

## Lec. 5

## Inflammation

**Inflammation** is part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants.

is also a protective immunovascular response that involves immune cells, blood vessels, and molecular mediators. The purpose 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 to initiate tissue repair

### ▪ **Causes**

The inflammatory RESPONSE can be provoked by physical, chemical, and biologic agents,

#### Physical:

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

#### Biological:

- Infection by pathogens
- Immune reactions due to hypersensitivity
- Stress

#### Chemical:

- Chemical irritants
- Toxins
- Alcohol

- **The physiologic changes that occur during the inflammatory process**

The three major components of this process are :-

(1) **changes in the caliber of blood vessels and the rate of blood flow through them (hemodynamic changes);**

Hemodynamic changes begin soon after injury and progress at varying rates, according to the extent of injury. They start with dilation of the arterioles and the opening of new capillaries and venular beds in the area. This causes an accelerated flow of blood, accounting for the signs of heat and redness.

(2) **Increased permeability** of the microcirculation, which permits leakage of protein-rich fluid out of small blood vessels and into the extravascular fluid compartment, accounting for the inflammatory edema .

(3) **Leukocytic exudation** occurs in the following sequence. First, the LEUKOCYTES move to the endothelial lining of the small blood vessels (*margination*) and line the endothelium in a tightly packed formation (*pavementing*). Eventually, these leukocytes move through the endothelial spaces and escape into the extravascular space (*emigration*).

Once they are outside the blood vessels they are free to move and, by CHEMOTAXIS, are drawn to the site of injury. Accumulations of NEUTROPHILS and MACROPHAGES at the area of inflammation act to neutralize foreign particles by PHAGOCYTOSIS.

- **Chemical mediators of the inflammatory**

process include a variety of substances originating in the plasma and the cells of uninjured tissue, and possibly from the damaged tissue. The major kinds of mediators are

1- *vasoactive amines*, such as HISTAMINE and SEROTONIN;

2- *plasma endopeptidases* that comprise three interrelated systems, the kinin system that produces BRADYKININ, the complement system

that produces proteins that interact with antigen--antibody complexes and mediate immunologic injury and inflammation, and the clotting system that increases vascular permeability and chemotactic activity for the leukocytes;

3- **PROSTAGLANDINS**, which can reproduce several aspects of the inflammatory process;

4- **neutrophil products**;

5- **lymphocyte factors**

6- **other mediators**, such as slow-reacting SUBSTANCE of anaphylaxis and endogenous PYROGEN.

- Inflammation can be classified as either acute or chronic
- **Acute inflammation**

**Acute inflammation** is a short-term process, usually appearing within a few minutes or hours and ceasing upon the removal of the injurious stimulus.

**It is characterized by five cardinal signs:**

- **Pain** - the inflamed area is likely to be painful, especially when touched. Chemicals that stimulate nerve endings are released, making the area much more sensitive.
- **Redness** - this is because the capillaries are filled up with more blood than usual
- **Immobility** - there may be some loss of function
- **Swelling** - caused by an accumulation of fluid
- **Heat** - as with the reason for the redness, more blood in the affected area makes it feel hot to the touch.



infected ingrown toenail showing the characteristic redness and swelling associated with acute inflammation

## ▪ **Chronic Inflammation**

**chronic inflammation** prolonged and persistent inflammation marked chiefly by new connective tissue formation; it may be a continuation of an acute form or a prolonged low-grade form.

**It can result from:**

- Failure to eliminate whatever was causing an acute inflammation
- An autoimmune response to a self antigen - the immune system attacks healthy tissue, mistaking it (them) for harmful pathogens
- A chronic irritant of low intensity that persists.

**Examples of diseases and conditions with chronic inflammation include:**

- Asthma
- Chronic peptic ulcer
- Tuberculosis
- Rheumatoid arthritis
- Chronic periodontitis
- Ulcerative colitis and Crohn's disease
- Chronic sinusitis
- Chronic active hepatitis (there are many more).

## ▪ **Acute and chronic inflammation compared**

The table below show the difference between chronic and acute inflammation regarding the causative agents, which major cells are involved, features regarding onset, duration, and outcomes:

<b>Comparison between acute and chronic inflammation</b>		
	Acute	Chronic
<b><i>Causative agent</i></b>	Bacterial pathogens, injured tissues	Persistent acute inflammation Due to non-degradable pathogens, viral infection, persistent foreign bodies, or autoimmune reactions
<b><i>Major cells Involved</i></b>	neutrophils (primarily), basophils (inflammatory response), and eosinophils (response to helminth worms and parasites) mononuclear cells (monocytes, macrophage)	Mononuclear cells (monocytes, macrophages, lymphocytes, plasma cells), fibroblasts
<b><i>Primary mediators</i></b>	Vasoactive amines, eicosanoids	IFN- $\gamma$ and other cytokines, growth factors, reactive oxygen species, hydrolytic enzymes
<b><i>Onset</i></b>	Immediate	Delayed
<b><i>Duration</i></b>	Few days	Up to many months, or years
<b><i>Outcomes</i></b>	Resolution, abscess formation, chronic inflammation	Tissue destruction, fibrosis, necrosis

▪ **Fast facts on inflammation , Here are some key points about inflammation.**

- Inflammation is the body's attempt at self-protection to remove harmful stimuli and begin the healing process.
- Inflammation is part of the body's immune response.
- Our infections, wounds and any damage to tissue would never heal without inflammation - tissue would become more and more damaged and the body, or any organism, would eventually perish.
- Chronic inflammation can eventually cause several diseases and conditions, including some cancers, rheumatoid arthritis, atherosclerosis, periodontitis, and hay fever.
- It should be remembered that inflammation is part of the healing process. Sometimes reducing inflammation is necessary, but not always.

- **What are the possible treatments for inflammation**

- **Anti-inflammatory medications**

**NSAIDs** (non-steroidal anti-inflammatory drugs) are taken to alleviate pain caused by inflammation. They counteract the COX (cyclooxygenase) enzyme, which synthesizes prostaglandins which create inflammation. If prostaglandin synthesis can be blocked, pain is either eliminated or reduced.



Examples of NSAIDs include naproxen, ibuprofen and aspirin.

People should not use NSAIDs long-term without being under the supervision of a doctor, because there is a risk of stomach ulcers, and even severe and life-threatening hemorrhage. NSAIDs may also worsen asthma symptoms and cause kidney damage. NSAID medications, with the exception of aspirin, can also increase the risk of stroke and myocardial infarction (heart attack).

**Acetaminophen** (paracetamol, Tylenol) can reduce pain associated with inflammatory conditions, but have no anti-inflammatory effects. They may be ideal for those wishing to treat just the pain, while allowing the inflammation to run its course.

**Corticosteroids** - these are a class of steroid hormones naturally produced in the cortex (outer portion) of the adrenal gland. They are synthesized in laboratories and added to medications. Corticosteroids, such as cortisol are anti-inflammatory; they prevent phospholipid release, which undermines eosinophil action and a number of other mechanisms involved in inflammation.

- **Other treatments for inflammation**

**Applying ice** - do not place the ice in direct contact with skin, wrap it in a cloth or a purpose-made ice bag. Applying ice has been shown to reduce inflammation. Athletes commonly use ice treatment for managing pain and inflammation. Inflammation can go down more rapidly if you rest, apply ice, compression, and elevate the affected area (have your ankle raised if the swelling is there, for example).

**Green tea** - researchers appear regular green tea drinking enhances bone health and reduces inflammation in postmenopausal women.

**Fish oil (Omega-3)** - the daily consumption of fish oil, omega-3 reduced both inflammation and anxiety in a group of young healthy people.