Inflammation

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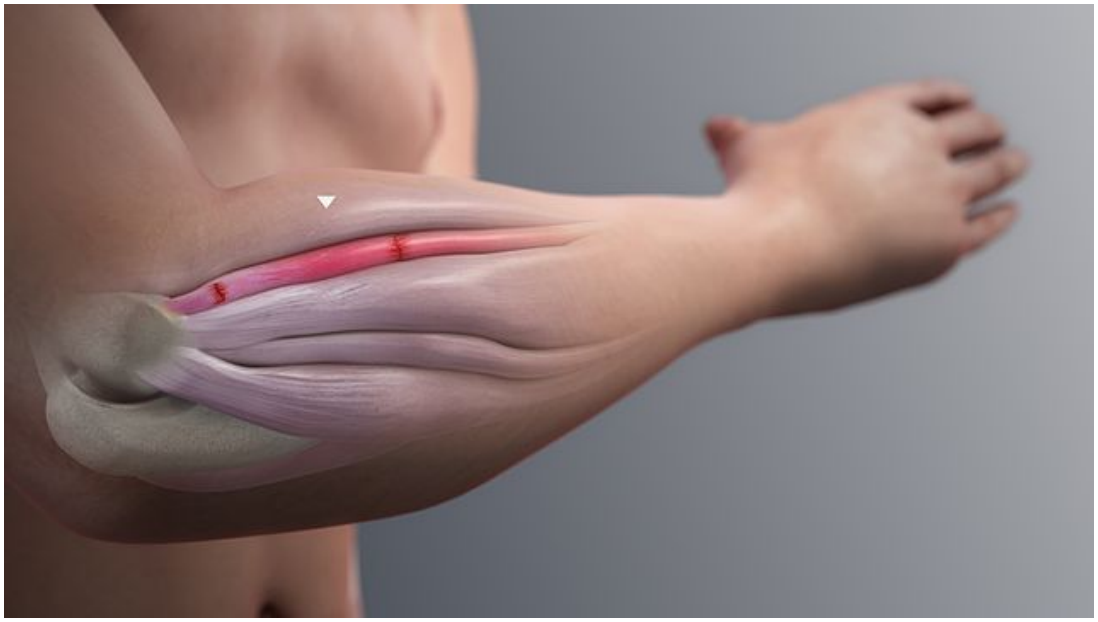
Inflammation is the physiologic body reaction in response to injury. The body tries to protect itself from harmful pathogens and physical or chemical irritants. Immune cells, fibroblasts, intra- and extra-cellular mediators are all involved in protecting the body, clearing the inflammatory products and help with the healing damaged parts. Sometimes the whole pathologic disorder is secondary to the body's reaction and inflammation as in cases of hypersensitivity, granulomas and autoimmune diseases. The following article describes various forms of inflammation as well as the body's reaction to them.



Definition of Inflammation

Inflammation is defined as the body’s response to injurious stimuli in the form of trauma or colonization with bacterial organisms. It is a protective reaction focused on getting rid of the original source of cell injury as well as the cells and tissues that have undergone necrosis. Without inflammation, infections would be rampant and wounds would fail to heal normally. Inflammation forms part of **innate immunity.**

Inflammatory response and repair mechanism can also cause significant harm when its components are destroyed and eliminated. Microbes and dead tissues can contribute to the destruction of normal tissues if the inflammatory response is severe or prolonged.

Causes of Inflammation

Some common causes of inflammation include:

- Pathogenic Infections by bacteria, viruses, fungi and, parasites.
- Injuries such as scratches and trauma from foreign bodies.
- Radiation
- Burns
- Chemical injury, e.g. toxins and alcohol
- Hypersensitivity reactions against environmental substances or against self-tissues.(Autoimmune reactions)

Clinical Picture

The five cardinal signs of inflammation form the basic principle of pathology and include:

1. Rubor/redness: arises from increased blood flow and accumulation at the point of injury or inflammation.
2. Calor/Hotness due to accumulation of warm flow of blow and the heat produced from local reaction/ irritation.
3. Tumor/Swelling the released inflammatory mediators at the site lead to increased fluid extravasation causing edema and swelling.
4. Dolor/Painis mediated by **cytokines** like bradykinins and prostaglandins
5. Functional laesa/loss of bodily functions occurs with the affection of an organ.

Pathophysiology and Stages of Inflammation

Inflammation can be acute or chronic. **Acute inflammation** is the immediate innate body response to harmful agents which are usually bacterial pathogens and physical tissue injuries. The involved cells which are part of the cellular complexity of the inflamed tissue e.g. **macrophages**, **histiocytes**, and **Kupffer cells**, recognize pathogens and damaged cellular debris through pathogen-associated molecular patterns and damage-associated molecular patterns, **PAMs** and **DAMs**. These are surface receptors that recognize pathogenic antigens and cellular debris.

Activation of these surface receptors leads to a release of **histamine**, **nitric oxide** and **prostaglandins** from tissue macrophages, mast cells and vascular endothelial cells. These mediators are responsible for the **dilatation of blood vessels** at the inflamed area and increase **capillary permeability** known as **a vascular phase**.

Fluid shift into the inflamed tissue space will establish an inflammatory response which results in redness and hotness with exudation of fluids containing proteins e.g. **fibrin**, **antibodies** and **complement proteins**. These proteins function to fight the invading pathogen and limit the infection process.

Exudation of plasma from the blood will lead to stasis with subsequent **extravasation** of inflammatory cells from stagnant blood to the injured tissues which are known as **a cellular phase**.

Vascular phase

Tissue macrophages and **mast cells** release **inflammatory mediators**, which lead to **vasodilatation** and **increase tissue permeability**. These mediators are also responsible for recruiting **more inflammatory cells** from the blood to the site of injury.

Inflammatory cells function to **phagocytize** foreign materials, **promote** the immune

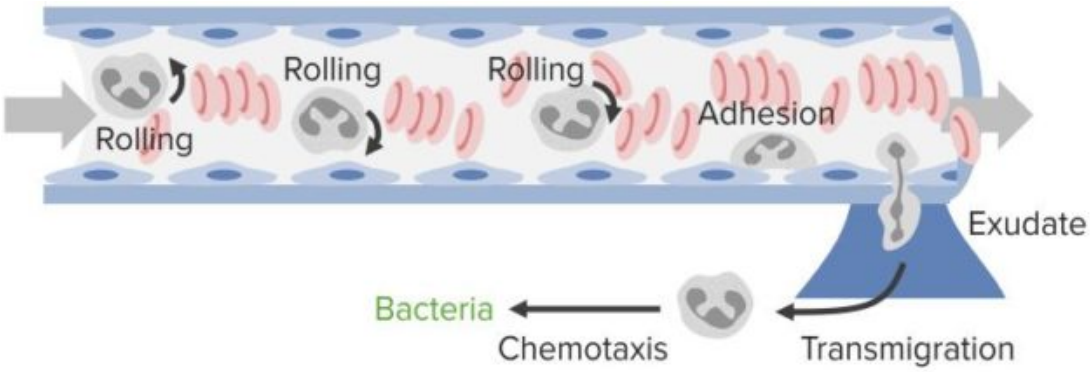
response and **secrete** other mediators. Inflammatory cells in acute inflammation are mainly **granulocytes** while in chronic inflammation they are **lymphocytes** and **monocytes**.

Extravasation of cells from the blood to the tissue space starts with margination of the cell towards the endothelial surface of the blood vessels due to **interleukins** and **TNF-α**. These mediators enhance the expression of **ICAM-1**, **P-selectin** and **E-selectin** on the endothelial cell surface to induce their adhesion with blood leukocytes before their migration.

Cellular phase

Chemokines-activated leukocytes find their way to the inflamed tissue through transmigration across the endothelium and basement membrane via acquiring foot processes to move between endothelial cells; a process called **diapedsis**.

Chemotactic factors e.g. C3a and C5 then guide leukocytes towards the site of tissue injury within the intercellular space via protein adhesions and binding to tissue integrins.

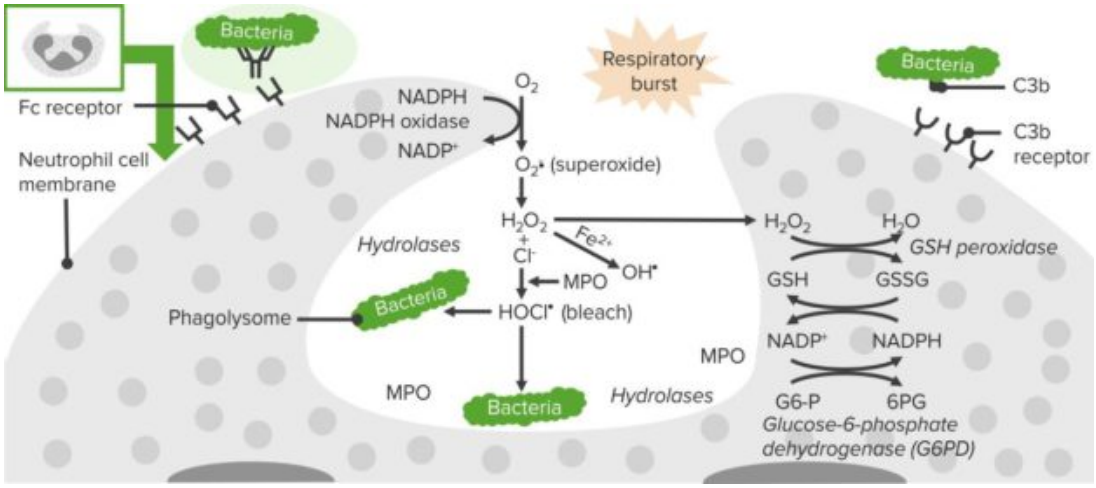


"Acute Inflammation" Image created by Lecturio

Neutrophils that migrate to the inflammation site act as **phagocytes** for the foreign organisms and cellular debris. The cells destroy the engulfed microorganisms via lysosomal enzymes and reactive oxygen species that can be introduced later as **antigen presenting cells**.

Phagocytosis is the process of engulfing foreign materials by phagocytes. These foreign materials include pathogens, dead cells, foreign debris and abnormal cells. Phagocytes can recognize the foreign material via surface receptors including **PRRs** that bind to PAMPs, **opsonin receptors** that bind to bacteria coated with complement and antibodies opsonization proteins and scavenger receptors.

Opsonization occurs after complement protein C3b with the foreign antigen binds to CR1 complement receptor on the surface of phagocytes to facilitate its immune destruction.



"Phagocytosis" Image created by Lecturio

Types of Inflammation

Serous inflammation occurs with **mild irritation of the epithelial or mesothelial surfaces** with resultant homogenous watery exudate from the plasma or lymph. It is more common on the **skin** and **mesothelial membranes**.

Mucinous or catarrhal inflammation occurs with **cuboidal cells** where the exudate is mainly **mucin**. It is more common in the **respiratory tract**.

Purulent inflammation occurs when the inflammatory process is **secondary to violent organisms** e.g. staphylococci that result in large amounts of pus composed of neutrophils and dead cells. Pus isolation with fibrosis and histiocytes is known as **an abscess**.

Fibrinous inflammation occurs in fibrin-rich exudate which will organize to form fibrous mesh. It occurs mainly in **viral inflammation** and **chemical or physical irritation**. Fibrinous inflammation will lead to a **permanent dysfunction** in the affected tissue as fibrosis lack parenchymal cells e.g. scars on the skin surface, liver fibrosis in viral and alcoholic hepatitis. Fibrosis can also occur on the surface of tissues leading to **pseudo-membrane formation** which is a devitalized membrane of fibrous tissue as in pseudomembranous colitis.

Hemorrhagic inflammation occurs with exudate full of erythrocytes or blood. It is common with **viral infection** and **physical irritation**. The hemorrhagic exudate is rich in cellular components and fibrin, which form into a clot limiting organ functions.

Ulcerative inflammation occurs with loss of necrotic epithelial integrity leading to **ulcer formation** on epithelial surfaces.

Granulomatous inflammation occurs with persistent inflammation leading to formation of walls of histiocytes, known as **granulomas**, surrounding the area of inflammatory focus. It is common in **chronic inflammatory conditions** e.g. tuberculosis and sarcoidosis. They can be either caseating where the central area is made up of dead foreign body surrounded by immunocompetent cells or non- caseating granulomas.

Fate of Acute Inflammation

The results of acute inflammation are dependent on the nature and intensity of the injury, the site and tissue affected, and the ability of the host to evoke a response. Interestingly, these mediators are **short-acting** and they are active only as long as there is a **pathogenic stimulation**. After resolution of the offending stimulus, fibrin mesh act to guide wound healing and resolution of the inflammatory products by **macrophages** and **lymphatic drainage** to the regional lymph nodes.

Persistence of the offending agent will lead to **fibrosis** to control the infection, **abscess formation** or **chronic inflammation** lasting for months or years with delayed healing. Chronic inflammation is characterized by replacement of neutrophils with macrophages and fibroblasts releasing IFN-γ and reactive oxygen species characterized by more fibrosis and more tissue destruction.

Chronic inflammation

Chronic inflammation is a prolonged inflammation whereactive inflammation, tissue injury, and healing proceed concurrently, leading toan increased number of lymphocytes and macrophages resulting to vascular proliferation and fibrosis.

Acute inflammation may progress to chronic inflammation. This is evident when the acute response cannot be regulated, either due to persistence of the injurious agent or as a result of interference with the normal healing process.

Chronic inflammation arises in the following settings:

- **Persistent infections** – by microbes that are difficult to eradicate. For example, mycobacteria and certain viruses and fungi
- **Immune-mediated inflammatory diseases (hypersensitivity diseases)** – These arises from excessive and inappropriate activation of the immune system.

Prolonged exposure to potentially toxic agents – They include non-degradable exogenous materials such as inhaled particulate silica, which causes a chronic inflammatory known as silicosis and endogenous agents that chronically elevated plasma lipid components, which leads to atherosclerosis.

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Notes