# Inflammation II.

## 1 Definitions

Inflammation is defined as local reaction of *vascularized living* tissue to local injury, characterized by movement of fluid and leukocytes from the blood into the extravascular space. According the time frame is divided into two categories: acute and chronic.

Function:

- destroys, dilutes or walls off injurious agents
- one of body's non-specific defense mechanisms
- begins the process of healing and repair

### 1.1 Acute Inflammation

Rapid onset, usually short duration

**Microscopy**

- neutrophils dominate
- other cellular elements are also involved (monocytes/macrophages, platelets, mast cells)
- protein rich exudate, especially fibrin

**Associations**

- necrosis
- pyogenic bacteria

### 1.2 Chronic Inflammation

Usually long duration, but in some cases may be short. May follow acute inflammation or may have an insiduous onset (without an apparent prelude of acute inflammation).

**Microscopy**

- *mononuclear cells* dominate
  - lymphocytes
  - plasma cells (plasmocytes)
  - monocytes/macrophages
- other cellular elements are also involved (eosinophils, neutrophils in „active" inflammation)[1]
- In *granulomas* are typical *Langhans cells*, large, multinuclear elements on the periphery of tuberculous granulomas. Nuclei are sometimes arranged in a horseshoe shape formation. *Foreign body* cells are similar, usually smaller, the horseshape formation of nuclei is not present. Both these elements are modified macrophages.
- evidence of *healing* — fibroblasts, capillaries, fibrosis

**Associations**

- long term stimulation of immune system, autoimmunity
- viral infections
- persistent intracellular organisms (e.g. Mycobacteria)
- prologned exposure to non-degradable substances — *foreign bodies*

[1] It is the microscopic appearance, that helps a pathologist to define „acute" vs. „chronic" inflammation in tissues:

- mostly neutrophils = acute inflammation
- mostly lymphocytes = chronic inflammation
- combination of neutrophils & lymphocytes = „mixed" inflammation or „active" chronic inflammation

## 1.3 Classical Clinical Signs of Acute Inflammation

1. *Rubor* (redness) due to increased blood flow
2. *Calor* (heat) due to increased blood flow
3. *Tumor* (swelling) due to edema
4. *Dolor* (pain) due to chemical mediators of inflammation
5. *Functio laesa* (malfunctioning) due to variety of reasons (pain, destruction of parenchyma)

## 1.4 Systemic Effects of Inflammation[2]

**Fever** caused by cytokines (Interleukin-1, Tumor Necrosis Factor — TNF), which act on thermoregulatory center of the hypothalamus, causing vasoconstriction of skin vessels, decreased dissipation of heat and elevation of core body temperature.

**Leukocytosis** increased number of WBC[3] in peripheral blood mostly due to release of WBC from bone marrow. Specific types of WBC may be elevated depending on the type of inflammatory reaction or the kind of agent evoking the inflammation:

- *neutrophilia* (often associated with bacterial infections)
- *lymphocytosis* viral infections
- *eosinophilia* allergic and parasitic reactions

**Lymphadenopathy** abnormally enlarged lymphnodes reflect lymphocyte proliferation response.

**Lymphangiitis, lymphadenitis** is inflammation of lymphatic vessels or lymphnodes. Usually reflects extension of inflammation from a site that these lymphatics drain. If infectious organisms are not stopped by lymph nodes, enter the blood (bacteriemia, viremia).

**Acute Phase Protein production** Most of these proteins are produced by the liver. They include

- C-reactive protein
- serum amyloid A
- complement
- coagulation factors (especially fibrinogen)

This results in icreased Erythrocyte Sedimentation Rate (ESR).

## 1.5 Alterative inflammation

Necrosis of the cells dominates. Usually caused by toxins (toxic necroses of myocardial myocytes in diphteria) or viruses (poliomyelitis, hepatitis).

## 1.6 Exudative inflammation

Exudative inflammation can be classified according to:

- the inflammed tissue (*superficial:* skin, mucous membranes; *intersticial:* deep tissues and organs
- the characteristics of exudation
  1. serous
  2. non-purulent (lymphoplasmocytic)
  3. purulent
  4. fibrinous
  5. gangrenous

[2] usually *acute* inflammation
[3] White Blood Cells

### 1.6.1 Serous inflammation

Limited alteration, low density of exudate: *catarrhal* inflammation. Sometimes hemorrhagic, small amount of fibrin in the exudate is common.

- *skin:* spongiotic vesicles
- *mucous membranes:* erythema, small ulcerations, edema; if longlasting hypertrophy or atrophy may follow (e.g. nasal polyps or atrophic gastritis)
- *serous membranes:* erythema, dull surface (fibrin)
- *interstitial:* edema (e.g. urticaria, weal)

Serous inflammation usually heals completely.

### 1.6.2 Lymphoplasmocytic inflammation

Small mononuclear cells (lymphocytes, plasmatic cells, histiocytes) dominate the infiltration. Viral etiology is common. Heals completely, but if chronic leads to atrophy and fibrosis of the tissue (e.g. myocarditis).

### 1.6.3 Purulent inflammation

Exsudate contains large amount of neutrophils; the amount of fibrin is usually small. Tendency to *liquefaction* which causes destruction of tissues. Therefore, healing is usually limited, damage of inflammed tissues is common. If extensive intoxicates the whole organism.

- *mucous membranes:* covered with pus, which may accumulate in preformed body cavities — pseudoabsces (pyosalpinx, empyema)
- *serous membranes:* accumulation of pus, absorption of toxins (peritonitis)
- *interstitial:* accumulation of neutrophils, colliquation:
  *Abscess* (has a membrane, may slowly enlarge).
  *Phlegmone* has no membrane, spreads and destroys tissues

In chronic inflammation necrotic debris is accumulated in cytoplasm of macrophages and later even extracellularly (post inflammatory *pseudoxanthoma*). The inflammation can attack blood and lymphatic vessels, causing hematogenous and lymphatic spread to distant locations. Purulent *thrombophlebitis* leads to *bacteriemia* or *pyemia* and *sepsis*.

### 1.6.4 Fibrinous inflammation

The exsudate contains large amount of fibrin. Healing is usually difficult, especially if fibrin is not removed quickly enough. Fibrin attracts fibrocytes and stimulates formation of *granulation tissue*. This newly formed connective tissue later gradually loses its vascularity and cellularity forming the *scar*.

- *skin, mucous membranes:* the *pseudomembrane* composed of necrotic tissue, fibrin and possibly bacteria covers the surface.
  *Croupous* located superficially, usually heals completely
  *Diphteric* the mucous membrane is damaged deeper, the pseudomembrane cannot be pealed off without haemorrhage. Important examples are *diphteria* (larynx) or *dysenteria* (colon, *Shigella*)
  *Necrotic* (escharotic) is characterized by pronounced alteration (necrosis), healing with deep ulcerations and scarring. Examples: necrotizing tracheitis, karnification in lobar pneumonia.
- *serous membranes:* surface coated with fibrin, leads almost always to proliferation and formation of scars and concrescence. This process can lead to further complications (peritoneal fibrous concrescences can cause ileus, inflammatory obliteration of pericardial or pleural cavities can prevent normal functioning of the heart or lungs). Dystrophic *calcification* is common.
- *interstitial:* fibrin is located in interstitium as in acute rheumatic fever. *Fibrinoid necroses* of blood vessel walls, granulomas with *Aschoff cells* on the priphery and necroses of connective tissue are typical. Small scars are formed later. Repeated attacs are common, the damage accumulates (myocarditis rheumatica, *endocarditis rheumatica*).

### 1.6.5 Gangrenous Inflammation

Gangrene was already mentioned in the chapter describing necrosis. The (bacterial) toxins can cause tissue necrosis, preparing the tissue for easy bacterial invasion. Proteolytic enzymes cause tissue colliquation.

## 1.7 Productive Inflammation

Characterized by proliferation of fibroblasts, endothelium and formation of collagenous fibrils. Tendency to scar formation. Can be found in
*Acute inflammation reparation*
*Reparation of numeric atrophy* (sclerosis, fibrosis)
*Primary proliferative inflammation* is rare. Examples: fasciitis proliferans (of Dupuytren — palmar aponeurosis), fibromatoses

# 2 Regeneration and Repair

Regeneration occurs when the damaged tissue is substituted by the tissue which is morphologically and functionally equal. Unfortunately in man this occures to a limited extend only.

Epithelial tissues heal well if the reticular network remains preserved (necroses of individual cells or small groups of cells), namely if the cause of tissue damage is removed quickly. Reticulin network serves as a scafolding for epithelial cells.

If the reticulin is damaged (abscess, long standing inflammation) the tissues heal only partially (scars, fibrosis).

Some tissues (CNS, heart) have very limited or no capacity for healing. The tissue defect leads to formation of a cavity (CNS) or scar.