Inflammation

Is part of the complex biological response of body tissues to harmful stimuli, such as pathogens, damaged cells, or irritants, and is a protective response involving immune cells, blood vessels, and molecular mediators. The function of inflammation is to eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult and the inflammatory process, and initiate tissue repair.

The **five cardinal signs** are heat, pain, redness, swelling, and loss of function.

Inflammation is a generic response, and therefore it is considered as a mechanism of innate immunity, as compared to adaptive immunity, which is specific for each pathogen. Too little inflammation could lead to progressive tissue destruction by the harmful stimulus (e.g. bacteria) and compromise the survival of the organism. In contrast, too much inflammation, in the form of chronic inflammation, is associated with various diseases, such as hay fever, periodontal disease, atherosclerosis, and osteoarthritis.

Inflammation can be classified as either ***acute*** or ***chronic***.

Acute inflammation:

Is the initial response of the body to harmful stimuli, and is achieved by the increased movement of plasma and leukocytes from the blood into the injured tissues.

Acute inflammation occurs immediately upon injury, lasting only a few days. Cytokines and chemokines promote the migration of neutrophils and macrophages to the site of inflammation. Pathogens, allergens, toxins, burns, and frostbite are some of the typical causes of acute inflammation. Toll-like receptors (TLRs) recognize microbial pathogens. Acute inflammation can be a defensive mechanism to protect tissues against injury. Inflammation lasting 2–6 weeks is designated subacute inflammation.

A series of biochemical events propagates and matures the inflammatory response, involving the local vascular system, the immune system, and various cells within the injured tissue.

Chronic inflammation:

Chronic inflammation is inflammation that lasts for months or years. Macrophages, lymphocytes, and plasma cells predominate in chronic inflammation, in contrast to the neutrophils that predominate in acute inflammation. Diabetes, cardiovascular disease, allergies,

and chronic obstructive pulmonary disease (COPD) are examples of diseases mediated by chronic inflammation. Obesity, smoking, stress, insufficient diet and poor diet are some of the factors that promote chronic inflammation.

Inflammation is not a synonym for infection. Infection describes the interaction between the action of microbial invasion and the reaction of the body's inflammatory response—the two components are considered together when discussing an infection, and the word is used to imply a microbial invasive cause for the observed inflammatory reaction.

Inflammation, on the other hand, describes purely the body's immunovascular response—whatever the cause may be. But because of how often the two are correlated, words ending in the suffix *-itis* (which refers to inflammation) are sometimes informally described as referring to infection. For example, the word *urethritis* strictly means only "urethral inflammation", but clinical health care providers usually discuss urethritis as a urethral infection because urethral microbial invasion is the most common cause of urethritis.

However, the inflammation-infection distinction becomes crucial for situations in pathology and medical diagnosis where inflammation is not driven by microbial invasion, such as the cases of atherosclerosis, trauma, ischemia, and autoimmune diseases (including type III hypersensitivity).

Causes:

1. Physical:

- Burns.
- Frostbite.
- Physical injury, blunt or penetrating.
- Foreign bodies, including splinters, dirt and debris.
- Trauma.
- Ionizing radiation.

2. Biological:

- Infection by pathogens.

Types:

- Appendicitis
- Bursitis
- Colitis
- Cystitis
- Pharyngitis
- Phlebitis
- Prostatitis
- Rhinitis

- Dermatitis
- Epididymitis
- Encephalitis
- Gingivitis
- Meningitis
- Myelitis
- Nephritis
- Neuritis
- Pancreatitis
- Sinusitis
- Tendonitis
- Tonsillitis
- Urethritis
- Vasculitis
- Vaginitis

Cardinal signs:

Acute inflammation is a short-term process, usually appearing within a few minutes or hours and begins to cease upon the removal of the injurious stimulus. It involves a coordinated and systemic mobilization response locally of various immune, endocrine and neurological mediators of acute inflammation. In a normal healthy response, it becomes activated, clears the pathogen and begins a repair process and then ceases. It is characterized by five cardinal signs:

- Redness.
- Pain.
- Heat.
- Swelling.
- Loss of function.

Redness and heat are due to increased blood flow at body core temperature to the inflamed site.

Swelling is caused by accumulation of fluid.

Pain is due to the release of chemicals such as bradykinin and histamine that stimulate nerve endings.

Loss of function has multiple causes.

Acute inflammation of the lung (usually as in response to pneumonia) does not cause pain unless the inflammation involves the parietal pleura, which does have pain-sensitive nerve endings.

Examples:

Atherosclerosis:

Atherosclerosis, formerly considered a bland lipid storage disease, actually involves an ongoing inflammatory response. Recent advances in

basic science have established a fundamental role for inflammation in mediating all stages of atherosclerosis from initiation through progression and, ultimately, the thrombotic complications from it. These new findings provide important links between risk factors and the mechanisms of atherogenesis.

Clinical studies have shown that this emerging biology of inflammation in atherosclerosis applies directly to human patients. Elevation in markers of inflammation predicts outcomes of patients with acute coronary syndromes, independently of myocardial damage.

In addition, low-grade chronic inflammation, as indicated by levels of the inflammatory marker C-reactive protein, prospectively defines risk of atherosclerotic complications, thus adding to prognostic information provided by traditional risk factors.

Moreover, certain treatments that reduce coronary risk also limit inflammation. In the case of lipid lowering with statins, the anti-inflammatory effect does not appear to correlate with reduction in low-density lipoprotein levels. These new insights on inflammation contribute to the etiology of atherosclerosis, and the practical clinical applications in risk stratification and the targeting of therapy for atherosclerosis.

Allergy:

An allergic reaction, formally known as type 1 hypersensitivity, is the result of an inappropriate immune response triggering inflammation, vasodilation, and nerve irritation. A common example is hay fever, which is caused by a hypersensitive response by mast cells to allergens. Pre-sensitised mast cells respond by degranulating, releasing vasoactive chemicals such as histamine.

These chemicals propagate an excessive inflammatory response characterised by blood vessel dilation, production of pro-inflammatory molecules, cytokine release, and recruitment of leukocytes. Severe inflammatory response may mature into a systemic response known as anaphylaxis.

Cancer:

Inflammation orchestrates the microenvironment around tumours, contributing to proliferation, survival and migration. Cancer cells use selectins, chemokines and their receptors for invasion, migration and metastasis. On the other hand, many cells of the immune system contribute to cancer immunology, suppressing cancer

This capacity of a mediator of inflammation to influence the effects of steroid hormones in cells is very likely to affect carcinogenesis. On the

other hand, due to the modular nature of many steroid hormone receptors, this interaction may offer ways to interfere with cancer progression, through targeting of a specific protein domain in a specific cell type. Such an approach may limit side effects that are unrelated to the tumor of interest, and may help preserve vital homeostatic functions and developmental processes in the organism.

Outcome:

The outcome in a particular circumstance will be determined by the tissue in which the injury has occurred—and the injurious agent that is causing it. Here are the possible outcomes to inflammation:

1. Resolution:

The complete restoration of the inflamed tissue back to a normal status. Inflammatory measures such as vasodilation, chemical production, and leukocyte infiltration cease, and damaged parenchymal cells regenerate. Such is usually the outcome when limited or short-lived inflammation has occurred.

2. Fibrosis:

Large amounts of tissue destruction, or damage in tissues unable to regenerate, cannot be regenerated completely by the body.
Fibrous scarring occurs in these areas of damage, forming a scar composed primarily of collagen. The scar will not contain any specialized structures, such as parenchymal cells, hence functional impairment may occur.

3. Abscess formation:

A cavity is formed containing pus, an opaque liquid containing dead white blood cells and bacteria with general debris from destroyed cells.

4. Chronic inflammation:

In acute inflammation, if the injurious agent persists then chronic inflammation will ensue. This process, marked by inflammation lasting many days, months or even years, may lead to the formation of a chronic wound. Chronic inflammation is characterised by the dominating presence of macrophages in the injured tissue. These cells are powerful defensive agents of the body, but the toxins they release—including reactive oxygen species—are injurious to the organism's own tissues as well as invading agents. As a consequence, chronic inflammation is almost always accompanied by tissue destruction.