INFLAMMATION

Introduction

Definition: Inflammation is a local response (reaction) of living vascularized tissues to endogenous and exogenous stimuli. The term is derived from the Latin "inflammare" meaning to burn. Inflammation is fundamentally destined to localize and eliminate the causative agent and to limit tissue injury. Thus, inflammation is a physiologic (protective) response to injury. Inflammation is itself not to be considered as a disease but as a salutary operation consequent either to some violence or to some diseases".

Causes:

Causes of inflammation are apparently causes of diseases such as:

1. physical agents - mechanical injuries, alteration in temperatures and pressure, radiation injuries.
2. chemical agents- including the increasing lists of drugs and toxins.
3. biologic agents (infectious)- bacteria, viruses, fungi, parasites
4. immunologic disorders- hypersensitivity reactions, autoimmunity, immunodeficiency states etc
5. genetic/metabolic disorders- examples gout, diabetes mellitus etc…

Examples of diseases with specific inflammation

- syphilis
- tuberculosis
- leprosy
- glanders (syn: equinia, farcy, or malleus)
- scleroma

Classification:

Inflammation is classified crudely based on duration of the lesion and histologic appearances into acute and chronic inflammation.

Acute inflammation

A. Acute inflammation is an immediate and early response to an injurious agent and it is relatively of short duration, lasting for minutes, several hours or few days.

B. It is characterized by exudation of fluids and plasma proteins and the emigration of predominantly neutrophilic leucocytes to the site of injury.

The five cardinal signs of acute inflammation are

1. Redness (rubor) which is due to dilation of small blood vessels within damaged tissue as it occurs in cellulitis.

2. Heat (calor) which results from increased blood flow (hyperemia) due to regional vascular dilation
3. Swelling (tumor) which is due to accumulation of fluid in the extravascular space which, in turn, is due to increased vascular permeability.
4. Pain (dolor), which partly results from the stretching & destruction of tissues due to inflammatory edema and in part from pus under pressure in, as abscess cavity. Some chemicals of acute inflammation, including bradykinins, prostaglandins and serotonin are also known to induce pain.
5. Loss of function: The inflamed area is inhibited by pain while severe swelling may also physically immobilize the tissue.

Events of acute inflammation:
Acute inflammation is categorized into an early vascular and a late cellular responses.
1) The **Vascular response** has the following steps:
a) Immediate (momentary) vasoconstriction in seconds due to neurogenic or chemical stimuli.
b) Vasodilatation of arterioles and venules resulting in increased blood flow.
c) After the phase of increased blood flow there is a slowing of blood flow & stasis due to increased vascular permeability that is most remarkably seen in the post□capillary venules. The increased vascular permeability oozes protein-rich fluid into extravascular tissues. Due to this, the already dilated blood vessels are now packed with red blood cells resulting in stasis. The protein-rich fluid which is now found in the extravascular space is called exudate. The presence of the exudates clinically appears as swelling. Chemical mediators mediate the vascular events of acute inflammation.
2) Cellular response
The cellular response has the following stages:
A. Migration, rolling, pavementing, & adhesion of leukocytes
B. Transmigration of leukocytes.
C. Chemotaxis
D. Phagocytosis
Normally blood cells particularly erythrocytes in venules are confined to the central (axial) zone and plasma assumes the peripheral zone. As a result of increased vascular permeability , more and more neutrophils accumulate along the endothelial surfaces (peripheral zone).
A) Migration, rolling, pavementing, and adhesion of leukocytes
Margination is a peripheral positioning of white cells along the endothelial cells.
Subsequently, rows of leukocytes tumble slowly along the endothelium in a process known as rolling.
In time, the endothelium can be virtually lined by white cells. This appearance is called pavementing
Thereafter, the binding of leukocytes with endothelial cells is facilitated by cell adhesion molecules such as selectins, immunoglobulins, integrins, etc which result in adhesion of leukocytes with the endothelium.
B). Transmigration of leukocytes

Leukocytes escape from venules and small veins but only occasionally from capillaries. The movement of leukocytes by extending pseudopodia through the vascular wall occurs by a process called diapedesis

The most important mechanism of leukocyte emigration is via widening of inter-endothelial junctions after endothelial cells contractions. The basement membrane is disrupted and resealed thereafter immediately.

C). Chemotaxis:

Chemotaxis is a unidirectional attraction of leukocytes from vascular channels towards the site of inflammation within the tissue space guided by chemical gradients (including bacteria and cellular debris) .

The most important chemotactic factors for neutrophils are components of the complement system (C5a), bacterial and mitochondrial products of arachidonic acid metabolism such as leukotriene B4 and cytokines , Interleukin-L(IL-8).

All granulocytes, monocytes and to lesser extent lymphocytes respond to chemotactic stimuli.

How do leukocytes "see" or "smell" the chemotactic agent? This is because receptors on cell membrane of the leukocytes react with the chemo-attractants, resulting in the activation of phospholipase C that ultimately leads to release of cytosolic calcium ions and these ions trigger cell movement towards the stimulus.

Chemical mediators of inflammation

Chemical mediators account for the events of inflammation. Inflammation has the following sequence:

Cell injury Chemical mediators Acute inflammation (i.e. the vascular & cellular events).

Sources of mediators:

The chemical mediators of inflammation can be derived from plasma or cells.

a) Plasma-derived mediators:

i) Complement activation

- increases vascular permeability (C3a,C5a)
- activates chemo-taxis (C5a)
- opsonization (C3b,C3bi)

ii) Factor XII (Hageman factor) activation

Its activation results in recruitment of four systems: the kinin, the clotting, the fibrinolysis and the compliment systems.

b) Cell-derived chemical mediators:

Cell-derived chemical mediators include

Most mediators perform their biologic activities by initially binding to specific receptors on target cells. Once activated and released from the cells, most of these mediators are short lived. Most mediators have the potential to cause harmful effect.