Doctor 021

PATHOLOGY

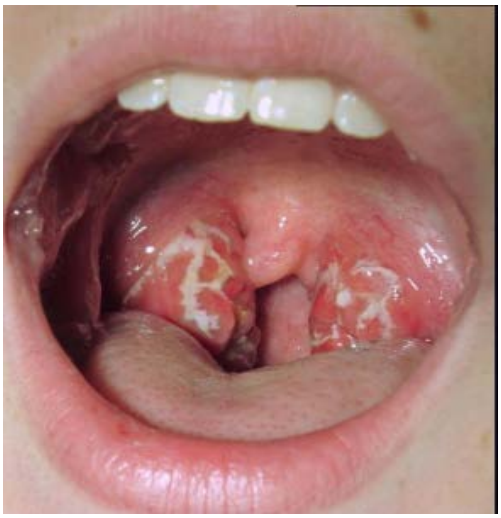
Sheet no. 1

Writer : Ahmad Al-laham

Corrector : Saba Al Smadi

Doctor : Dr.Mousa Alabbadi

INFLAMATION



Let us start our lecture observing this picture:

-we can clearly see some deviations From the normal state you can See that the tonsils are enlarged And there is a formed pus(the white color) Which is clearly a sign of inflammation.

-So what is inflammation?

It is the "Response of vascularized tissue to injury(infections or tissue damage) recruitment of cells and molecules from circulation to the sites of need to eliminate the offending agent"

-so according to the definition inflammation is a mechanism the body uses to protect itself against injurious agents of vascularized tissues

-pay attention to vascularized which is supplied with blood- so cadavers(dead bodies) won't respond to invading agents because they aren't viable/ vascularized as the doctor implied. And in the end the main goal is to eliminate the invader and heal the injured site.

From the book:

- Although in common medical and lay parlance, inflammation suggests a harmful reaction, it is actually a protective response that is essential for survival. It serves to rid the 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).

- The mediators of defense include phagocytic leukocytes, antibodies, and complement proteins. Most of these normally circulate in the blood, where they are sequestered so they cannot damage normal tissues but can be rapidly recruited to any site in the body.

-Some of the cells involved in inflammatory responses also reside in tissues, where they function as sentinels on the lookout for threats. The process of inflammation delivers leukocytes and proteins to foreign invaders, such as microbes, and to damaged or necrotic tissues, and it activates the recruited cells and molecules, which then function to eliminate the harmful or unwanted substances.

-you should know that there are certain defensive cells that circulate in your blood and once an injury happens they are called and recruited towards the injury site to eliminate the invader(enemy) and heal the damaged tissues.

-so we can conclude that inflammation has certain properties some of which are:

- **Protective**

In general the response is protective to prevent the spreading of the disease to all sites of your body for ex. Covid 19 there weren't proper treatment initially so it was able to target every organ inside of your body mainly the lungs so a lot of people died because of this harmful virus.

- **With no inflammation: infections can be fatal, wounds would never heal and injured tissue may sustain permanent damage.**

So without inflammatory response such as in severe immunodeficiency diseases a disease like simple tonsillitis,and simple injuries can kill them so you are in danger without this response That's why patients with severe Immunodeficiency diseases die early.

Also without proper response healing will be delayed and imperfect and not very efficient because healing is part of this amazing response.

Immunodeficiency ⟶ no inflammatory response.

The typical inflammatory reaction develops through a series of sequential steps:

- **Offending agent recognized by cells and Molecules.**
- **WBCs & Pl. proteins recruited to injury Site.**
- **WBCs and Pl. proteins work together to destroy and eliminate the enemy.**
- **Rx. Is then controlled and terminated**
- **Repair of damaged tissue (regeneration & fibrosis).**

Explanation:

- The offending agent which is the one that provides a stimulus, which is located in extravascular tissues, is recognized by host cells and molecules.

Your cells can screen and recognize the offending agent which causes the stimulus and in response they secrete chemical mediators through mainly macrophages and neutrophils also lymphocytes also called cytokines and then they recruit:

- Leukocytes and plasma proteins are recruited from the circulation to the site where the offending agent is located.
- The leukocytes and proteins are activated and work together to destroy and eliminate the offending substance.

-the doctor calls the neutrophils micky mouse cells because they have 3-5 nuclei also called polymorphonuclear leukocytes(scientific name).

So the recruited cells make changes some of which increased vascular permeability and vasodilation which results in swelling(edema) and the macrophages will be stimulated more to eliminate and eat the offending agent.

The macrophage cell when it is circulating in the blood vessels we call it monocyte it has a short life span if not used it will die in a short time however when it is recruited to the tissues we call it tissue macrophage it has more organelles in the cytoplasm and the cytoplasm gets larger it gets matured.

When we talk about cell differentiation (maturation) when we go from the most primitive (mother cell) to terminally differentiated cells nucleus gets smaller cytoplasm gets larger and the cell will have more organelles and nucleus to cytoplasm ratio gets smaller.

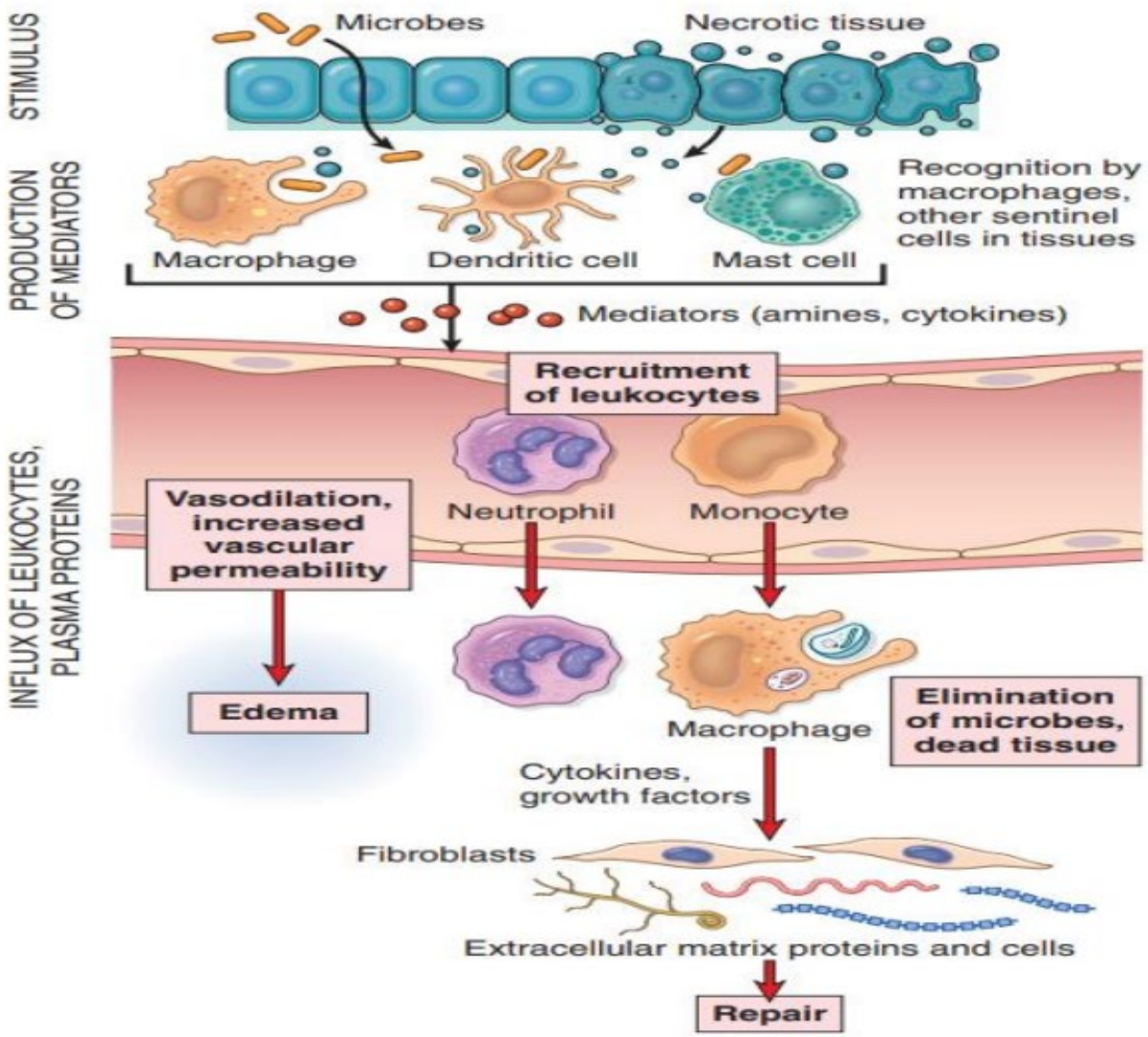
probably the last step in the response is the repair so those steps which we talked about are the major steps of the inflammatory response. And in particular in acute response.

Further explanation from the book:

When a microbe enters a tissue or the tissue is injured, the presence of the infection or damage is sensed by resident cells, including macrophages, dendritic cells, mast cells, and other cell types. These cells secrete molecules (cytokines and other mediators) that induce and regulate the subsequent inflammatory response. Inflammatory mediators are also produced from plasma proteins that react to the microbes or to products of necrotic cells. Some of these mediators promote the efflux of plasma and the recruitment of circulating leukocytes to the site where the offending agent is located. Mediators also activate the recruited leukocytes, enhancing their ability to destroy and remove the offending agent. Understanding the role of chemical mediators is important because most anti-inflammatory drugs target specific mediators. We shall discuss the mediators of inflammation in detail later, after we review the main steps in inflammatory reactions.

-know that these steps happen in sequence however there can be some overlap between these steps and in the end when the invader is eliminated you control the inflammatory response because you don’t need it anymore and it could damage the tissues if not controlled.

-everything we have covered up until now is summarized in this pic:



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. When acute inflammation achieves its desired goal of eliminating the offenders, the reaction subsides and residual injury is repaired. But if the initial response fails to clear the stimulus, the reaction progresses to a protracted type of inflammation that is called chronic inflammation. But this is not always true however it is enough to know that for our level. It is of longer duration and is associated with more tissue destruction, the presence of lymphocytes and macrophages, the proliferation of blood vessels, and fibrosis. Sometimes chronic may have no symptoms.

TABLE 3.1 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

-local and systemic signs:

Sometimes the inflammation can be local such as the swelling of your appendix or Tonsils but you also suffer from fever which your whole body feels it so it is systemic and when you find -after doing a blood sample test- that the white blood cells count has increased or the Creactive protein level elevated this is systemic signs.

In acute the signs are prominent because at first there is high elevated levels of what we talked about so you will feel tired and rest in your home however chronic even though it is less prominent it causes you more damage since it acts upon you over long period of times.

For ex. The liver weighs 1.3 kg and you remain normal although 85 percent of it has been damaged because the reserve capacity of it is high so when you begin to feel sick you will be certainly in a bad state and condition the same for if you lost one of your kidneys.

-To know fibrosis refers to the healing of the wound and since you sustain more damage in chronic inflammation fibrosis will be greater.
Cellular filtrate looking at microscope after taking a section from inflamed tissue and it means what are the main cells present in this tissue.

there will be a question about it memorize it well the doctor said.

-chronic diseases are insidious.
Hepatitis B/C acute attacks with chronic inflammation
Hypertension/diabetes are chronic diseases so watch out for yourselfs
Hypertension could cause heartfailure.
The external manifestations of inflammation, often called its cardinal signs, are heat (calor in Latin), redness (rubor), swelling (tumor), pain (dolor), and loss of function (functio laesa)

Cardinal signs of inflammation:

- **HEAT (calor)**
- **REDNESS (rubor)**
- **SWELLING (tumor)**
- **PAIN (dolor)**
- **LOSS OF FUNCTION (function laesa)**

Can inflammation be bad?

- **Too much...damage**
- **Too little... damage**
- **Misdirected inflammation...autoimmune diseases and allergies**
- **Chronic inflammation...chronic diseases**

TABLE 3.2 Disorders Caused by Inflammatory Reactions

Disorders	Cells and Molecules Involved in Injury
Acute	
Acute respiratory distress syndrome	Neutrophils
Asthma	Eosinophils; IgE antibodies
Glomerulonephritis	Antibodies and complement; neutrophils, monocytes
Septic shock	Cytokines
Chronic	
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.

in some situations, the inflammatory reaction becomes the cause of disease, and the damage it produces is its dominant feature. For example, inflammatory reactions to infections are often accompanied by local tissue damage and its associated signs and symptoms (e.g., pain and functional impairment). Typically, however, these harmful consequences are self-limited and resolve as the inflammation abates, leaving little or no permanent damage. In contrast, there are many diseases in which the

inflammatory reaction is misdirected (e.g., against self tissues in autoimmune diseases), occurs against normally harmless environmental substances that evoke an immune response (e.g., in allergies), or is excessively prolonged (e.g., in infections by microbes that resist eradication). Not only excessive inflammation but also defective inflammation is responsible for serious illness.

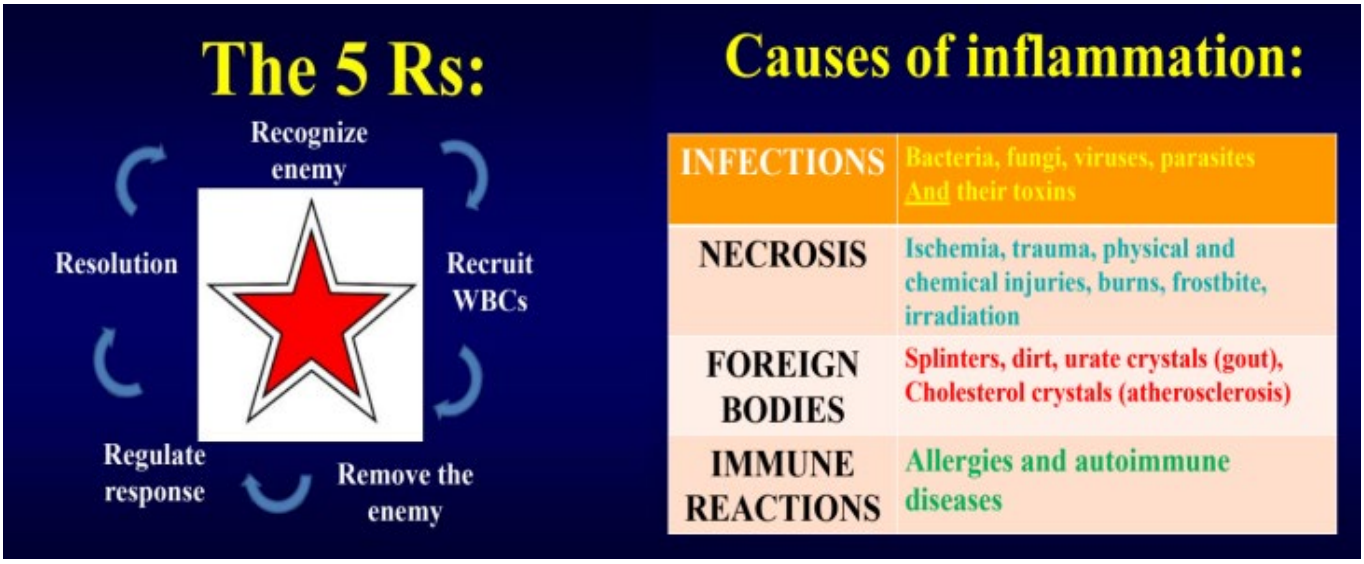
Too little inflammation, which is typically manifested by increased susceptibility to infections.

-final notes the doctor said focus on the contents of the macrophage in the pic at page 6.

-Glomerulonephritis: involves tissue injury on kidneys and sometimes in neurons.

-Acute bronchial asthma: severe bronchospasm, wheezing, difficulty in swallowing

-Septic shock (septicemia)—blood poising due to severe bacterial overgrowth in the blood results in secreting too many cytokines are released which impacts vital functions gram-negative bacterial septicemia is lethal.



In the end goodluck to all of you my dear fellows

We wish you the best work hard and you will be on top

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