INFLAMMATION

- “Inflame” – to set fire.
- Inflammation is “A dynamic response of vascularised tissue to injury.”
- It is a protective response.
- It serves to bring defense & healing mechanisms to the site of injury.

What is Inflammation?

- A reaction of a living tissue & its micro-circulation to a pathogenic insult.
- A defense mechanism for survival.
- Reaction of tissues to injury, characterized clinically by: heat, swelling, redness, pain, and loss of function.
- Pathologically by: vasoconstriction followed by vasodilatation, stasis, hyperemia, accumulation of leukocytes, exudation of fluid, and deposition of fibrin.
- The processes followed by repair, the production of new capillaries and fibroblasts, organization, and cicatrization.

How Does It Occur?

The vascular & cellular responses of inflammation are mediated by chemical factors (derived from blood plasma or some cells) & triggered by inflammatory stimulus.

Tissue injury or death ---> Release mediators

Etiologies

- Microbial infections: bacterial, viral, fungal, etc.
- Physical agents: burns, trauma--like cuts, radiation
- Chemicals: drugs, toxins, or caustic substances like battery acid.
- Immunologic reactions: rheumatoid arthritis.
Cardinal Signs of Inflammation

- Redness : Hyperaemia.
- Pain : Nerve, Chemical mediators.
- Loss of Function
- Warm : Hyperaemia.
- Swelling : Exudation

Time course

- Acute inflammation: Less than 48 hours
- Chronic inflammation: Greater than 48 hours (weeks, months, years)

Cell type

- Acute inflammation: Polymorphonuclear leukocyte (PMN)
- Chronic inflammation: Mononuclear cells (Macrophages, Lymphocytes, Plasma cells).

Acute inflammation:

• Changes which take place usually within the first few minutes to several hours to days after an injury
• Most commonly involves PMN’s as mediators

Key physiologic events:

• Changes in vascular flow (hemodynamic changes)
• Changes in vascular permeability (vascular leakage)
• Leukocyte exudation

PATHOGENESIS: Three main processes occur at the site of inflammation, due to the release of chemical mediators:

- Increased blood flow (redness and warmth).
- Increased vascular permeability (swelling, pain & loss of function).
- Leukocytic Infiltration.

The major local manifestations of acute inflammation, compared to normal.

(1) Vascular dilation and increased blood flow (causing erythema and warmth)
(2) Extravasation and deposition of plasma fluid and proteins (edema)
(3) Leukocyte emigration and accumulation in the site of injury.

Changes in vascular flow and caliber (hemodynamic changes)

• Vasoconstriction: transient and inconstant, then followed by
• Vasodilatation: first the arterioles, and then the capillaries
- **Slowing of the circulation**: outpouring of albumin rich fluid into the extravascular tissues results in the concentration of RBCs in small vessels and increased viscosity of blood.

- **Leukocyte margination**: PMNs become oriented at the periphery of vessels and start to stick.

**Changes in vascular flow (hemodynamic changes)**

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**Time scale**

- Variable: minor damage ---- 15-30 minutes
  - severe damage ---- a few minutes

**Lymphatics in inflammation**: Lymphatics are responsible for draining edema.

**Edema**: An excess of fluid in the interstitial tissue or serous cavities; either a **transudate** or an **exudate**

**Transudate**:

- An ultrafiltrate of blood plasma
- permeability of endothelium is usually normal.
- low protein content (mostly albumin)

**Exudate**:

- A filtrate of blood plasma mixed with inflammatory cells and cellular debris.
- permeability of endothelium is usually altered
- high protein content.

**Pus**: A purulent exudate: an inflammatory exudate rich in leukocytes (mostly neutrophils) and parenchymal cell debris.

**Leukocyte exudation**

- divided into 4 steps
- Margination, rolling, and adhesion to endothelium
- Diapedesis (trans-migration across the endothelium)
- Migration toward a chemotactic stimuli from the source of tissue injury.
- Phagocytosis

Different molecules play predominant roles in different steps of this process: **selectins** in rolling; **chemokines** in activating the neutrophils to increase avidity of integrins (in green); **integrins** in firm adhesion; and **CD31 (PECAM-1)** in transmigration.

**Phagocytosis**

- 3 distinct steps
  - Recognition and attachment
  - Engulfment
  - Killing or degradation

**Defects in leukocyte function:**

- Margination and adhesion caused by: steroids, leukocyte adhesion deficiency
- Emigration toward a chemotactic stimulus caused by: drugs; chemotaxis inhibitors
- Phagocytosis caused by: Chronic granulomatous disease (CGD)

**Chemical Mediators:** Chemical substances synthesised or released and mediate the changes in inflammation.

- **Histamine**: by mast cells --------- vasodilatation.
- **Prostaglandins** --------------- Cause pain & fever.
- **Bradykinin** ---------------------- Causes pain.

**Chemical mediators of inflammation**

- Platelet activating factor (PAF)
- Cytokines (IL-1, TNF, IL-8, IL-12)
- Nitric oxide (vasodilator, cytotoxin)
- Lysosomal constituents of leukocytes
- Oxygen derived free radicals

**Another view of chemical mediators**

- **Vasodilatation** (vascular flow/ caliber; hemodynamic changes)
  - Prostaglandins, Nitric oxide
- **Increased vascular permeability** (vascular leakage)
  - Vasoactive amines (histamine, serotonin)
  - C3a and C5a (through liberating amines)
• Bradykinin
• Leukotrienes C4, D4, E4

Another view of chemical mediators

<table>
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<tr>
<th>Fever</th>
<th>IL-1, IL-6, TNF</th>
<th>Prostaglandins</th>
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<tr>
<td>Pain</td>
<td>Prostaglandins</td>
<td>Bradykinin</td>
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Morphologic types of acute inflammation

- Exudative or catarrhal inflammation: excess fluid. TB lung.
- Fibrinous – pneumonia – fibrin
- Membranous (fibrino-necrotic) inflammation
- Suppuration/Purulent – Bacterial – neutrophils
- Serous – excess clear fluid – Heart, lung
- Allergic inflammation
- Haemorrhagic – b.v. damage - anthrax.
- Necrotising inflammation.

Acute inflammation has one of four outcomes:

- Abscess formation
- Progression to chronic inflammation
- Resolution--tissue goes back to normal
- Repair--healing by scarring or fibrosis

Abscess formation:

"A circumscribed collection of pus (suppurative inflammation) appearing in an acute or chronic localized infection, and associated with tissue destruction, and frequently, swelling."

It is usually the result of a pyogenic organism.

- Site: skin, subcutaneous tissue, internal organs like brain, lung, liver, kidney..
- Pathogenesis: the necrotic tissue is surrounded by pyogenic membrane, which is formed by fibrin and help in localize the infection.

- Abscess is formed of 3 zones:
  - The center of necrotic tissue caused by byogenic organism.
  - Swelling or edema and epidermal atrophy.
  - Abscess opining through the weak point.
Carbuncle

- It is an extensive form of abscess in which pus is present in multiple loci open at the surface by sinuses.
- Occur in the back of the neck and the scalp.

Furuncle or boil

- It is a small abscess related to hair follicles or sebaceous glands, could be multiple furunclosis.

Cellulitis

- It is an acute diffuse suppurative inflammation caused by streptococci, which secrete hyaluronidase & streptokinase enzymes that dissolve the ground substances and facilitate the spread of infection.

   **Sites:**
   - Areolar tissue; orbit, pelvis, …
   - Lax subcutaneous tissue

Sinus: It is a tract of granulation tissue a cavity (abscess) to the outside (skin), and has a blind end

Fistula: It is a tract of granulation tissue connecting two epithelial surfaces; i.e. two ends open.

   - Types of fistula: Congenital or Acquired.
   - The acquired form could be: traumatic; inflammatory; neoplastic.