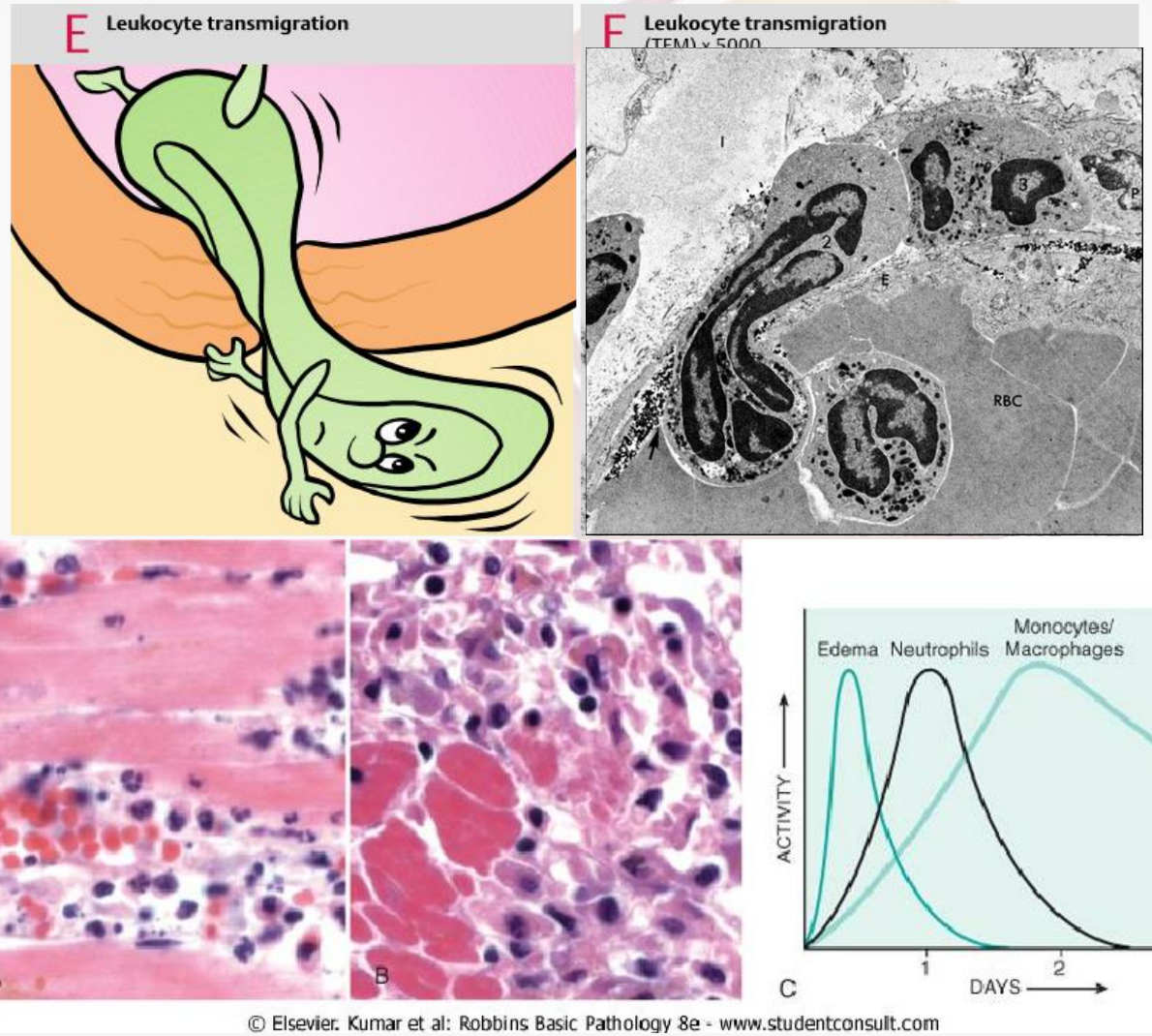


FIGURE 2-22. Neutrophil adhesion and extravasation. Inflammatory mediators activate endothelial cells to increase expression of adhesion molecules. Sialyl-Lewis X on neutrophil P-selectin glycoprotein-1 (PSGL-1) and E-selectin ligand (ESL-1) binds to P- and E-selectins to facilitate tethering and rolling of neutrophils. Increased integrins on activated neutrophils bind to intercellular adhesion molecule-1 (ICAM-1) on endothelial cells to form a firm attachment. Endothelial cell attachments to one another are released and neutrophils then pass between separated cells to enter the tissue. *EC* = endothelial cell; *IL* = interleukin; *PAF* = platelet-activating factor; *PMN* = polymorphonuclear neutrophil; *TNF* = tumor necrosis factor.


A Leukocyte margination
B Leukocyte margination
(intravital microscopy) x 100
C Leukocyte adhesion
D Leukocyte adhesion
(HE) x 100



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