



# Pathology

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● Sheet

○ Slides

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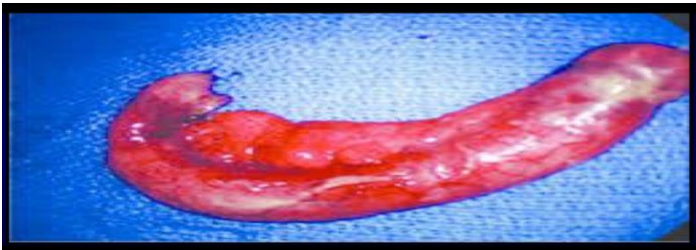
## Inflammation and repair

**Inflammation** is a response of vascularized (Alive) tissue to infections and tissue damage that brings cells and molecules of host defense from the circulation to the sites where they are needed, to eliminate the offending agents.

\*Inflammation does not occur in dead tissue for example in the case of gangrene.

Inflammatory response is **most** of the time protective response that is essential for survival, **BUT** not always. It serves to rid host of both the initial cause of cell injury (e.g., microbes, toxins) and the consequences of such injury (e.g., necrotic cells and tissues). So, without inflammation, infections would go unchecked, wounds would never heal, and injured tissues might remain permanent festering sores.

An example of inflammation...



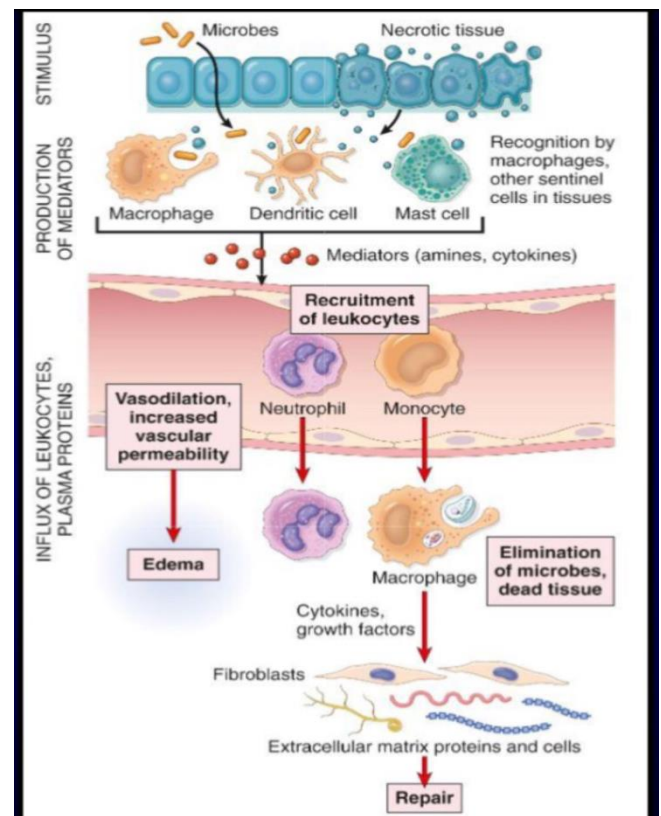
Note: Please pay attention to each picture in the slide as the Dr. said he will bring pictures in the exam.

It is an acute appendicitis as it is appeared in red color (congested).

### **Steps of inflammation:**

The typical inflammatory reaction develops through a series of sequential steps, (5 major steps- they overlap each other sometimes, BUT the sequence is very important so step 1 comes before step 2 and step 2 comes before step 3 and so on):

1. The offending agent, which is located in the extra-vascular tissues, is recognized by host cells and molecules.
2. (WBC)Leukocytes and plasma proteins are recruited from the circulation to



the site where the offending agent is located and vascular changes happen.

3. Leukocytes and proteins are activated and work together to destroy and eliminate the offending substance.
4. The reaction is controlled and the response is terminated.
5. The damaged tissue is repaired or resolved.

(Most of the time the tissue goes back to normal, not 100% but almost).



\*All these steps include cellular response and they all need stimulation by chemicals and proteins called chemical mediators of inflammation.

**Inflammation may be of two types, Acute and Chronic.**

- The initial, rapid response to infections and tissue damage is called acute inflammation. It typically develops within minutes or hours and is of short duration, lasting for several hours or a few days with prominent symptoms.
- But if the initial response fails to clear the stimulus, the reaction progresses to a protracted type of inflammation that is called chronic inflammation. It is of longer duration, and is associated with more tissue destruction.

\*Some forms of injury (immunologic reactions, some viral infections) cause a chronic inflammation from the outset.

\*Since the signs of chronic inflammation are not prominent, the inflammation can go unnoticed for a long time especially with organs like the liver where 80% of it can be destroyed and there would be no liver failure same goes for the kidneys, the body can survive with half a kidney so when the inflammation is finally detected it can be too late.

In the table, the features of Acute and Chronic inflammation:

| Feature                  | Acute                         | Chronic                               |
|--------------------------|-------------------------------|---------------------------------------|
| Onset                    | Fast: minutes or hours        | Slow: days                            |
| Cellular infiltrate      | Mainly neutrophils            | Monocytes/macrophages and lymphocytes |
| Tissue injury, fibrosis  | Usually mild and self-limited | May be severe and progressive         |
| Local and systemic signs | Prominent                     | Less                                  |

And Plasma cells

\*Neutrophils are sometimes called Polymorphonuclear cells because they have 3-5 nucleuses.  
 \*they have a short life span 1-2 days.  
 \*plasma cells are mature or hyper-mature B cells.

\*most cases that come in the E.R are acute, and in the clinic are usually chronic.

The external manifestation of inflammation, often called its **Cardinal Signs**, are:

- **Heat** (calor in Latin).
- **Redness** (*rubor*).
- **Swelling** (*tumor* – it is a Latin word which mean that something is big or swollen and here it has nothing to do with cancer "the term tumor" the inflamed organ gets bigger because of fluid and edema)
- **Pain** (*dolor*).(it can have physical causes and chemical causes)
- **Loss of function** (*function laesa*).

((NOTE: The Latin terms are very important))

**These manifestations occur as consequences of the vascular changes and leukocytes recruitment and activation.**

Although inflammation is normally protective, in some situations, the inflammatory reaction becomes the cause of disease, and the damage it produces is its dominant feature. For example:

- **Excessive inflammation** causes too much damage to the tissues and cells. It is an exaggerated inflammatory response which can be harmful and fatal to many people (for example, acute anaphylaxis).
- **Too little inflammation** Not only excessive inflammation, but also defective inflammation is responsible for serious illness.
- **inflammation reaction is misdirected** such as being against self-tissue in autoimmune diseases like rheumatoid arthritis and systemic lupus erythematosus, sometimes inflammation occurs against normally harmless environmental substances that evoke an immune response (e.g, allergies)which can be fatal, or is excessively prolonged (e.g., in infections by microbes that resist eradication).

(Pay attention to the table, it's an exam question):

TABLE 3.2 Disorders Caused by Inflammatory Reactions

| Disorders                                                                                                                                                                                                                                                                                                                  | Cells and Molecules Involved in Injury            |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| <b>Acute</b>                                                                                                                                                                                                                                                                                                               |                                                   |
| Acute respiratory distress syndrome                                                                                                                                                                                                                                                                                        | Neutrophils                                       |
| Asthma                                                                                                                                                                                                                                                                                                                     | Eosinophils; IgE antibodies                       |
| Glomerulonephritis                                                                                                                                                                                                                                                                                                         | Antibodies and complement; neutrophils, monocytes |
| Septic shock                                                                                                                                                                                                                                                                                                               | Cytokines                                         |
| <b>Chronic</b>                                                                                                                                                                                                                                                                                                             |                                                   |
| Arthritis                                                                                                                                                                                                                                                                                                                  | Lymphocytes, macrophages; antibodies?             |
| Asthma                                                                                                                                                                                                                                                                                                                     | Eosinophils; IgE antibodies                       |
| Atherosclerosis                                                                                                                                                                                                                                                                                                            | Macrophages; lymphocytes                          |
| Pulmonary fibrosis                                                                                                                                                                                                                                                                                                         | Macrophages; fibroblasts                          |
| Listed are selected examples of diseases in which the inflammatory response plays a significant role in tissue injury. Some, such as asthma, can present with acute inflammation or a chronic illness with repeated bouts of acute exacerbation. These diseases and their pathogenesis are discussed in relevant chapters. |                                                   |

To sum up:

The main cell infiltrates in Acute Inflammation is **Neutrophils**,  
and in chronic inflammation are **Lymphocytes and macrophages**.

## Acute inflammation

### Acute respiratory distress syndrome (ARDS)

-It is a severe inflammatory response in the lungs, the patient would be severely ill and it usually requires mechanical ventilation in an intensive care unit setting.

\*It can happen to people of all ages.

-In (ARDS) the neutrophils damage the \*hyaline alveolar membrane and the lungs would stop functioning causing what is called white lungs and the patient might end up dead.

-It used to have a high mortality rate (\*around 90%) but it has improved recently (30-40% can survive).

-When the lung is dissected after death it is heavy, thick and congested.

\*(ARDS is a clinical term not pathological).

**Asthma:** -sometimes called bronchial asthma- is a chronic disease of the airways that makes breathing difficult.

Asthma is characterized by bronchospasm and temporary airflow narrowing due to inflammation. This results in asthma symptoms, including coughing, wheezing, Tachypnea (breathing too fast) shortness of breath, and chest tightness.

**Eosinophils** are a type of white blood cell that are pinkish(eosinophilic) under the microscope and contain granules and are stimulated in acute allergic reactions like bronchial asthma where they rupture and release granules (Ige) into the blood stream causing the acute allergic reaction or acute anaphylaxis and if it is severe it can cause anaphylactic shock, where the blood pressure and heart rate drop and it can lead to death.

\*the doctor said that Ige molecules are released from Eosinophils however other resources mention that plasma cells are actually the ones that release Ige.

**Glomerulonephritis:** is a kidney disease (inflammation) caused by immunological reaction (\*type3) where the Antigen-antibody complex deposition in the kidney causes injury to it.

**Septic shock:** happens when there is a severe bacterial infection that the body could not eradicate and it spreads into the blood stream and to other organs and it may lead to organ failure and death ,cytokines which are inflammatory mediators secreted by the lymphocytes contribute in the septic shock.

\* Gram negative bacteria causes gram negative septicemia, it is more dangerous and is  
\*one of the main causes for patients that are present in the ICU.

### **Chronic inflammation**

**Atherosclerosis:** is a disease in which plaque builds up inside your arteries blocking them so the blood is unable to pass through \*platelets macrophages and endothelial cells are also involved.

It starts from **birth** and progresses as people get older.

**Asthma:** \*sometimes the attack is not severe and doesn't need medical care in the hospital (the ige molecules and Eosinophils are involved).

Example of an exam question:

The main cell infiltrate in: Acute asthmatic, allergic (anaphylactic) and parasitic reactions is "Eosinophils".

**Pulmonary fibrosis:** (called "scarring of the lungs") is a respiratory disease in which scars are formed in the lung tissues, leading to serious breathing problems and lung failure and the \*patent would need lung transplant.

### **Causes of inflammation:**

#### **Infection:**

Bacterial, viral, fungal, parasitic, and sometimes their microbial toxins (like in food poisoning-acute bacterial poisoning- where the bacteria usually Staphylococcus aureus produces toxins) are among the most common and medically important causes of inflammation.

#### **Tissue necrosis:**

It elicits inflammation regardless of the cause of cell death, which may include ischemia, trauma, Atherosclerosis, \*embolus (a blood clot, air bubble, piece of fatty deposit, or other object which has been carried in the bloodstream to lodge in a vessel and cause an embolism). gangrene, radiation, burns, frost bite, physical and chemical injury.

#### **Foreign body:**

Splinters, dirt, sutures may elicit inflammation by themselves or because they cause traumatic tissue injury or carry microbes. Even some endogenous substances stimulate potentially harmful inflammation if large amounts are deposited in tissues; such as uric acid crystals that are deposited in joints and causes acute arthritis (Gout), and cholesterol crystals in atherosclerosis.

#### **Immune reaction:**

The injurious immune responses may be directed against self antigens, causing autoimmune diseases, or may be inappropriate reactions against environmental substances, as in allergies or against microbes.

Best of luck....