

Inflammation

Inflammation: Introduction, Clinical Signs, and Types

- Inflammation is the body's natural response to injury, infection, or harmful stimuli.
- It is a complex biological process involving the immune system's cells, blood vessels, and molecular mediators.

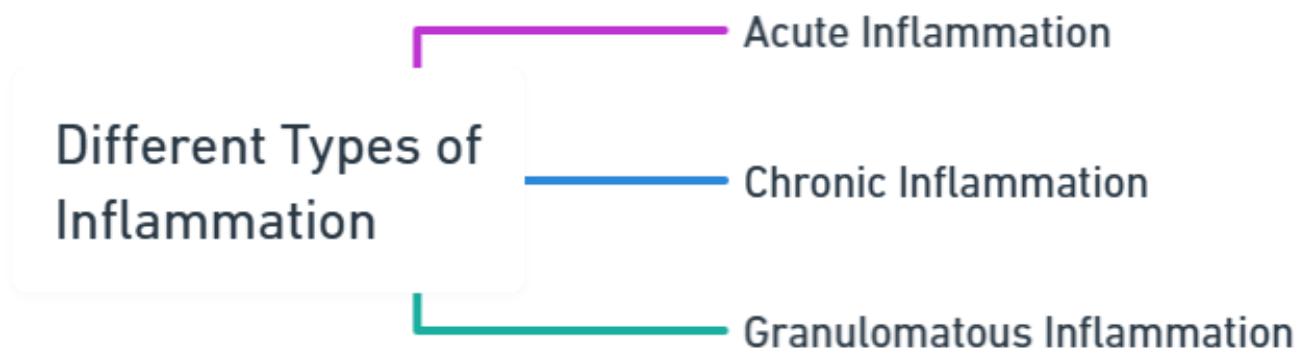
Primary Purposes of Inflammation:

- Eliminate the initial cause of cell injury
- Clear out damaged cells and tissues
- Establish a repair process
- While inflammation is essential for healing, **chronic or excessive inflammation** can contribute to various diseases, including:
 - Autoimmune disorders
 - Cardiovascular diseases
 - Cancer
- Understanding the types and signs of inflammation helps in diagnosing and treating various inflammatory conditions effectively.
- Proper management is crucial to prevent inflammation from contributing to chronic diseases.

Clinical Signs of Inflammation

- The classic signs of inflammation, also known as the five cardinal signs, are:
 1. **Redness (Rubor):** Increased blood flow to the affected area.
 2. **Heat (Calor):** Elevated temperature in the inflamed area due to increased blood flow.
 3. **Swelling (Tumor):** Accumulation of fluid in the tissues.
 4. **Pain (Dolor):** Release of chemicals that stimulate nerve endings.
 5. **Loss of Function (Functio Laesa):** Reduced function of the affected area due to pain and swelling.

Different Types of Inflammation



1. Acute Inflammation

- **Duration:** Short-term, lasting from a few hours to a few days.
- **Causes:** Infection, injury, or foreign bodies (e.g., splinters).
- **Characteristics:** Rapid onset, marked by the five cardinal signs. Involves the activation of immune cells like neutrophils.
- **Examples:** Cuts, burns, infections (e.g., bacterial, or viral).

2. Chronic Inflammation

- **Duration:** Long-term, lasting from weeks to years.
- **Causes:** Persistent infection, prolonged exposure to irritants (e.g., tobacco smoke), autoimmune diseases.
- **Characteristics:** Slow onset, less obvious symptoms. Involves different immune cells, such as macrophages and lymphocytes.
- **Examples:** Rheumatoid arthritis, inflammatory bowel disease, chronic infections (e.g., tuberculosis).

3. Granulomatous Inflammation

- **Duration:** Can be acute or chronic.
- **Causes:** Persistent pathogens (e.g., mycobacteria), foreign substances that the immune system cannot eradicate.
- **Characteristics:** Formation of granulomas, which are small nodules of immune cells that form around the foreign material.
- **Examples:** Tuberculosis, sarcoidosis, leprosy.

Pathogenesis of Acute Inflammation

- Acute inflammation is the early and immediate response to tissue injury or infection. It typically develops within minutes to hours and is characterized by five cardinal signs:
 - **Redness (rubor)**
 - **Heat (calor)**
 - **Swelling (tumor)**
 - **Pain (dolor)**
 - **Loss of function (functio laesa)**

A. Initial Trigger

- The process is initiated when **tissue injury** occurs due to trauma, infection, necrosis, or chemical exposure.

- Damaged cells release **danger signals** known as **DAMPs** (Damage-Associated Molecular Patterns) and **PAMPs** (Pathogen-Associated Molecular Patterns) in case of infection.
- These are recognized by **Pattern Recognition Receptors (PRRs)** such as **Toll-like Receptors (TLRs)** on innate immune cells (e.g., macrophages, dendritic cells, mast cells).

B. Vascular Changes

- There are three major vascular responses:

1. Vasodilation

- The earliest response; arterioles dilate to increase blood flow.
- Mediated by **histamine**, **nitric oxide**, and **prostaglandins**.
- Causes **redness** and **heat**.

2. Increased Vascular Permeability

- Endothelial cells contract or become damaged, creating gaps in vessel walls.
- Plasma proteins (especially **fibrinogen**, **complement**, **immunoglobulins**) and fluids leak into the interstitial space.
- Leads to **swelling (edema)**.

Mechanisms of increased permeability:

- Endothelial contraction (immediate transient response)
- Direct injury (e.g., burns, microbial toxins)
- Delayed prolonged leakage (e.g., sunburn)

3. Stasis and Leukocyte Margination

- Blood flow slows (stasis) due to fluid loss and increased viscosity.
- White blood cells move to the periphery of blood vessels (margination), roll, and adhere to the endothelium (mediated by selectins and integrins).
- Then they transmigrate (diapedesis) across the endothelium into the tissue.

C. Cellular Events

- Once in the tissue, leukocytes (mostly **neutrophils** in early stages) perform:

1. Chemotaxis

- Movement along a chemical gradient toward the site of injury.
- Chemotactic agents: **C5a**, **IL-8**, **LTB4**, **bacterial products**.

2. Phagocytosis

- Recognition and ingestion of microbes or necrotic tissue.
- Steps:
 - Recognition and attachment

- Engulfment (formation of phagosome)
- Killing and degradation (via ROS, nitric oxide, and lysosomal enzymes)

3. Killing of Microbes

- Occurs via oxygen-dependent mechanisms (e.g., reactive oxygen species) and oxygen-independent mechanisms (e.g., defensins, lysosomal enzymes).

Chemical Mediators in Inflammation

- Chemical mediators are responsible for orchestrating the complex series of events in inflammation.

They can be classified into cell-derived and plasma-derived mediators.

Cell-Derived Mediators

1. Histamine

- Source: Mast cells, basophils, platelets.
- Action: Vasodilation, increased vascular permeability, endothelial activation.
- Released by trauma, IgE crosslinking, complement (C3a, C5a).

2. Serotonin

- Source: Platelets.
- Action: Vasoconstriction (minor), permeability changes.

3. Arachidonic Acid Metabolites

- Formed via cyclooxygenase (COX) or lipoxygenase pathways.
- **Prostaglandins (PGs):**
 - Produced by mast cells, macrophages.
 - PGI₂: Vasodilation, inhibits platelet aggregation.
 - TXA₂: Vasoconstriction, promotes aggregation.
 - PGE₂: Fever, pain sensitization.
- **Leukotrienes (LTs):**
 - LTB₄: Chemotaxis of neutrophils.
 - LTC₄, LTD₄, LTE₄: Vasoconstriction, bronchospasm, increased permeability.
- **Lipoxins:**
 - Anti-inflammatory, inhibit neutrophil chemotaxis.

4. Platelet-Activating Factor (PAF)

- Source: Leukocytes, endothelial cells.
- Actions: Platelet aggregation, vasodilation, increased permeability, leukocyte adhesion.

5. Cytokines

- **TNF- α and IL-1:**
 - Produced by macrophages, dendritic cells.
 - Induce fever, leukocyte recruitment, expression of adhesion molecules.
- **Chemokines:**
 - IL-8: Neutrophil chemoattractant.
 - Monocyte Chemoattractant Protein-1 (MCP-1): Attracts monocytes.

Plasma-Derived Mediators

1. Complement System

- Key components: C3a, C5a, C3b, MAC (C5b-9).
- C3a and C5a: Anaphylatoxins (vasodilation, permeability, mast cell degranulation).
- C5a: Potent chemotactic factor.
- C3b: Opsonization.
- MAC: Lyses microbes.

2. Kinins (e.g., Bradykinin)

- Source: Kinin cascade.
- Actions: Vasodilation, increased permeability, pain, bronchoconstriction.

3. Clotting and Fibrinolytic Systems

- **Thrombin:** Enhances leukocyte adhesion, increases permeability.
- **Fibrin degradation products:** Increase permeability and are chemotactic.

Types of Chronic Inflammation

- Chronic inflammation is a prolonged response (weeks to years) in which inflammation, tissue destruction, and healing occur simultaneously.
- It can arise due to:
 - Persistent infections (e.g., tuberculosis)
 - Prolonged exposure to toxic agents (e.g., silica)
 - Autoimmune diseases (e.g., rheumatoid arthritis)

General Features



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