Inflammation

Inflammation is **a normal part of the body's deafens to injury or infection**, and, in this way, it is beneficial. But inflammation is damaging when it occurs in healthy tissues or lasts too long. Known as chronic inflammation, it may persist for months or years.

Inflammation may result from many factors, such as:

* Environmental chemicals
* Injuries like scrapes, insect stings, or a splinter in your finger
* Pathogens (germs) like bacteria, viruses, or fungi
* Radiation
* TYPES OF INFLAMMATION. Depending upon the defense capacity of the host and duration of response, inflammation can be classified as acute and chronic.
* [Inflammation](https://www.webmd.com/arthritis/about-inflammation) can be either short-lived (**acute**) or long-lasting (**chronic**). Acute inflammation goes away within hours or days. Chronic inflammation can last months or years, even after the first trigger is gone.
* A. Acute inflammation is of short duration (lasting less than 2 weeks) and represents the early body reaction, resolves quickly and is usually followed by healing. The main features of acute inflammation are:
* 1. accumulation of fluid and plasma at the affected site;
* 2. intravascular activation of platelets; and
* 3. polymorphonuclear neutrophils as inflammatory cells. Sometimes, the acute inflammatory response may be quite severe and is termed as fulminant acute inflammation.
* B. Chronic inflammation is of longer duration and occurs either after the causative agent of acute inflammation persists for a long time, or the stimulus is such that it induces chronic inflammation from the beginning. A variant, chronic active inflammation, is the type of chronic inflammation in which during the course of disease there are acute exacerbations of activity.
* The characteristic feature of chronic inflammation is presence of chronic inflammatory cells such as lymphocytes, plasma cells and macrophages, granulation tissue formation, and in specific situations as granulomatous inflammation. In some instances, the term sub-acute inflammation is used for the state of inflammation between acute and chronic.

DEFINITION AND CAUSES. Inflammation is defined as the local response of living mammalian tissues to injury due to any agent. It is a body defense reaction in order to eliminate or limit the spread of injurious agent, followed by removal of the necrosed cells and tissues. The agents causing inflammation may be as under:

1. Infective agents like bacteria, viruses and their toxins, fungi, parasites.

2. Immunological agents like cell-mediated and antigenantibody reactions.

3. Physical agents like heat, cold, radiation, mechanical trauma.

4. Chemical agents like organic and inorganic poisons.

5. Inert materials such as foreign bodies

inflammation is distinct from infection—while inflammation is a protective response by the body to variety of etiologic agents (infectious or non-infectious), while infection is invasion into the body by harmful microbes and their resultant ill-effects by toxins. Inflammation involves 2 basic processes with some overlapping, early inflammatory response and later followed by healing. Though both these processes generally have protective role against injurious agents, i

SIGNS OF INFLAMMATION. The Roman writer Celsus in 1st century A.D. named the famous 4 cardinal signs of inflammation as: rubor (redness); tumor (swelling); calor (heat); and dolor (pain). To these, fifth sign functio laesa (loss of function)

it can be divided into following two events: I. Vascular events.

II. Cellular events

1. VASCULAR EVENTS

Alteration in the microvasculature (arterioles, capillaries and venules) is the earliest response to tissue injury. These alterations include: haemodynamic changes and changes in vascular permeability.

Haemodynamic Changes

The earliest features of inflammatory response result from changes in the vascular flow and calibre of small blood vessels in the injured tissue. The sequence of these changes is as under:

1. Irrespective of the type of injury, immediate vascular response is of transient vasoconstriction of arterioles., the blood flow may be re-established in 3-5 seconds while with more severe injury the vasoconstriction may last for about 5 minutes.

2. Next follows persistent progressive vasodilatation which involves mainly the arterioles, but to a lesser extent, affects other components of the microcirculation like venules and capillaries. This change is obvious within half an hour of injury. Vasodilatation results in increased blood volume in microvascular bed of the area, which is responsible for redness and warmth at the site of acute inflammation.

3. Progressive vasodilatation, in turn, may elevate the local hydrostatic pressure resulting in transudation of fluid into the extracellular space. This is responsible for swelling at the local site of acute inflammation.

4. Slowing or stasis of microcirculation follows which causes increased concentration of red cells, and thus, raised blood viscosity.

5. Stasis or slowing is followed by leucocytic margination or peripheral orientation of leucocytes (mainly neutrophils) along the vascular endothelium. The leucocytes stick to the vascular endothelium briefly, and then move and migrate through the gaps between the endothelial cells into the extravascular space. This process is known as emigration.

Altered Vascular Permeability

In and around the inflamed tissue, there is accumulation of oedema fluid in the interstitial compartment which comes from blood plasma by its escape through the endothelial wall of peripheral vascular bed. In the initial stage, the escape of fluid is due to vasodilatation and consequent elevation in hydrostatic pressure. This is transudate in nature.

1. CELLULAR EVENTS

The cellular phase of inflammation consists of 2 processes:

1. exudation of leucocytes; *and*

2. phagocytosis.

Exudation of Leucocytes The escape of leucocytes from the lumen of microvasculature to the interstitial tissue is the most important feature of inflammatory response. In acute inflammation, polymorphonuclear neutrophils (PMNs) comprise the first line of body defense, followed later by monocytes and macrophages. The changes leading to migration of leucocytes

The normal axial flow consists of central stream of cells comprised by leucocytes and RBCs and peripheral cellfree layer of plasma close to vessel wall. Due to slowing and stasis, the central stream of cells widens and peripheral plasma zone becomes narrower because of loss of plasma by exudation. This phenomenon is known as margination. As a result of this redistribution, the neutrophils of the central column come close to the vessel wall; this is known as pavementing. الرصف

2. ROLLING AND ADHESION.

Peripherally marginated and pavemented neutrophils slowly roll over the endothelial cells lining the vessel wall (rolling phase). This is followed by the transient bond between the leucocytes and endothelial cells becoming firmer (adhesion phase). The following molecules bring about rolling and adhesion phases:

1. Selectins are expressed on the surface of activated endothelial cells which recognise specific carbohydrate groups found on the surface of neutrophils, the most important of which is s-Lewis X molecule. While P-selectin (preformed and stored in endothelial cells and platelets) is involved in rolling, E-selectin (synthesised by cytokineactivated endothelial cells) is associated with both rolling and adhesion; L-selectin (expressed on the surface of lymphocytes and neutrophils) is responsible for homing of circulating lymphocytes to the endothelial cells in lymph nodes.
2. ii) Integrins on the endothelial cell surface are activated during the process of loose and transient adhesions between endothelial cells and leucocytes. At the same time the receptors for integrins on the neutrophils are also stimulated. This process brings about firm adhesion between leucocyte and endothelium.
3. iii) Immunoglobulin gene superfamily adhesion molecule such as intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) allow a tighter adhesion and stabilise the interaction between leucocytes and endothelial cells. Platelet-endothelial cell adhesion molecule1 (PECAM-1) or CD31 may also be involved in leucocyte migration from the endothelial surface.

3. EMIGRATION. After sticking of neutrophils to endothelium, the former move along the endothelial surface till a suitable site between the endothelial cells is found where the neutrophils throw out cytoplasmic pseudopods. Subsequently, the neutrophils lodged between the endothelial cells and basement membrane cross the basement membrane by damaging it locally with secreted collagenases and escape out into the extravascular space; this is known as emigration. The damaged basement membrane is repaired almost immediately. As already mentioned, neutrophils are the dominant cells in acute inflammatory exudate in the first 24 hours, and monocyte-macrophages appear in the next 24-48 hours. However, neutrophils are short-lived (24-48 hours) while monocyte-macrophages survive much longer. Simultaneous to emigration of leucocytes, escape of red cells through gaps between the endothelial cells, diapedesis, takes place. It is a passive phenomenon—RBCs being forced out either by raised hydrostatic pressure or may escape through the endothelial defects left after emigration of leucocytes. Diapedesis gives haemorrhagic appearance to the inflammatory exudate.

Phagocytosis

Phagocytosis is defined as the process of engulfment of solid particulate material by the cells (cell-eating). The cells performing this function are called phagocytes.

There are 2 main types of phagocytic cells: i) Polymorphonuclear neutrophils (PMNs) which appear early in acute inflammatory response, sometimes called as microphages.

ii) Circulating monocytes and fixed tissue mononuclear phagocytes, commonly called as macrophages. Neutrophils and macrophages on reaching the tissue spaces produce several proteolyitc enzymes—lysozyme, protease, collagenase, elastase, lipase, proteinase, gelatinase, and acid hydrolases. These enzymes degrade collagen and extracellular matrix. The microbe undergoes the process of phagocytosis by polymorphs and macrophages and involves

1. Recognition and attachment 2. Engulfment 3. Killing and degradationز
2. CHEMOTAXIS. The chemotactic factor-mediated transmigration of leucocytes after crossing several barriers (endothelium, basement membrane, perivascular myofibroblasts and matrix) to reach the interstitial tissues is called chemotaxis. The concept of chemotaxis is well illustrated by Boyden’s chamber experiment. In this, a millipore filter (3 μm pore size) separates the suspension of leucocytes from the test solution in tissue culture chamber. If the test solution contains chemotactic agent, the leucocytes migrate through the pores of filter towards the chemotactic agent (Fig. 6.5). The following agents act as potent chemotactic substances or chemokines for neutophils: i) Leukotriene B4 (LT-B4), a product of lipooxygenase pathway of arachidonic acid metabolites ii) Components of complement system (C5a and C3a in particular) iii) Cytokines (Interleukins, in particular IL-8) iv) Soluble bacterial products (such as formylated peptides). In addition to neutrophils, other inflammatory cells too respond and partake in inflammation and there are chemokines for them, e.g. monocyte chemoattractant protein (MCP-1), eotaxin chemotactic for eosinophils, NK cells for recognising virally infected cells etc.