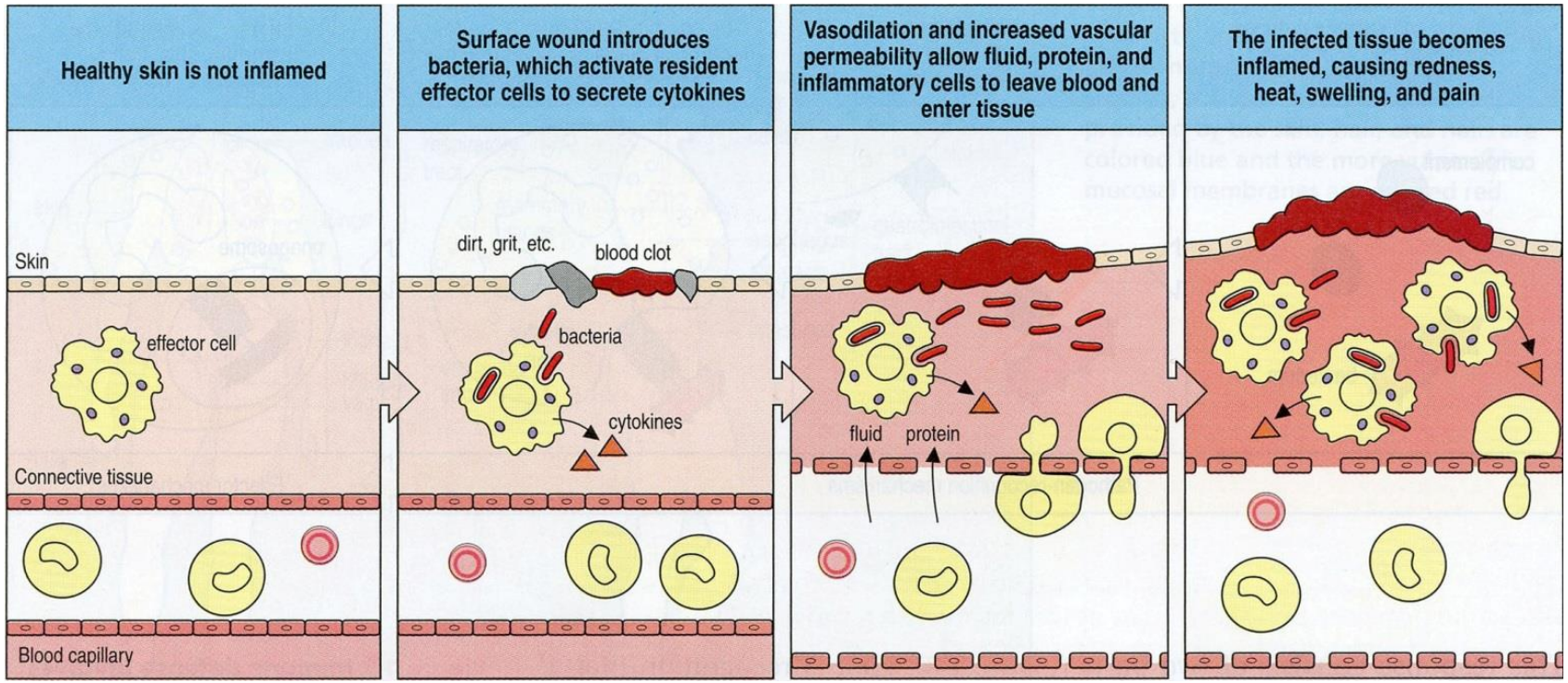
Inflammation

Inflammation

Cellular and soluble factors in the tissue detect the invading pathogens



From Parham 4th edition

PRRs are Germline-encoded receptors:

Two families of signalling membrane receptors:

1. **Toll-like receptors (TLRs)**
2. **C-type lectin receptors (CLRs)**

PRRs	Localization	Ligand	Origin of the Ligand
TLR			
TLR1	Plasma membrane	Triacyl lipoprotein	Bacteria
TLR2	Plasma membrane	Lipoprotein	Bacteria, viruses, parasites, self
TLR3	Endolysosome	dsRNA	Virus
TLR4	Plasma membrane	LPS	Bacteria, viruses, self
TLR5	Plasma membrane	Flagellin	Bacteria
TLR6	Plasma membrane	Diacyl lipoprotein	Bacteria, viruses
TLR7 (human TLR8)	Endolysosome	ssRNA	Virus, bacteria, self
TLR9	Endolysosome	CpG-DNA	Virus, bacteria, protozoa, self
TLR10	Endolysosome	Unknown	Unknown
TLR11	Plasma membrane	Profilin-like molecule	Protozoa
CLR			
Dectin-1	Plasma membrane	β-Glucan	Fungi
Dectin-2	Plasma membrane	β-Glucan	Fungi
MINCLE	Plasma membrane	SAP130	Self, fungi

PRRs are Germline-encoded receptors:

Two families of signalling cytoplasmic receptors.

1. **Retinoic acid-inducible gene (RIG)-I-like receptors (RLRs).**
2. **NOD-like receptors (NLRs).**

PRRs	Localization	Ligand	Origin of the Ligand
RLR			
RIG-I	Cytoplasm	Short dsRNA, 5′triphosphate dsRNA	RNA viruses, DNA virus
MDA5	Cytoplasm	Long dsRNA	RNA viruses (Picornaviridae)
LGP2	Cytoplasm	Unknown	RNA viruses
NLR			
NOD1	Cytoplasm	iE-DAP	Bacteria
NOD2	Cytoplasm	MDP	Bacteria

Inflammation:

■ **Initiation** of the inflammatory response is mediated by:

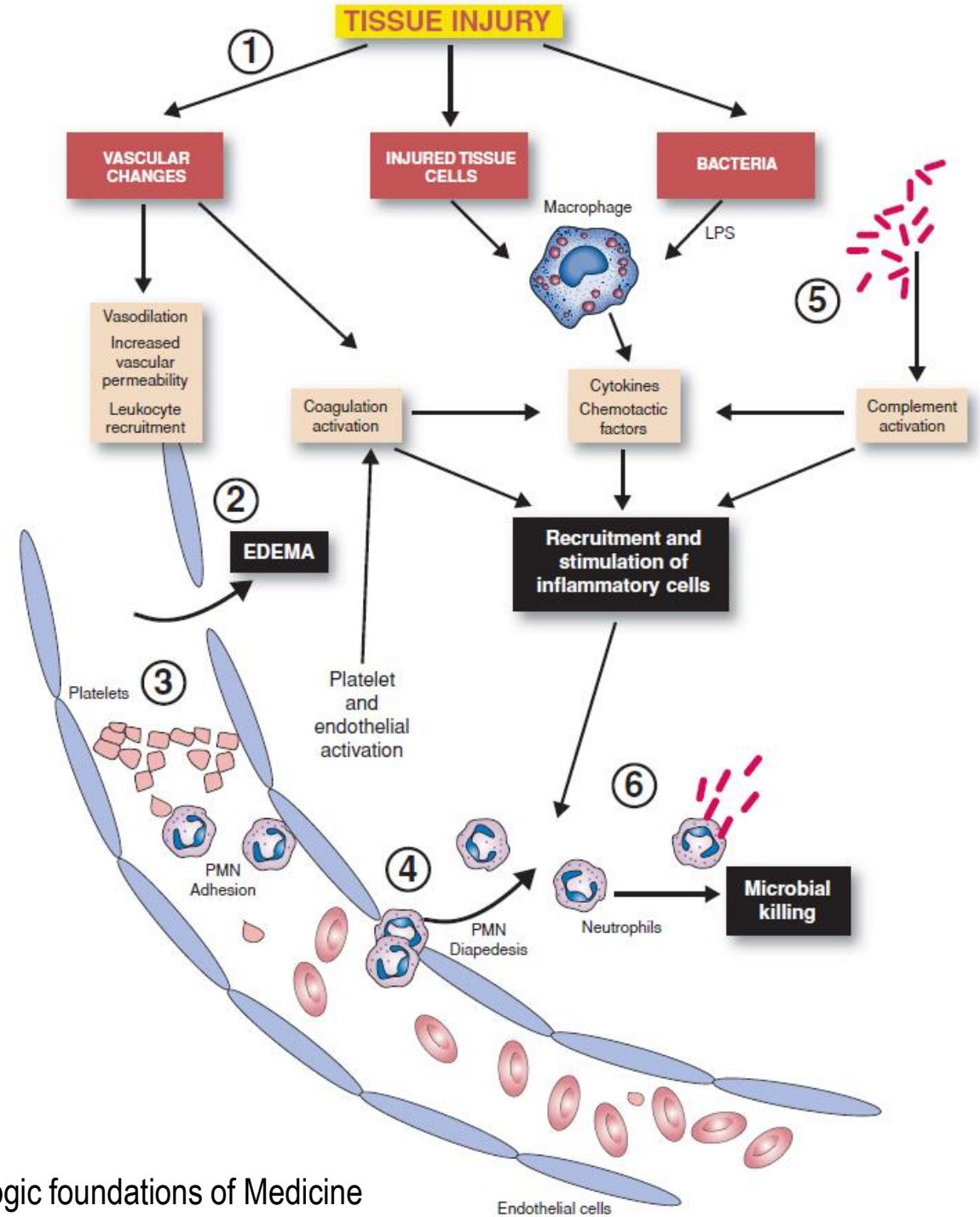
- Activation of soluble mediators
  - Altering the permeability of nearby blood vessels to plasma, soluble molecules
  - Triggering the recruitment of inflammatory cells to the area.
  - Rapid flooding of injured tissues with fluid, coagulation factors, cytokines, chemokines, platelets and inflammatory cells, neutrophils in particular.
  - **This overall process is acute inflammation.**

■ **Amplification** depends on the extent of injury and activation of mediators such as kinins and complement components. Additional leukocytes and macrophages are recruited to the area.

Inflammation:

- Eliminate a pathogenic insult.
- Remove injured tissue components.
- Allow tissue repair.

Responses to many damaging agents are immediate and stereotypical.



Rubin's PATHOLOGY Clinicopathologic foundations of Medicine

Inflammation:

- **Destruction** of the damaging agent brings the process under control.
  - Enzymatic digestion and phagocytosis reduce or eliminate foreign material or infectious organisms.
  - Damaged tissue components are also removed and debris is cleared, paving the way for repair to begin.

- **Termination** of the inflammatory response:
  - Is mediated by intrinsic anti-inflammatory mechanisms.
  - Limit tissue damage.
  - Allow repair and a return to normal physiologic function.
  - Alternatively, a scar may develop in place of normal tissue.
  - Prevent further influx of fluid, mediators and inflammatory cells; and prevent damage to normal cells and tissue.

Acute inflammatory responses: Usually works to defend the body.

- If not controlled may also be harmful. Acute inflammatory responses may be exaggerated.
    - Tissue damage may result
        - Ravages of bacterial pneumonia due to acute inflammation.
        - Joint destruction in septic arthritis.

Chronic inflammation:

When injured tissue and foreign agents are not cleared persistent responses occur.

- Infiltrates are largely lymphocytes, plasma cells and macrophages.
- Chronic inflammation may also damage tissue and cause scarring and loss of function.
- Indeed, chronic inflammation is the basis for many degenerative diseases.
- Weak inflammatory responses may lead to uncontrolled infection, as in immunocompromised hosts.
- In several congenital diseases, deficient inflammation is due to defects in inflammatory cell function or immunity.

A**cute and chronic inflammatory infiltrates often coexist.**

Inflammation

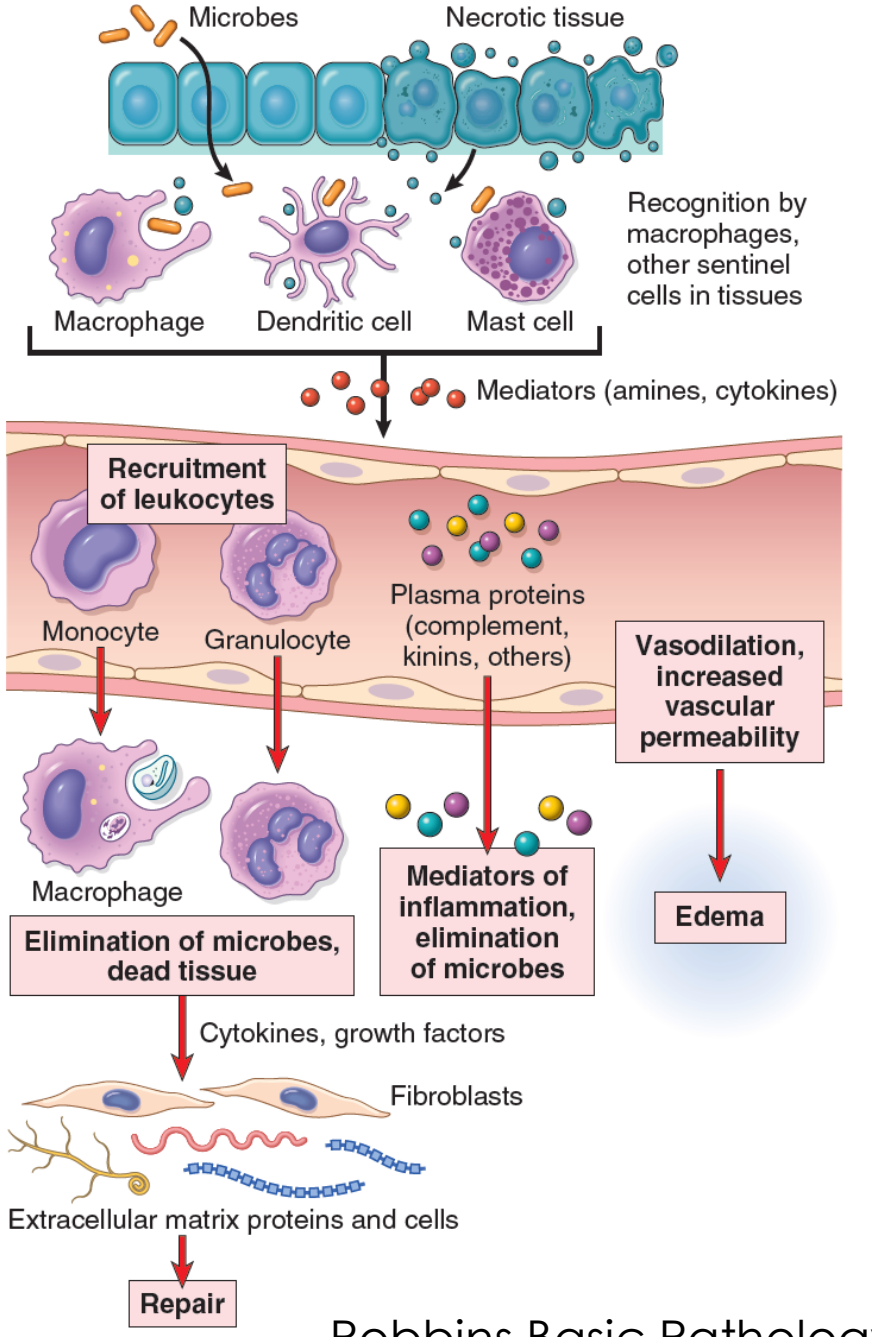
- Response to infections and damaged tissues (defense mechanism)
- Brings cells and molecules of host defence to the sites where needed
- Essential for survival as it rid the host of
  - Initial cause of cell injury (e.g., microbes, toxins)
  - Consequences of such injury (remove necrotic cells or tissues)
  - Initiate the repair process (wound healing)
- W/o inflammation
  - Infections would go unchecked,
  - Wounds would never heal,
  - Injured tissues might remain permanent
- Contribute with immune response in the elimination of the threat
- Inflammation is normally controlled and self limited
- Potentially harmful process:

  Components of inflammation that are capable of destroying pathogen can also injure bystander cells of surrounding tissues.

Inflammation

Inflammatory reaction is sequential:

- Pathogens/ substance are recognized
- Leukocytes and plasma proteins are recruited
- Eliminate the pathogens/substance.
- The reaction is controlled and terminated.
- The damaged tissue is repaired



Robbins Basic Pathology 9th Ed

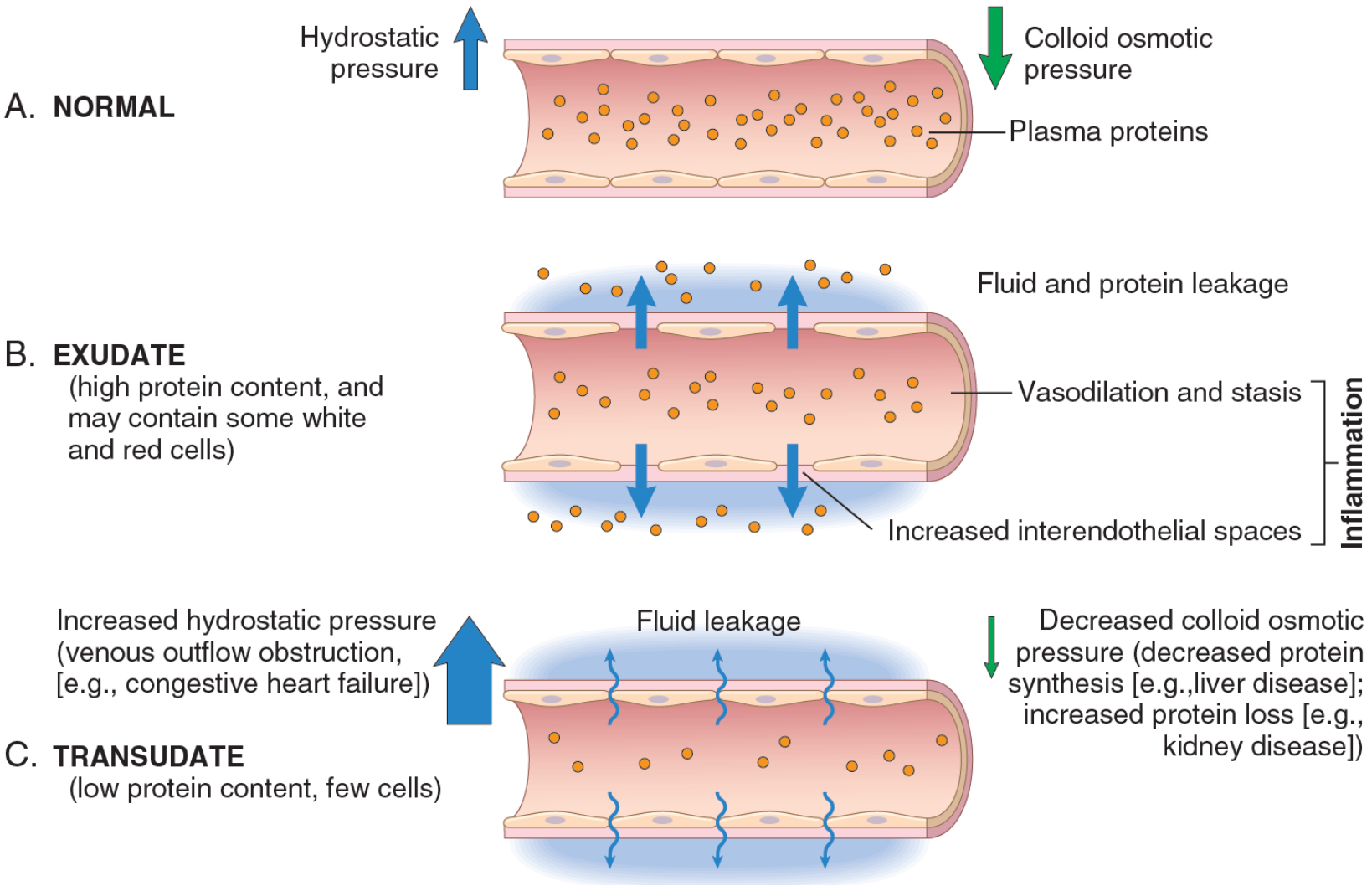
Components of the inflammatory response

The major participants in the inflammatory reaction in tissues are:

- Blood vessels
  - Dilate to slow down blood flow,
  - Increasing their permeability
  - Selected circulating proteins enter the site of infection or tissue damage
  - Endothelial cell express adhesion molecules

- leukocytes
  - Recruitment and activation
  - Ingest and destroy microbes and dead cells foreign bodies and unwanted materials in the tissues

Blood Vessels in Acute Inflammation



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Blood vessels

Vasodilation

Action of several mediators notably histamine on vascular smooth muscle.

- Increased blood flow (heat and redness, erythema)

Increased permeability of the microvasculature

- Outpouring of protein-rich fluid into the extravascular tissue
- Slower blood flow (loss of fluid + increased vessel diameter)
- Stasis (concentration of red cells in small vessels increasing blood viscosity)
- Leukocytes (neutrophils) accumulate along the vascular endothelium

Increased Vascular Permeability (Vascular Leakage)

Endothelial cell contraction (histamine, bradykinin, leukotrienes)

- Increased inter-endothelial spaces

Endothelial injury (severe injuries in burns, actions of microbes and microbial toxins

- leakage is immediate and sustained until damaged vessels are thrombosed or repaired

Lymphatic Vessels and Lymph Nodes

Increased lymph flow

- Drainage of oedema fluid
- Drainage of leukocytes and cell debris and microbes
- Proliferate of lymphatic vessels to handle the increased load

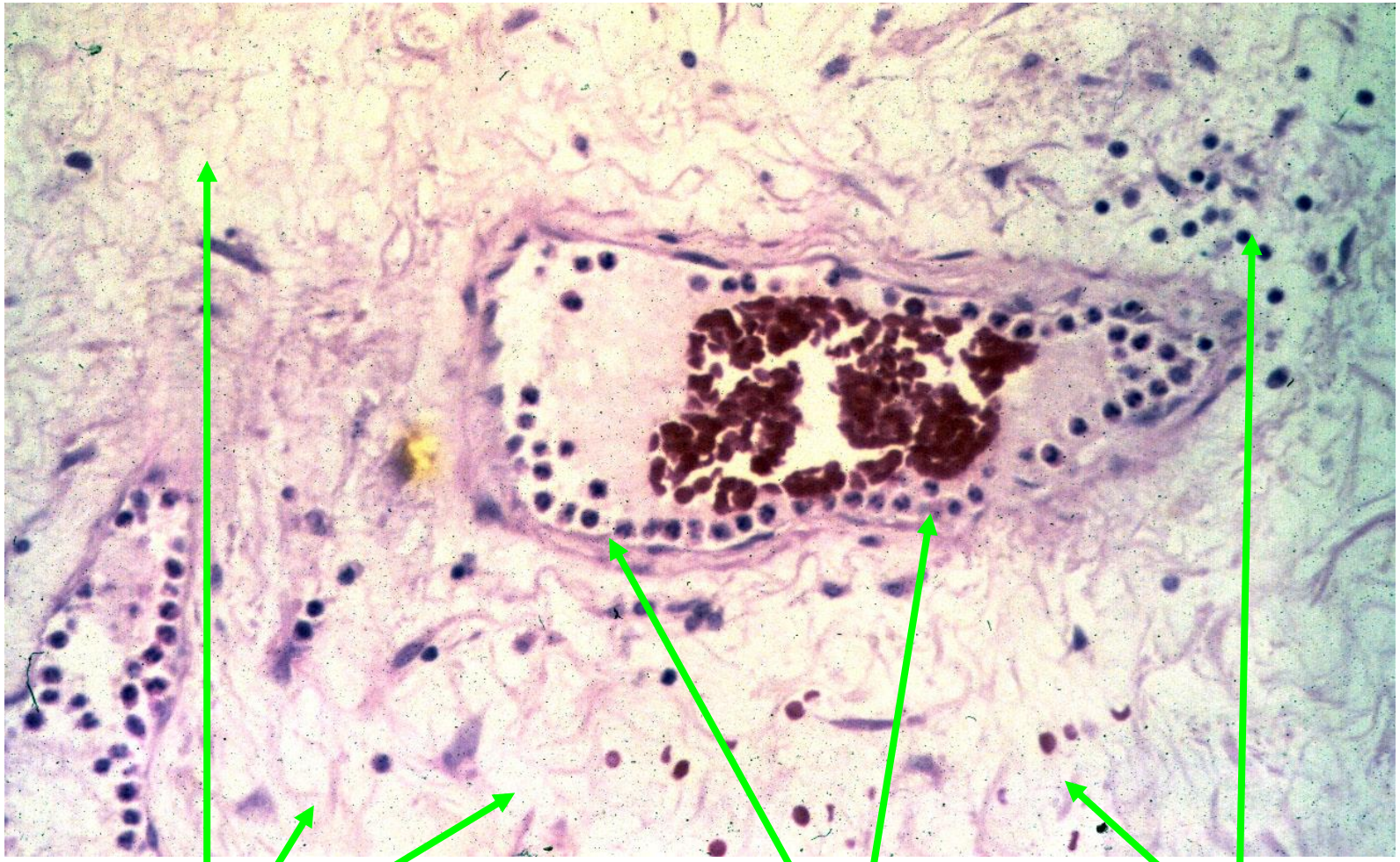
Lymphangitis

- *Secondary inflammation of lymphatic vessels*

Lymphadenitis

- *Secondary inflammation of lymph nodes*

Leukocyte extravasation



Leukocyte extravasation