Pathology

Second Year - First Semester Course

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Lecture 7

Acute Inflammation 1

- Inflammation is a **protective response** that is intended to eliminate the initial cause of cell injury, infectious agents, the necrotic cells, and to initiate the process of repair.

It also removes the debri that follows killing of infectious agents.

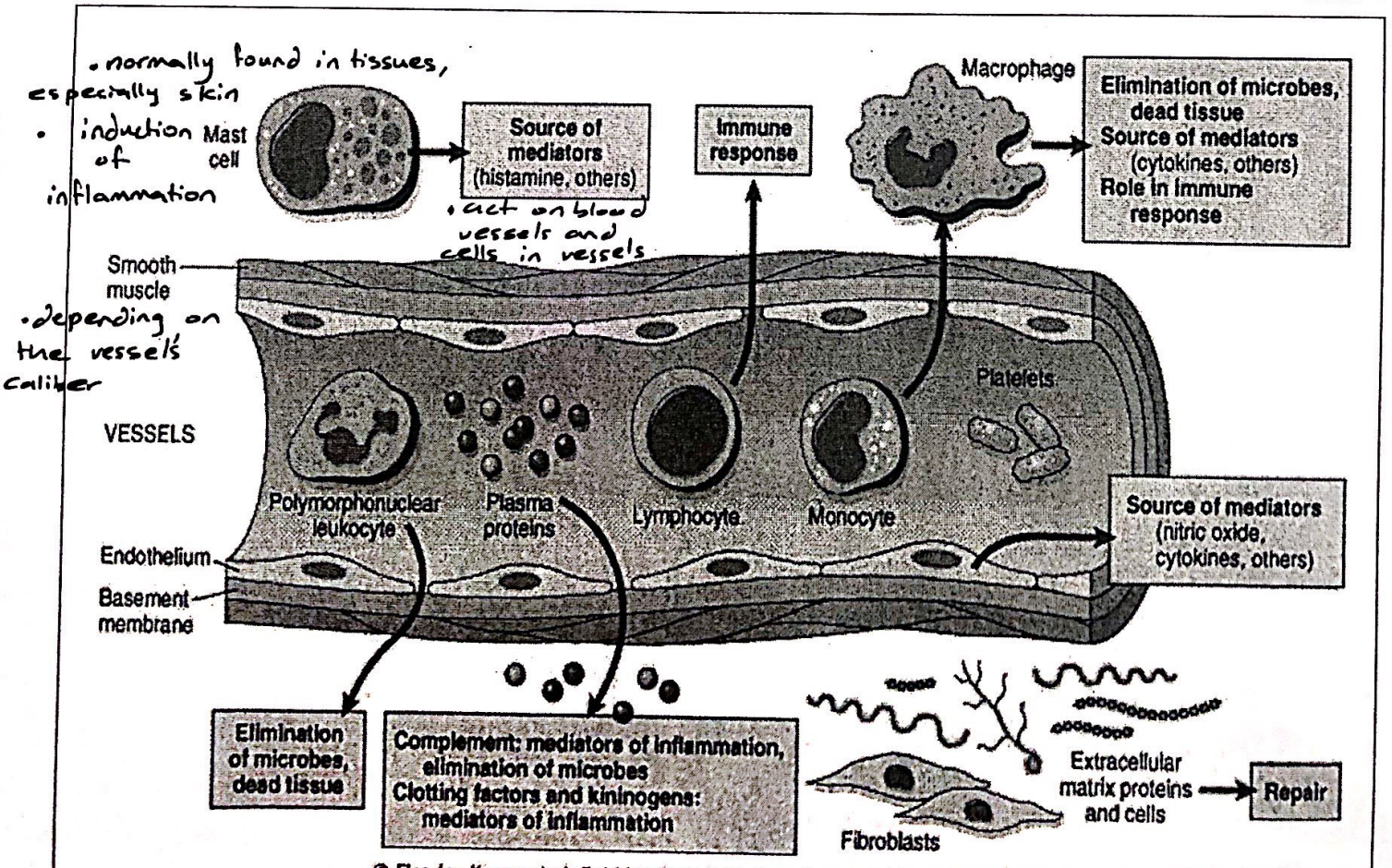
1. eliminate initial cause of injury
2. remove/clean up debri left behind
3. initiate repair process

Components of Inflammation

- Inflammatory responses involve an interaction of:
  - **Blood vessels** (endothelial cells and smooth muscles of vessels)
  - **White blood cells and platelets**
    - Neutrophils, monocytes, basophils lymphocytes, eosinophils.
  - **Plasma proteins and chemical mediators:**
    - Coagulation / fibrinolytic system, kinin system, complement system
  - **Extracellular matrix and stromal cells**
    - Mast cells, fibroblasts, macrophages & lymphocytes.
    - Structural fibrous proteins, adhesive glycoproteins, proteoglycans, basement membrane.

Vascular response → Blood vessels (endothelial cells and smooth muscles of vessels)

Vascular response ← → cellular response



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- normally found in tissues, especially skin
- induction of inflammation
- act on blood vessels and cells in vessels
- depending on the vessel's caliber
- if polymorphonucleur leukocytes, lymphocytes and monocytes exit the blood vessel and go to the tissues, they are called macrophages.

local sign : on site
· cut on hand
systemic sign : away from site
· increase in body temperature

Inflammation

Acute inflammation

- Onset: Fast: minutes to hours
- Duration: Short, from minutes to days
- Cellular infiltrate: Mainly neutrophils
- Tissue injury, fibrosis: usually mild and self limited, most of the time, the tissue recovers and restores its original function and structure
- Local and systemic signs: Prominent

Chronic inflammation

- Onset: Slow: days
- Duration: Long: days to years
- Cellular infiltrate: Monocytes/ macrophages and lymphocytes ★ (main)
- Tissue injury, fibrosis: Often severe and progressive, develops scar
- Local and systemic signs: Less prominent, may be subtle

chronic inflammation can start as:
· chronic (or) · acute ⟶ chronic (in case of persistant injury)

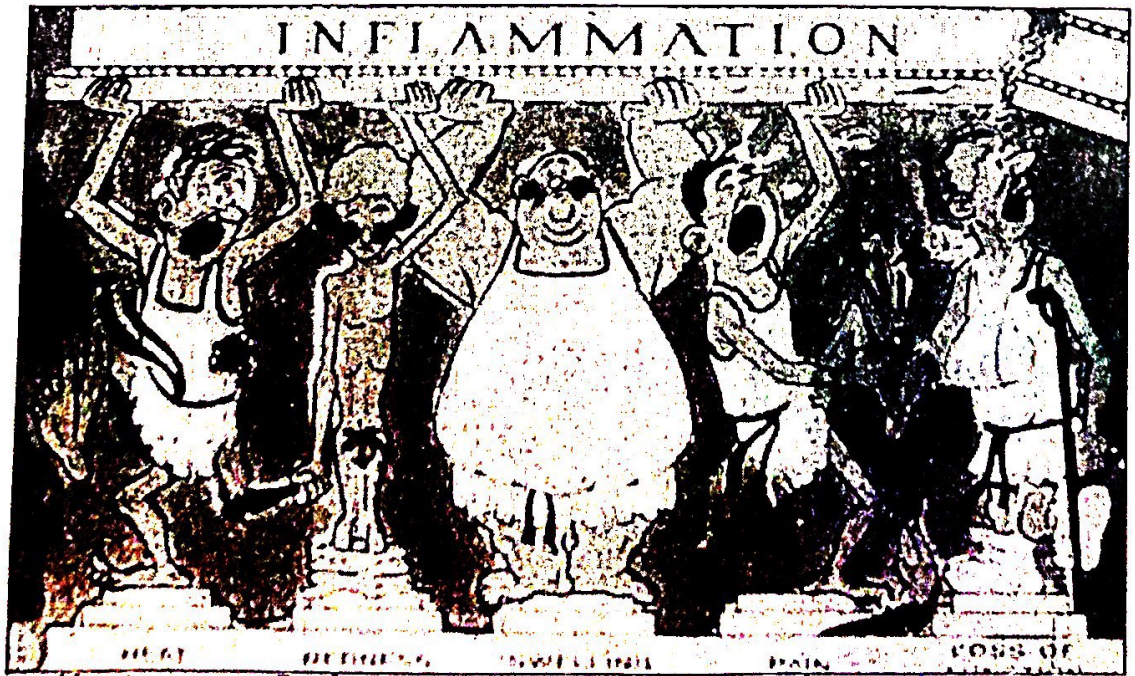
Acute inflammation

External manifestation of Inflammation

- Heat . cause: vasodilation
- Redness . cause: vasodilation
- Swelling. cause: edema
- Pain. Cause: some of the mediators
- Loss of function.

. usually those manifestations are localized (at the site of injury)
. example: bee sting (swollen, red, painful, restricted movement, heat)

The five classic signs of acute inflammation



Heat Redness Swelling Pain Loss Of Function.

Stimuli for Acute Inflammation

initiating agents

- *Infections* (bacteria, fungal, viruses, and parasites).
- *Trauma, various chemichal and physical agents* (heat, cold, burns, radiation).
- *Chemicals (*acids, alkali, bacterial toxins, metals).
- *Tissue necrosis* (from any cause)
- *Foreign bodies*
- *Immunologic reactions* (hypersensitivity reactions)

- *The steps of the inflammatory response can be remembered as the five Rs:*

(1) recognition of the injurious agent and differentiate between good, normal bacteria and pathogenic bacteria

(2) recruitment of leukocytes

(3) removal of the agent

(4) regulation (control) of the response, cannot be left ongoing

(5) resolution (repair).

Recognition of Microbes, Necrotic Cells, and Foreign Substances

- Phagocytes, dendritic cells ,and many other cells, such as epithelial cells, express receptors:

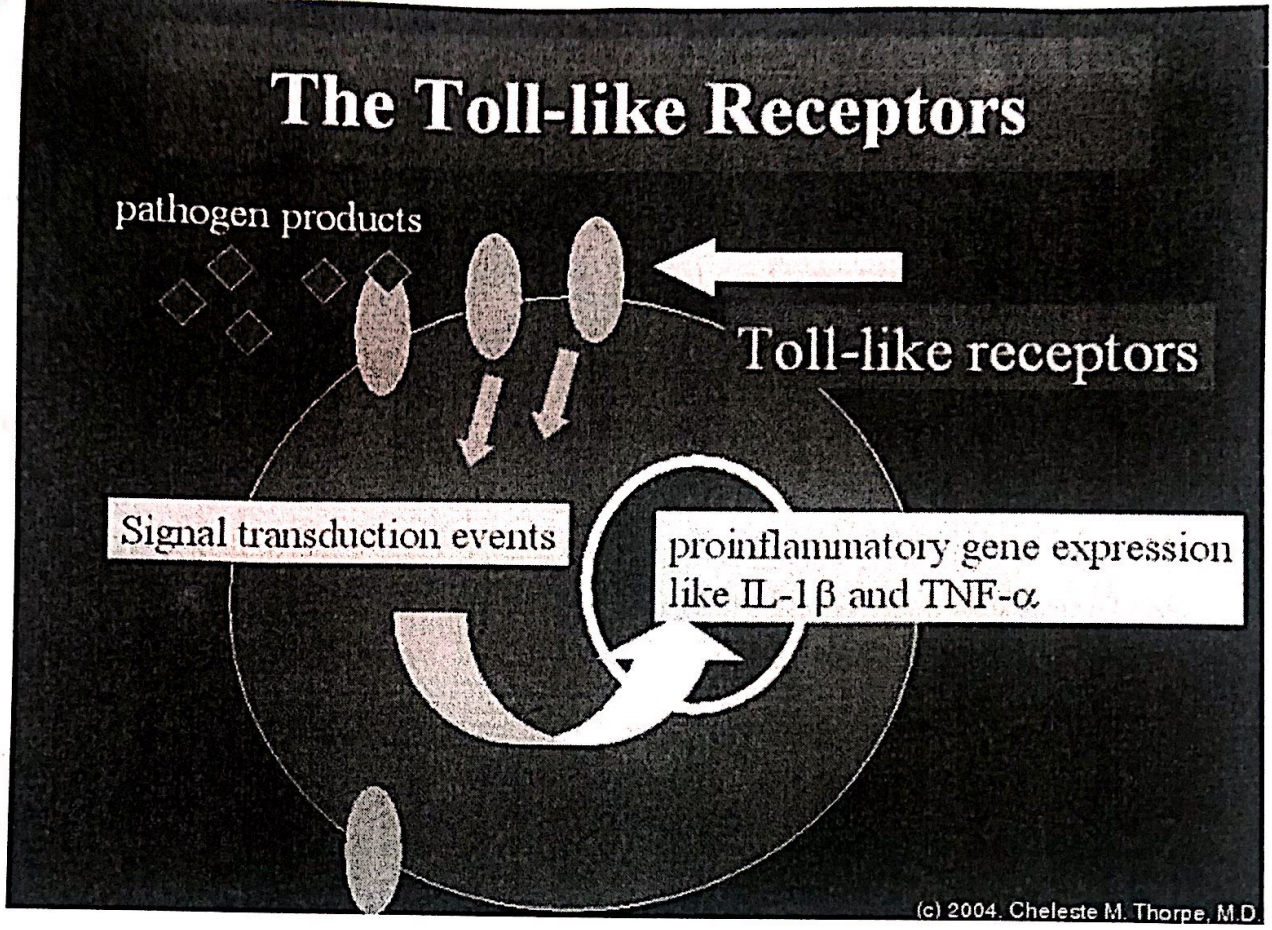
- Sense the presence of infectious pathogens and substances released from dead cells.
- They recognize structures on many microbes or dead cells.

① pathogenic products (bacterial, chemical agents) bind to TLRs.
② initiate signal transduction events that lead to increase in levels of pro-inflammatory factors

- The two most important families of these receptors are:

1- Toll-like receptors (TLRs):

- Microbial sensors: recognize products of bacteria (such as endotoxin and bacterial DNA), viruses (such as double-stranded RNA), and other pathogens.
- Recognition of microbes by these receptors activates transcription factors that stimulate the production of mediators of inflammation, and antiviral cytokines (interferons).



2- The inflammasome:

- Recognizes products of dead cells, such as uric acid and extracellular ATP, crystals and some microbial products.
- Triggering of the inflammasome results in IL-1 production.

Components of acute inflammation

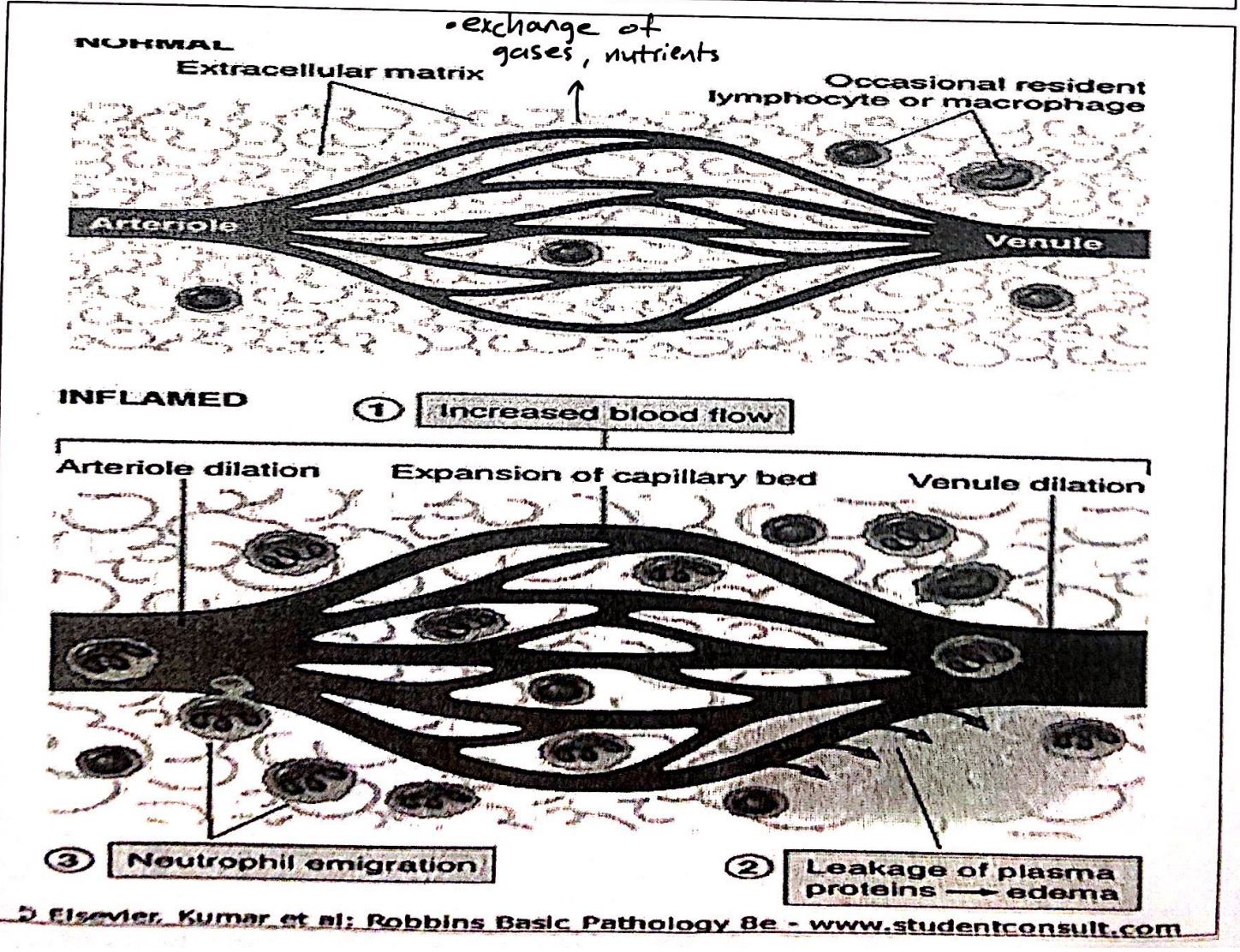
- **Vascular changes:** related to blood vessel walls → caliber / blood vessel walls & cells
  - Alterations in vessel caliber resulting in increased blood flow (***vasodilation***) → to slow the blood, giving cells time to leave and repair injury
  - Structural changes that permit plasma proteins to leave the circulation (***increased vascular permeability***).

① transient vasoconstriction (to stop bleeding) ② vasodilation ③ ↑ permeability

- ***Cellular events:***
  - Emigration of the leukocytes from the microcirculation and accumulation in the focus of injury (***cellular recruitment and activation***).
  - The principal leukocytes in acute inflammation: **neutrophils.**

① cellular recruitment (cells must be taken to site of inflammation)

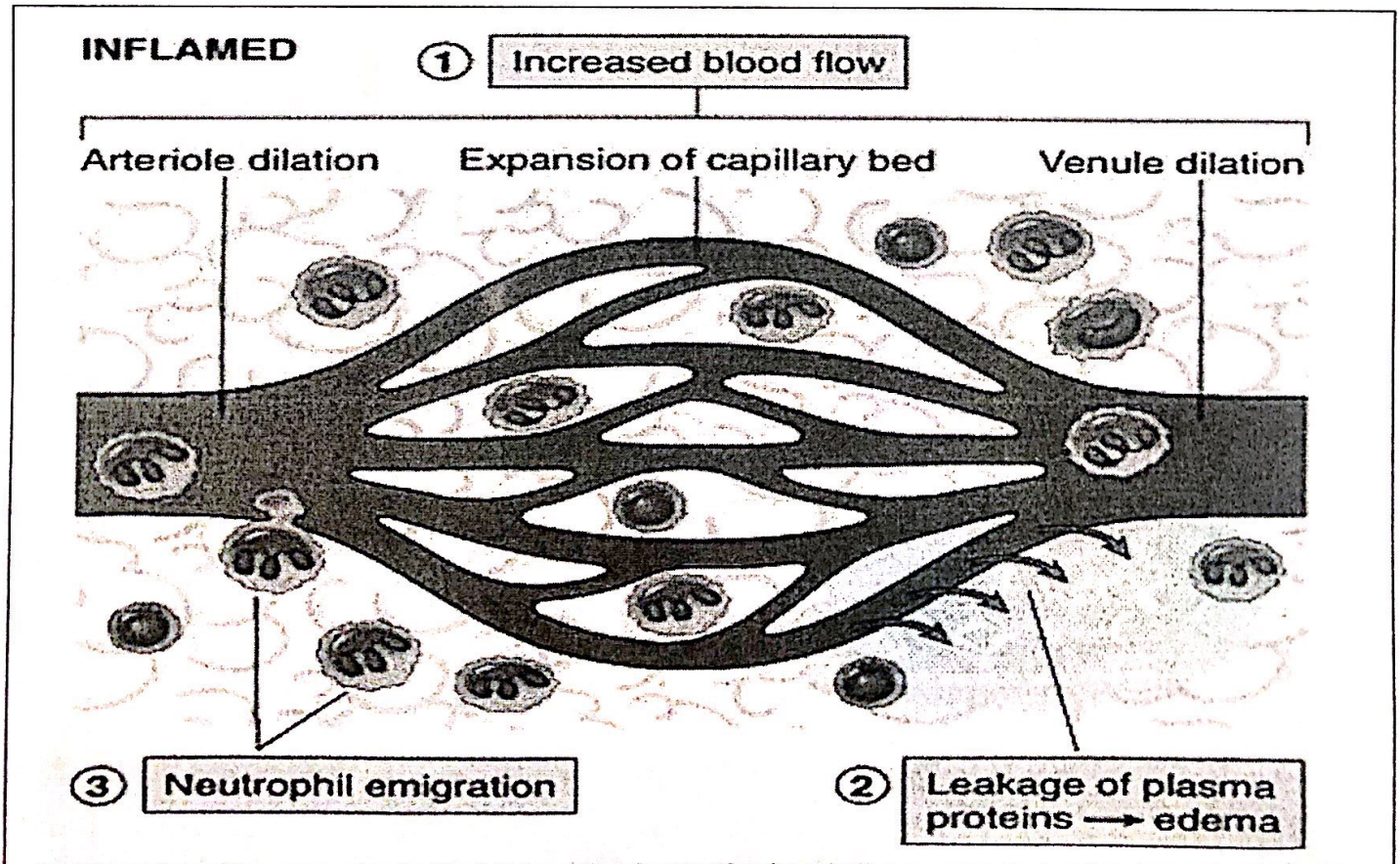
② cellular activation (cells must be activated to get rid of the initiating cause of inflammation and aid in repair)



Vascular Changes

1- Changes in Vascular Caliber and Flow:

- **Transient vasoconstriction** (lasting only for seconds) to stop blood loss
- **Arteriolar *vasodilation***, *the cause of erythema and warmth.* in area of injury

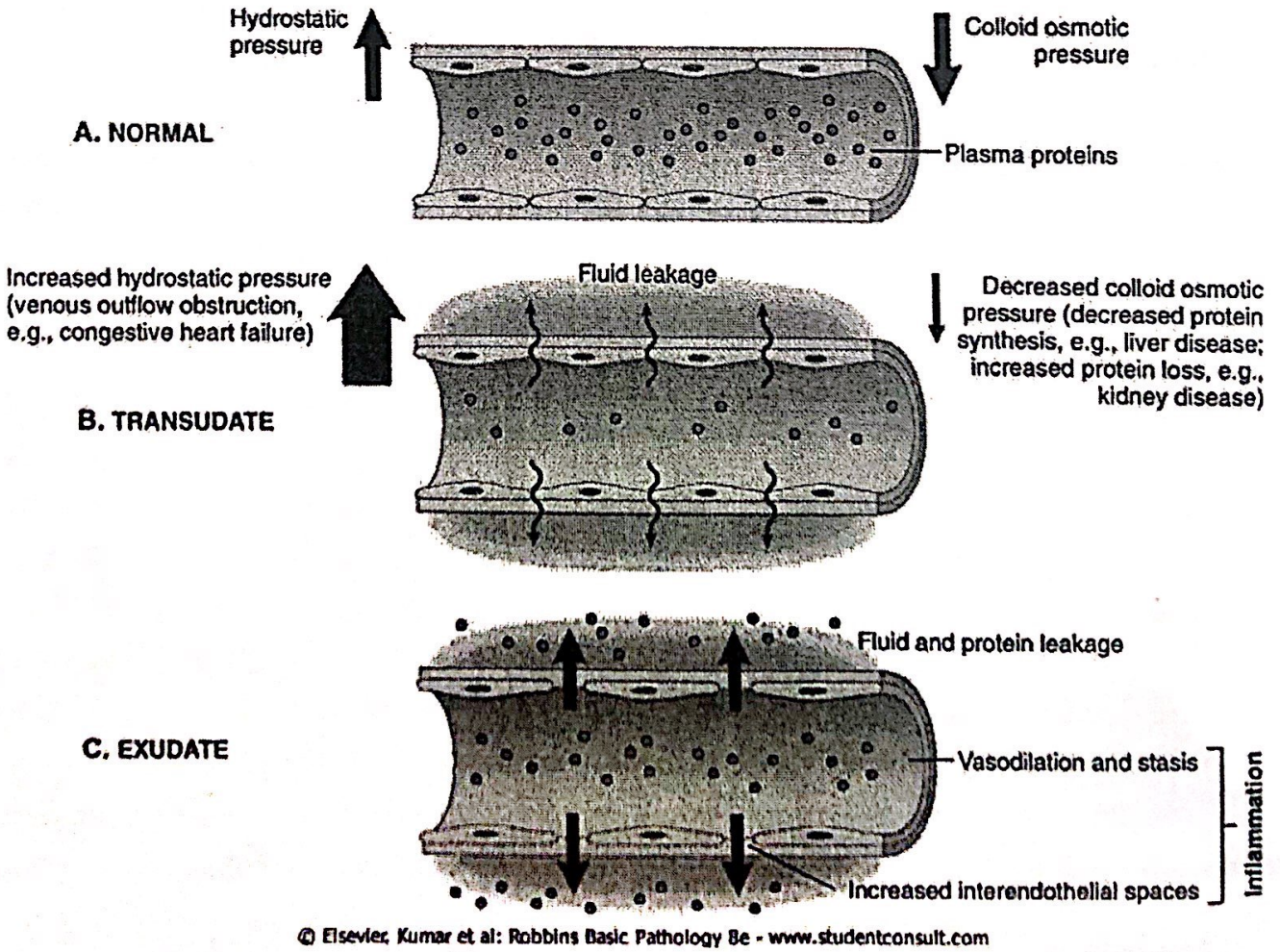


Vascular Changes

2- Increased Vascular Permeability

(exit) Leads to the movement of **protein-rich fluid and even blood cells** into the extravascular tissues . This in turn increases the osmotic pressure of the interstitial fluid, leading to more outflow of water from the blood into the tissues.

- More concentrated blood, slowing of the circulation (Stasis)
- Fluid accumulation in extravascular spaces produces tissue *edema*. → excess fluid, blood cells



Edema in Inflammation

2 types of edema fluid

TRANSUDATE

- Mechanism: Hydrostatic pressure imbalance across vascular endothelium
- Fluid of low protein content (ultrafiltrate of blood plasma)
- Typical in noninflammatory conditions

protein stays in blood vessel only water leaves vessel

example: kidney disease due to low protein content

EXUDATE

- Mechanism: Alteration in normal permeability of small blood vessels in area of injury
- Fluid of high protein content
- Typical in inflammation

proteins and water both exit blood vessel. proteins exiting leads to more fluid exiting due to hydrostatic pressure

Mechanisms of increased vascular permeability in acute inflammation

- **Endothelial cell contraction** (most common cause), formation of intercellular gaps in post capillary venules
- **Endothelial injury:** endothelial cell necrosis and detachment. (detach from lumen of blood vessels)
- **Increased transcytosis of proteins:** occurs through channels formed by fusion of intracellular vesicles. cells take up proteins and they pass right through the cell
- **Leakage from new blood vessels.**