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 acute 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

Net flow out

Arteriole

Capillaries

Venule

No net flow

B. ACUTE INFLAMMATION

Net flow out

Arteriole

Capillaries

Venule

Net flow out

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-1, 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