Inflammation and Repair

L1- Acute inflammation- vascular changes

L2- Acute inflammation- cellular changes

L3- Mediators of inflammation

L4- Mediators of inflammation

Tutorial

L5- Morphology of acute inflammation

L6- Chronic inflammation

L7- Chronic granulomatous diseases- Tuberculosis

L8- Other granulomatous diseases

Tutorial

L9- Tissue renewal

L10- Healing by repair

Tutorial

Inflammation

- Def: complex reaction to injurious agents and damaged cells that consists of vascular responses, activation of leukocytes and systemic reactions
- Protective response, potentially harmful
- Inflammation can occur anywhere

  - acutely in the skin around a wound or a sting

  - or in less visible sites such as the lining of the middle ear, or of the gall bladder

Types of inflammation

- Acute : characterized by vascular changes, edema and neutrophilic infiltration

- Chronic : infiltration of mononuclear cells i.e. macrophages, lymphocytes and plasma cells along with tissue destruction and repair by fibrosis

Stimuli for acute inflammation

- Infections
- Physical agents
- Chemical agents
- Trauma
- Tissue necrosis
- Immune reactions

Signs of inflammation

- *calor* (heat)
- *rubor* (redness)
- *tumor* (swelling)
- *dolor* (pain)
- *loss of function*

- They are the manifestations of the body's defence against injury or against invasion by foreign material or microorganisms
- means of removal or destruction of the offending agent
- restriction of the spread of infection and
- preparation for the healing process

- Redness and heat are due to increased blood flow to the inflamed site
- Swelling is caused by accumulation of fluid
- Pain is due to release of chemicals that stimulate nerve endings
- Pain only happens where the appropriate sensory nerve endings exist in the inflamed area — e.g. acute pneumonia does not cause pain unless the inflammation involves the parietal pleura, which has pain-sensitive nerve endings
- Loss of function has multiple causes

Process of acute inflammation

- Rapid host response that serves to deliver leukocytes and plasma proteins to site of infection or tissue injury
- These mediator molecules cause:

(1) changes in the caliber of blood vessels and the rate of blood flow through them (hemodynamic changes)

(2) increased capillary permeability

(3) leukocytic exudation

Acute inflammation

- Vascular changes
- Cellular events

Vascular changes

- Haemodynamic changes (changes in vascular flow and calibre)
- Changes in vascular permeability

Hemodynamic changes

- Transient vasoconstriction
  arterioles (3-5 secs or mins)
- Persistent progressive vasodilation
  opening of new microvascular beds - ↑blood flow
  heat & redness
- Increased hydrostatic pressure
  transudation of fluid→ swelling
- Slowing of circulation
  ↑ permeability of microvasculature → stasis
- Leukocytic margination

Lewis experiment

- Red line- vasodil of capillaries & venules
- Flare- (flush)- vasodil of arterioles
- Wheal (swelling) – transudation of fluid

Changes in vascular permeability

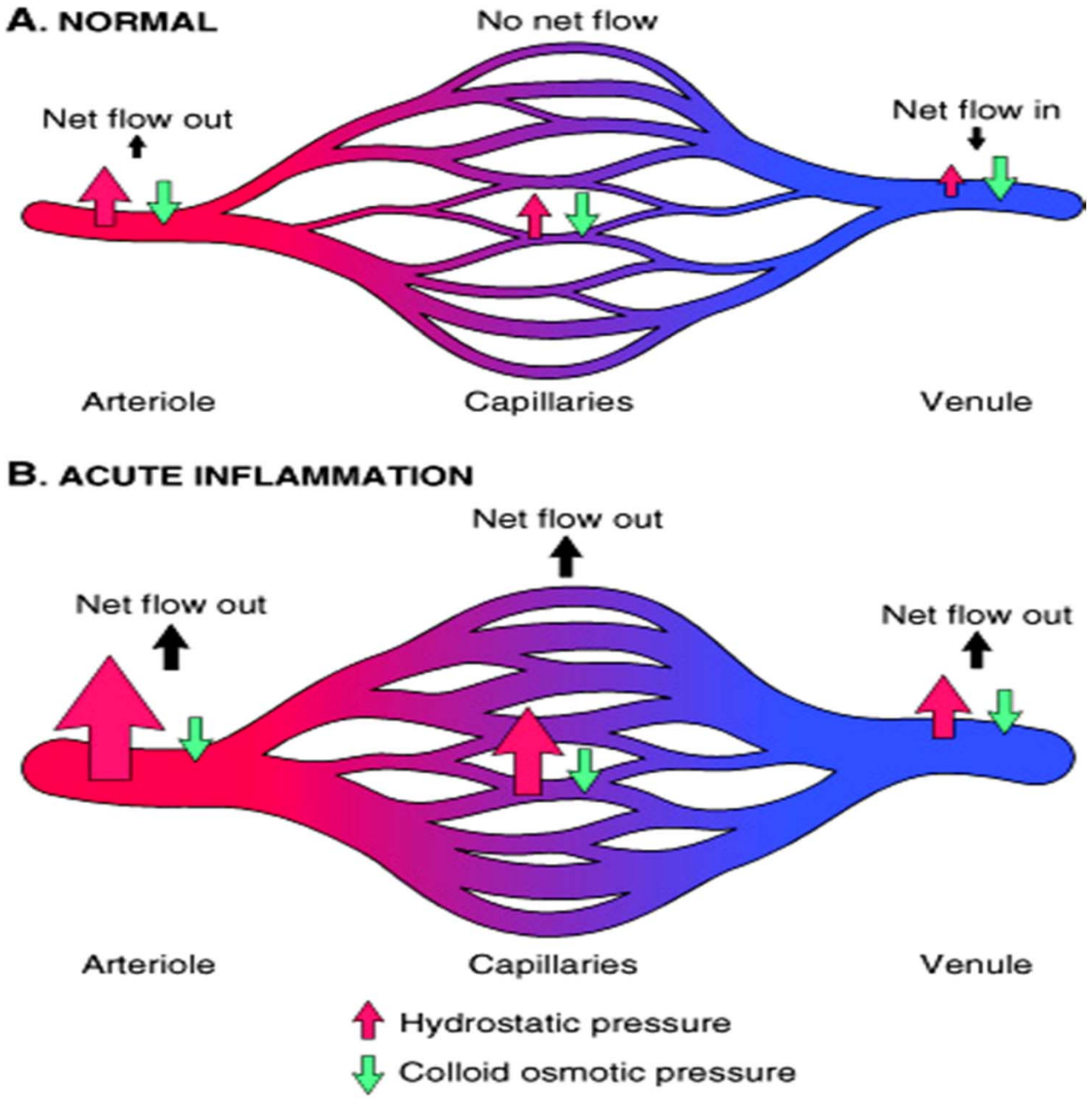
Hallmark of ac inflammation- increased vascular permeability

Pathogenesis

- Starling's hypothesis

  - outward movement: O.P of interstitial fluid & I.V hydrostatic pressure

  - inward movement: O.P of plasma protein & tissue hydrostatic pressure
- Initial transudation
- Inflammatory exudation


A. NORMAL
No net flow
Net flow out
Net flow in
Arteriole
Capillaries
Venule
B. ACUTE INFLAMMATION
Net flow out
Net flow out
Net flow out
Arteriole
Capillaries
Venule
Hydrostatic pressure
Colloid osmotic pressure

Mechanism of increased vascular permeability

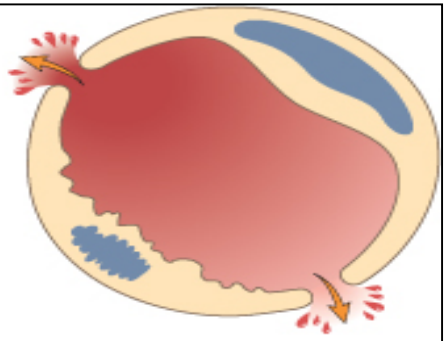
- Endothelial contraction (gaps)
  - venules
  - chemical mediators (histamine)
  - immediate transient response (15-30 mins)
  - mild thermal injury
- Endothelial retraction (cytoskeletal reorganisation)
  - venules, capillaries
  - cytokines (IL-I, TNF), hypoxia
  - delayed response (4-6 hrs after injury, lasts for 2-4 hrs)
- ↑ transcytosis
  - increased no. of channels
  - VEGF

Mechanism of increased vascular permeability

- Direct endothelial injury- resulting in necrosis & detachment
  - severe burns, lytic bacterial infections
  - venules, capillaries, arterioles
  - immediate sustained response, lasts for several hours & days
  - direct effect or cytokines
- Leukocyte mediated endothelial injury
  - pulmonary & glomerular capillaries
  - toxic oxygen species & proteolytic enzymes
- Neovascularization- leakage from new blood vessels

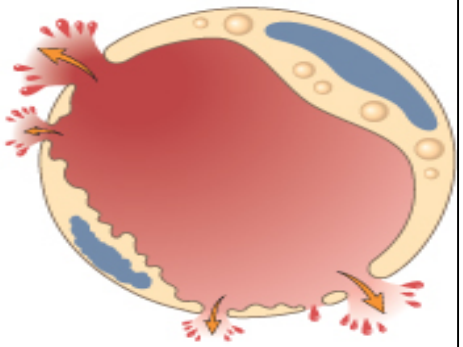
Gaps due to endothelial contraction

- Venules
- Vasoactive mediators (histamine, leukotrienes, etc.)
- Most common
- Fast and short-lived (minutes)



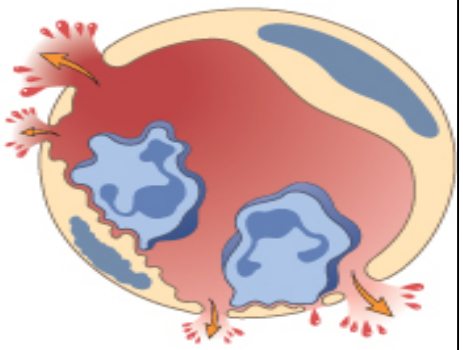
Direct injury

- Arterioles, capillaries, and venules
- Toxins, burns, chemicals
- Fast and may be long-lived (hours to days)



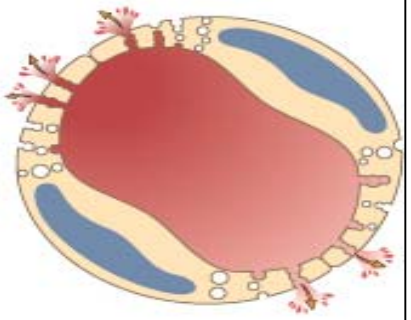
Leukocyte-dependent injury

- Mostly venules
- Pulmonary capillaries
- Late response
- Long-lived (hours)



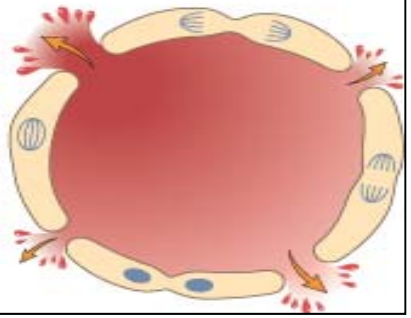
Increased transcytosis

- Venules
- Vascular endothelium–derived growth factor



New blood vessel formation

- Sites of angiogenesis
- Persists until intercellular junctions form



Response of lymphatic vessels

- Lymphatics drain the excess edema fluid
- Leukocytes & cell debris may find their way into lymphatics- lymphangitis, lymphadenitis