INFLAMMATION

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DEPT. OF CLINICAL MEDICINE

Learning Objectives

- By the end of this session, students are expected to be able to:
  - Define the term inflammation
  - Identify types and signs of inflammation
  - Describe factors causing inflammation
  - Explain vascular and cellular changes occurring during inflammation
  - Describe outcomes of inflammation
  - Describe chemical mediators of inflammation

DEFINITION OF INFLAMMATION

- The ability of vascularised living tissue to respond to any noxious agent or injury.
- It is a local response of the living mammalian tissues to injury due to an agent.
- It is a protective response intended to eliminate the initial cause of cell injury as well as the necrotic cells and tissues resulting from the original insult.
- It is a complex reaction which involves many other systemic changes despite of what is observed locally.

Causes of Inflammation

1. **Physical agents like**
   - heat,
   - cold,
   - radiation and
   - mechanical trauma
2. **Chemical agents like**
   - organic and
   - inorganic poisons
3. **Infective agents like**
   - bacteria virus and their toxins
4. **Immunological agents like**
   - cell mediated and antigen antibody reactions

Types or Classification of Inflammation

- Depending on the different capacity of the host and duration of response, inflammation can be classified into acute or chronic.

1. **Acute inflammation**
   - represents the early body reaction and usually followed by repair and is of short duration.

2. **Chronic inflammation**
   - occurs either after the causative agent of acute inflammation persists for the long time or the stimulus such as that which it induces chronic inflammation from the beginning. It is of long duration.

A) ACUTE INFLAMMATION

- It is a rapid response to injury or microbes and other foreign substances that is designed to deliver leukocytes and plasma proteins to sites of injury.

- The leukocytes clear the invaders and begin the process of digesting and getting rid of necrotic tissues.

Components of Acute Inflammation

- Two Major Components

a) **Vascular changes**

Alterations in vessel caliber resulting in increased blood flow (vasodilatation) and structural changes that permit plasma proteins to leave the circulation (increased vascular permeability)

a) **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 are neutrophils (polymorphonuclear

leukocytes)

Causes of Acute Inflammation

1. **Infections** (bacterial, viral, fungal, parasitic) are among the most common and medically important causes of inflammation
2. **Trauma** (blunt and penetrating)
3. **Physical and chemical agents** (thermal injury, e.g. burns or frostbite; irradiation; some environmental chemicals) injure host cells and elicit inflammatory reactions.
4. **Tissue necrosis** (from any cause), including ischemia (as in a myocardial infarct) and physical and chemical injury
5. **Foreign bodies** (splinters, dirt, sutures)
6. **Immune reactions against environmental substances** or **against self tissues** (hypersensitivity)

Clinical Features/Signs of Acute Inflammation

The five cardinal features of acute inflammation

1. Pain and tenderness (dolour)
2. Swelling (tumour)
3. Redness (rubor)
4. Hotness (colour)
5. Loss of function or reduced efficiency (function laesa)

Pain and tenderness (dolour)

- This is an early symptom in acute inflammation
- The pain in acute inflammation is due to
  - direct nerve injury,
  - tissue irritation by chemicals and agents released by cells involved in acute inflammation and
  - pressure due to accumulating exudates compressing nerves

Swelling (tumour)

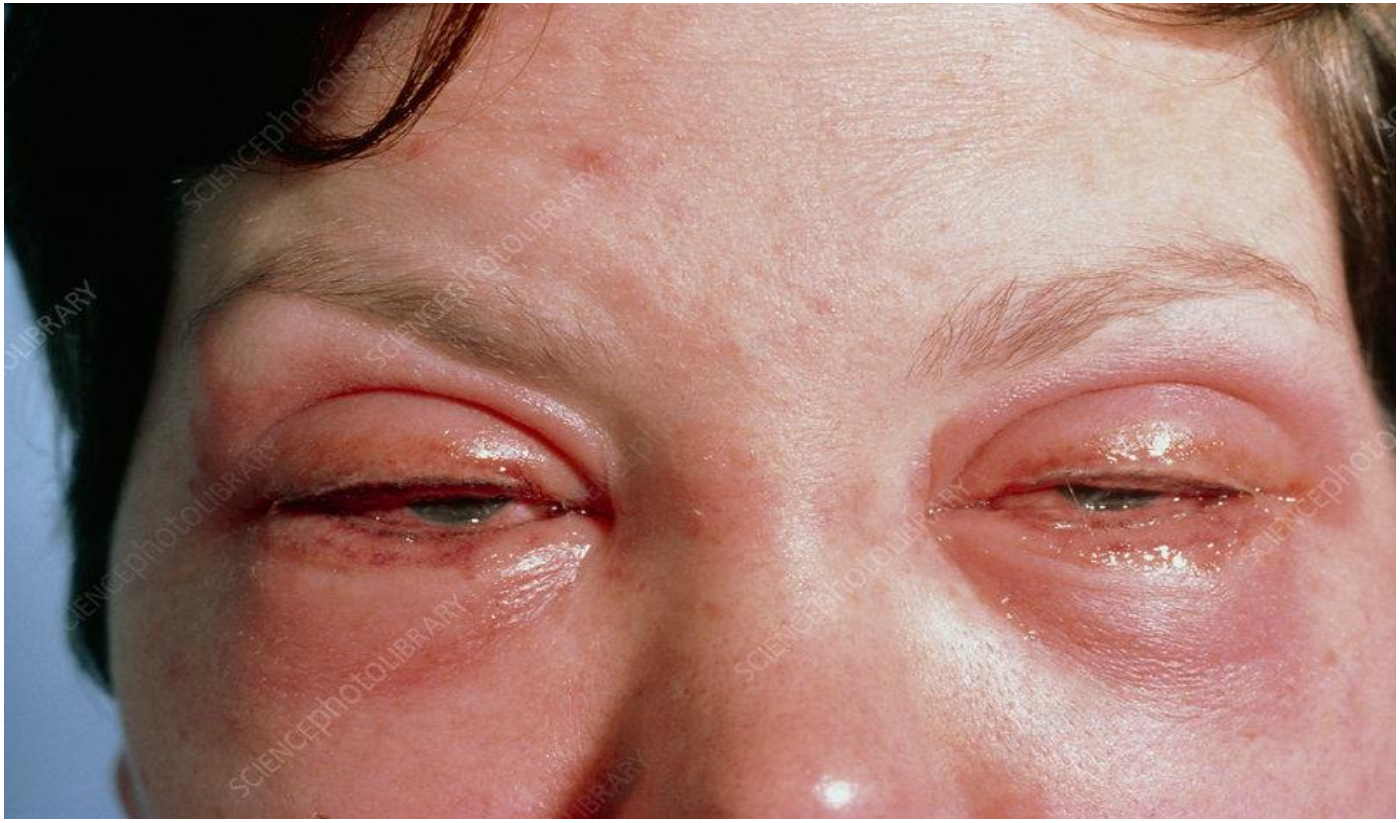
- This is due to **local accumulation** of inflammatory exudates
- Vascular changes occur within the affected area, which cause accumulation of **fluid and white blood cells** to escape from the intravascular compartment to the interstitial tissue in the inflamed area

Redness (rubor)

- This red coloration is due to
  i. local increase in blood flow to the inflamed zone,
  ii. increased permeability and blood flow
- The coloration is less prominent feature among dark skinned individuals

Hotness (colour)

- Inflamed area feels warmer than the surrounding areas due to increased blood flow to the affected area.



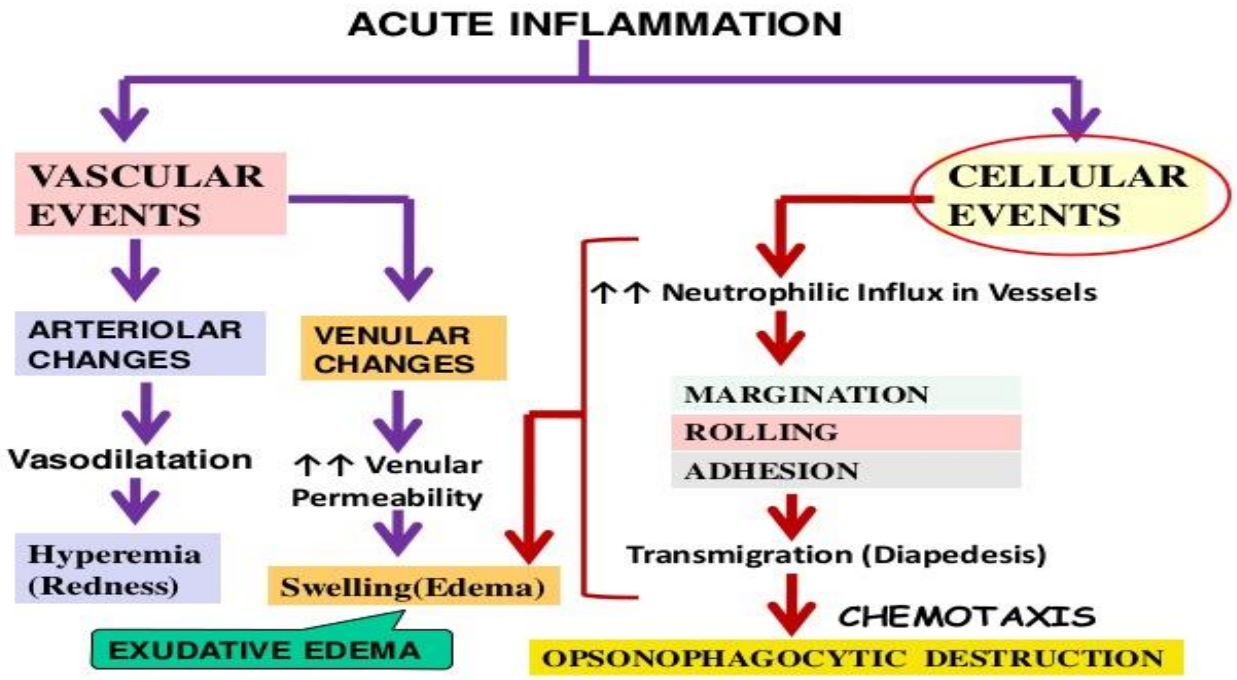
Loss of function or reduced efficiency (function laesa)

- Inflamed tissue or organ cannot perform its function as efficiently as a normal tissue

- Temporary or permanent structural damage to the tissue may lead to loss of function

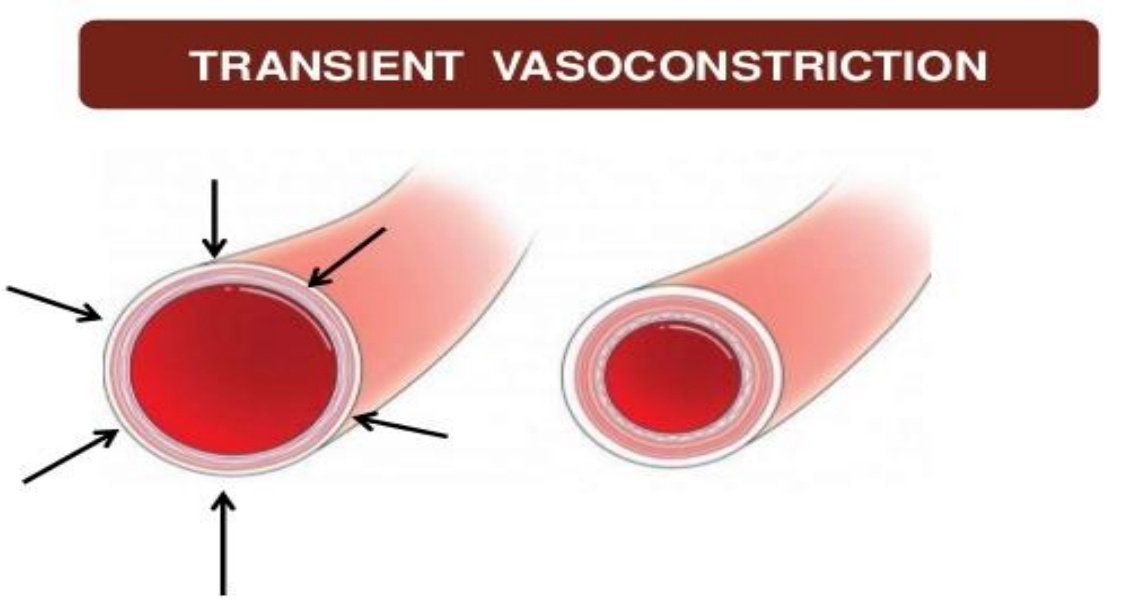
Vascular Changes During Acute Inflammation

1. Transient Vasoconstriction
2. Arteriolar Vasodilatation
3. Increased Vascular Permeability



1) Transient Vasoconstriction

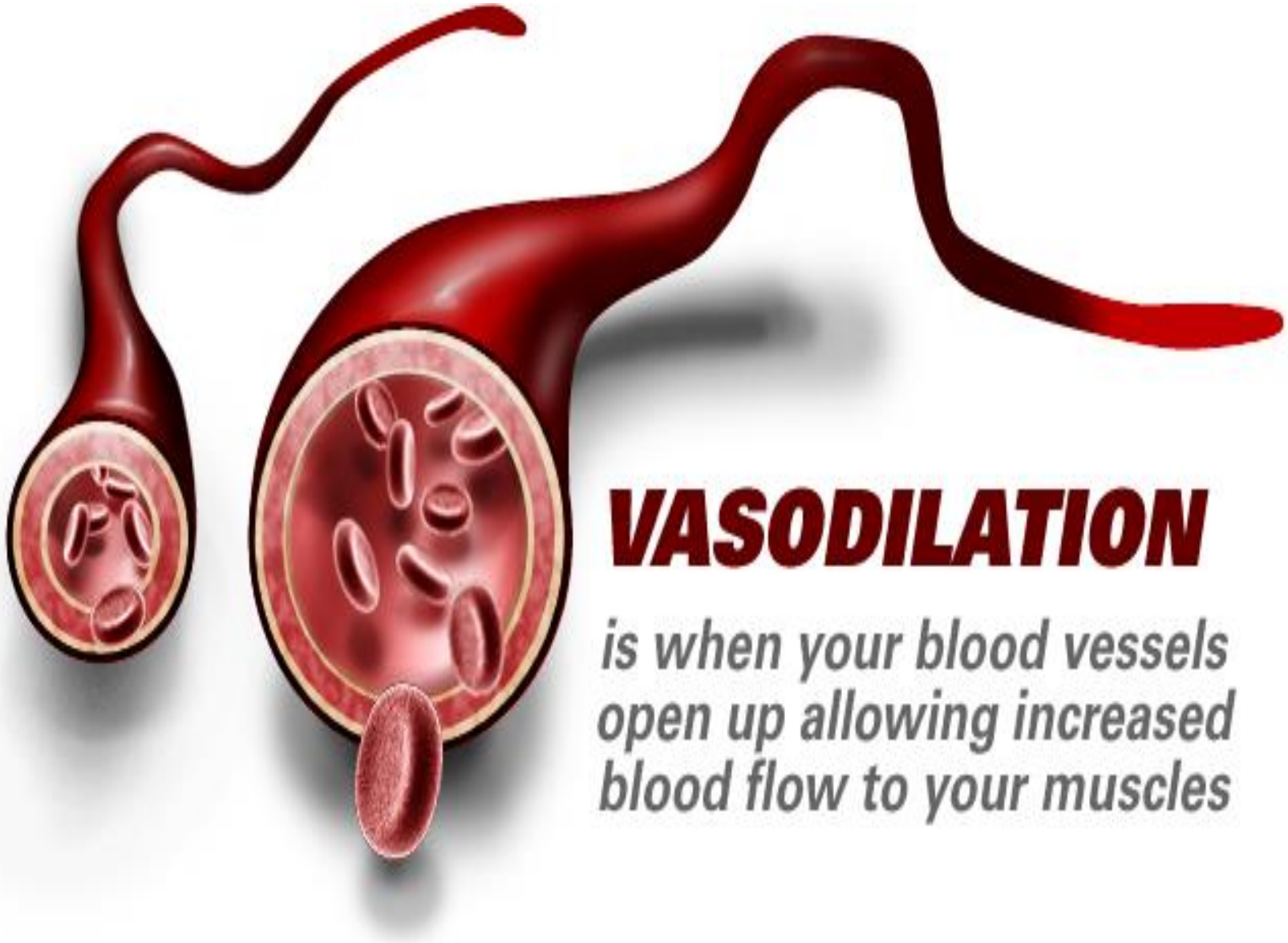
- This is a very short event lasting for a few seconds



- **Arterioles**
- **3-5 sec. in mild injury.....5 minutes ; severe injury**

2)Arteriolar Vasodilatation

- This is a predominant feature in acute inflammation.
- It occurs due to increased blood flow and engorgement of the down-stream capillary beds.
- This **vascular expansion** is the cause of the **redness** (erythema) and **warmth characteristically** seen in acute inflammation.
- As the microvasculature becomes more permeable, protein-rich fluid moves into the **extravascular tissues**.
- This causes the **red blood cells** to become more **concentrated**, thereby increasing blood viscosity and slowing the circulation



VASODILATION

is when your blood vessels open up allowing increased blood flow to your muscles

- These changes are reflected microscopically by numerous **dilated small vessels packed with erythrocytes** and slowly flowing blood, a process **called stasis**.
- As stasis develops, leukocytes (principally neutrophils) begin to accumulate along the vascular endothelial surface, a process called margination.
- This is the first step in the journey of the leukocytes through the vascular wall into the interstitial tissue (described later).

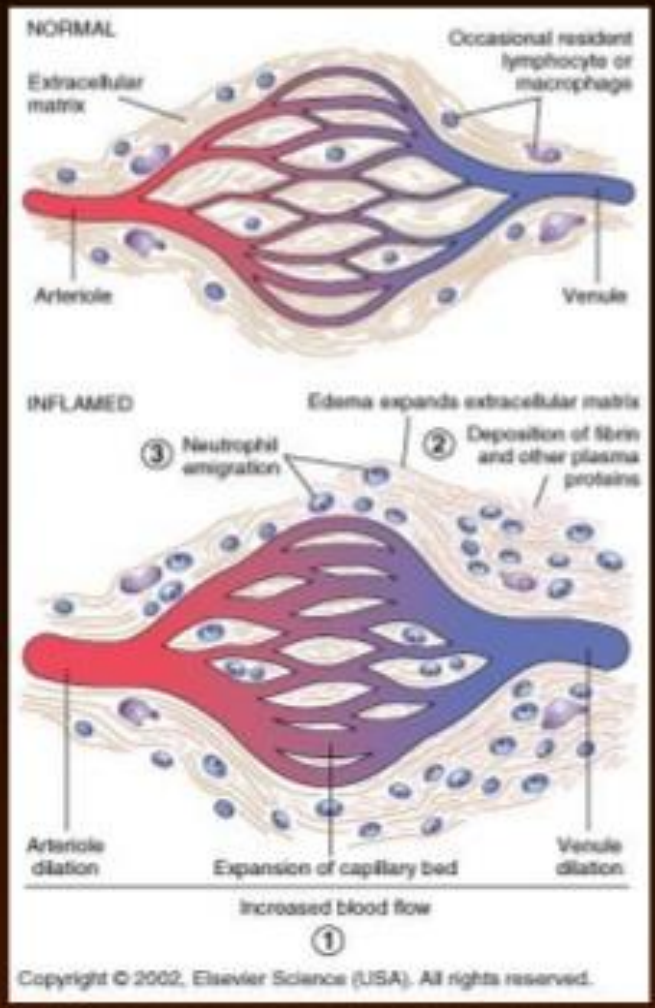
3)Increased Vascular Permeability

- In the early phase of inflammation, art**eriolar vasodilatation** and increased **volume of blood flow** lead to a rise in intravascular hydrostatic pressure, resulting in movement of fluid from capillaries into the tissues.
- This fluid, called a transudate, is essentially an ultra filtrate of blood plasma and contains little protein.
- However, transudation is soon eclipsed by increasing vascular permeability that allows the movement of protein-rich fluid and even cells into the interstitium, this protein rich fluid is called an exudate.

- The loss of protein-rich fluid into the perivascular space reduces the intravascular osmotic pressure and increases the osmotic pressure of the interstitial fluid.
- The net result is outflow of water and ions into the extravascular tissues.
- Fluid accumulation in extravascular spaces is called oedema, the fluid may be a **transudate or exudate.**
- Whereas **exudates are typical of inflammation, transudates** accumulate in various **non inflammatory conditions**

Stages of Inflammation

1. Transient vasoconstriction
2. Persistent vasodilatation
3. Increased Permeability
4. Fluid exudate (edema)
5. Cellular exudate (Neutrophil emigration & accumulation)
6. Resolution or progression



4)Exudation

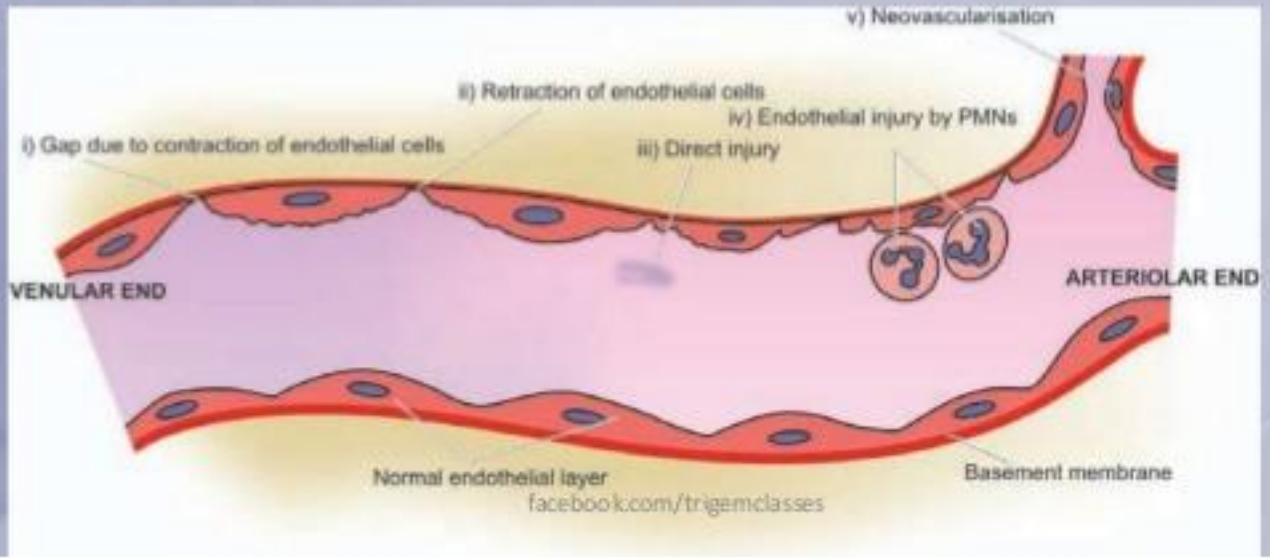
- The increase of protein-rich fluid from vessels to the interstitial space due to increased vascular permeability during an inflammatory condition.
- Components of exudates
  1. **Water**
  2. **Proteins** (immunoglobulins), albumin and fibrinogen in severe cases
  3. **Hormones**
  4. Natural antibacterial **opsonin**
  5. **Cells**-White blood cells (WBCs

Advantages of exudation

1. Dilute toxins in the area of inflammation
2. Globulins are protective antibodies
3. Fibrin helps in limiting the spread of factors causing inflammation and also assists wound healing

MECHANISMS OF INCREASED VASCULAR PERMEABILITY

1. Contraction of endothelial cells.
2. Retraction of endothelial cells
3. Direct injury to endothelial cells
4. Endothelial injury mediated by leucocytes
5. Leakiness and neo-vascularisation

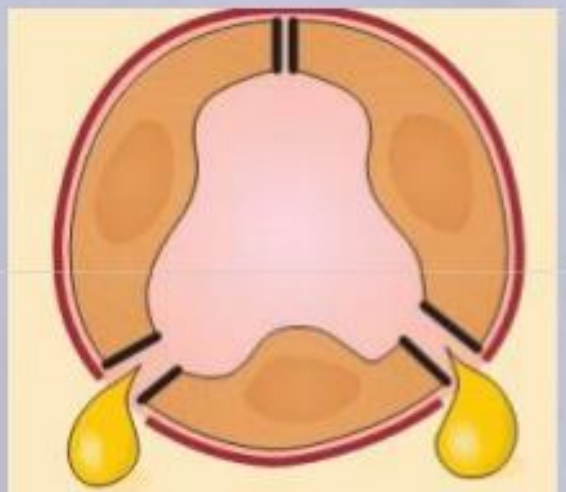


1) Endothelial cell contraction

- Endothelial cell contraction leading to **intercellular gaps** in post capillary venules .
- Its the most common cause of increased vascular permeability.
- It is a reversible process elicited by histamine, bradykinin, leukotrienes, and many other chemical mediators.
- Endothelial cell contraction is usually short-lived **(15-30 minutes)** it is also known as **the immediate transient response.**

Contraction of endothelial cells

- Affects venules exclusively.
- Endothelial cells develop temporary gaps
- Contraction resulting in vascular leakiness.
- Mediated by the release of **histamine**, **bradykinin** and **other chemical mediators.**
- Short duration (15-30 minutes) - immediately after injury.



Endothelial contraction

2) Endothelial injury

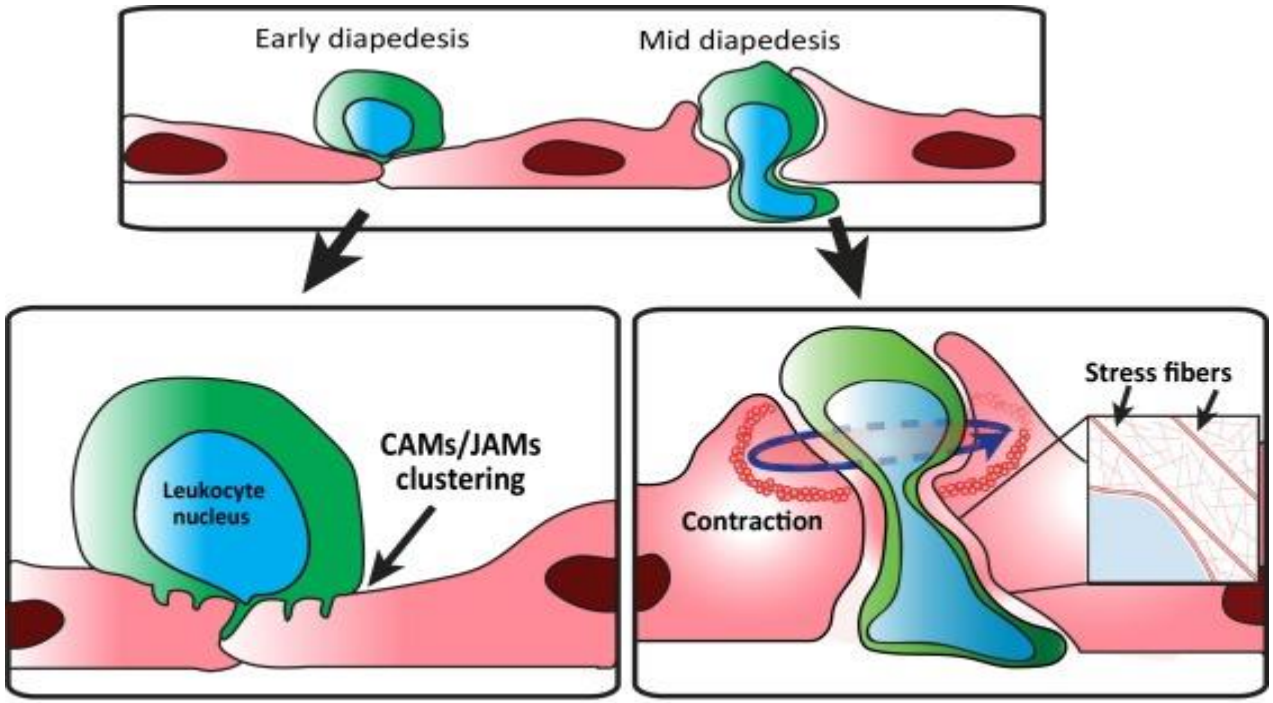
- Endothelial injury results in vascular leakage by causing endothelial cell necrosis and detachment.
- Direct injury to endothelial cells is usually seen after severe injuries (e.g. burns and some infections).
- In most cases leakage begins immediately after the injury and persists for several hours (or days) until the damaged vessels are thrombosed or repaired.
- Therefore, this reaction is known as the immediate sustained response

3) Direct Injury to Endothelial cells

- Direct injury to endothelial cells may also induce a **delayed prolonged leakage** that begins after a delay of **2 to 12 hours**, lasts for several hours or even days, and involves venules and capillaries.
- Examples include
  a) mild to moderate thermal injury,
  b) certain bacterial toxins, and
  c) X-rays or ultraviolet irradiation (i.e. the sunburn that appears in the evening after a day in the sun).

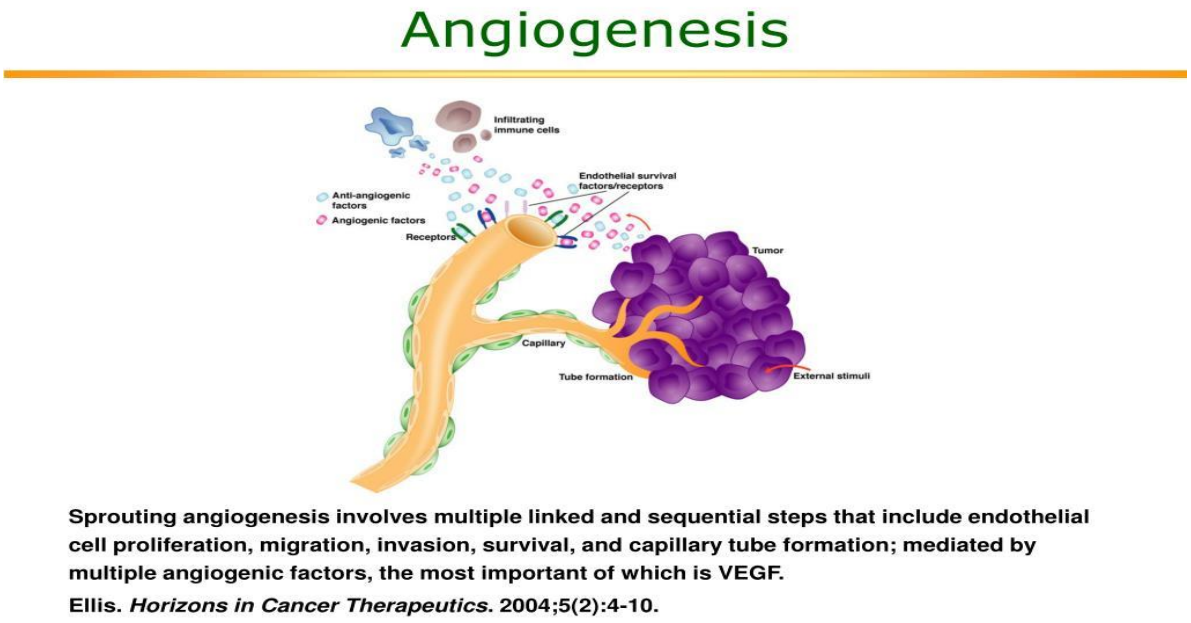
4) Leukocyte-mediated endothelial injury

- This may occur as a consequence of leukocyte accumulation along the vessel wall
- Activated leukocytes release many toxic mediators that may cause endothelial injury or detachment.



5)Leakage from new blood vessels

- Tissue repair involving **new blood vessels formation** (angiogenesis) which remain leaky until proliferating endothelial cells mature sufficiently to form intercellular junctions.



Sprouting angiogenesis involves multiple linked and sequential steps that include endothelial cell proliferation, migration, invasion, survival, and capillary tube formation; mediated by multiple angiogenic factors, the most important of which is VEGF.

Ellis. *Horizons in Cancer Therapeutics.* 2004;5(2):4-10.

END