SHEET NO.

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IMMUNOLOGY

DOCTOR 2019 | MEDICINE | JU

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The small red font in this sheet is additional information.

Immunology

The most important function of the immune system is resisting against any foreign body, so people who have immune deficiency are always exposed to various infections. Conversely, stimulating immune responses against microbes through vaccination is the most effective method for protecting individuals against infections.

((The immune system does more than provide protection against infections. It prevents the growth of some tumors, and different types of cancer can be treated by stimulating immune responses against tumor cells. Immune responses also participate in the clearance of dead cells and in initiating tissue repair.

In contrast to these beneficial roles, abnormal immune responses cause many inflammatory diseases with serious morbidity and mortality)).

Immunity is defined as resistance to disease, specifically infectious diseases. The collection of cells, tissues, and molecules that mediate resistance to infections is called the **immune system**, and the coordinated reaction of these cells and molecules to infectious microbes comprises an immune response.

It is important to understand that the immune system will resist any foreign body, even if this body does not belong to microbes or viruses, for example: if any cell of your body turned into a cancer cell, the immune system will kill it. Therefore, the immune system can harm your body.

Some examples on the previous paragraph:

1-the immune system in some cases resists bacteria in an excessive way, so it might cause your body more harm than bacterial poisons.

2-the most significant impediments in 'Organ Transplantation' is the immune system.

Immunology is the study of the immune system, including its responses to microbial pathogens and damaged tissues and its role in disease.

Immunology and its applications helped save millions of lives, and future breakthroughs are expected to save more.

First, we will study the biology of the immune system (e.g. Cells of the immune system, their activation and regulation)
then we will describe the role of the immune system in health and disease. (e.g. Role in fighting microbes, immunopathologies)
finally, we will go over applications of immunology (serology, immunotherapy).
It is worth mentioning that the immune system is one of the best discoveries in the modern time because it helped save millions of lives (especially in Vaccination), and future breakthroughs are expected to save more!

In ancient times, people thought that the cause of any disease is poisonous air, because they noticed that diseases spread in areas containing trash.

In Western society, it was not until the late eighteenth century that a rational approach to the origin of diseases developed.

Effectiveness of vaccination for some common infectious diseases.

Role of the immune system	Implications
Defense against infections	Deficient immunity results in increased susceptibility to infections; exemplified by AIDS Vaccination boosts immune defenses and protects against infections
Defense against tumors	Potential for immunotherapy of cancer
The immune system can injure cells and induce pathologic inflammation	Immune responses are the cause of allergic, autoimmune, and other inflammatory diseases
The immune system recognizes and responds to tissue grafts and newly introduced proteins	Immune responses are barriers to transplantation and gene therapy

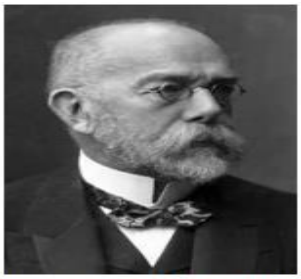
Importance of the immune system in health and disease.
This table summarizes some of the physiological functions of the immune system and its role in diseases. Such as AIDS, Acquired immunodeficiency syndrome.

In 1798, Edward Jenner, noticed that milkmaids were protected from smallpox if they had been first infected with cowpox microbe.

Some historical information:

Robert Koch was one of the main founders of modern bacteriology. He identified the specific causative agents of tuberculosis, cholera and anthrax and gave experimental support for the **concept of infectious disease (germ theory)**, which included experiments on humans and other animals.

Pasteur is renowned for his discoveries of the principles of **vaccination**, microbial fermentation and **pasteurization,** he was responsible for disproving the doctrine of **spontaneous generation.**



Robert Koch 1843 –1910

Louis Pasteur 1822 –1895

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The figure below illustrates Koch's postulates, criteria designed to establish a causal relationship between a causative and a disease.

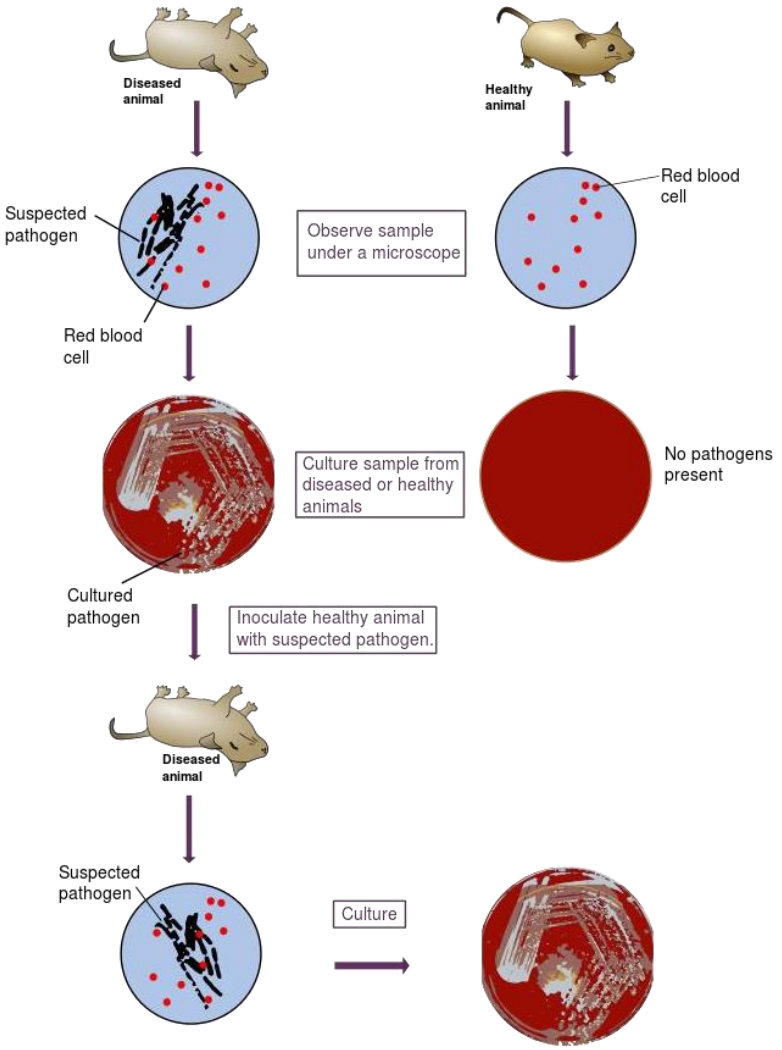
Koch's Postulates:

① The microorganism must be found in abundance in all organisms suffering from the disease, but should not be found in healthy organisms.

② The microorganism must be isolated from a diseased organism and grown in pure culture.

③ The cultured microorganism should cause disease when introduced into a healthy organism.

④ The microorganism must be reisolated from the inoculated, diseased experimental host and identified as being identical to the original specific causative agent.



Paul Ehrlich and others, recognized that a specific **antigen** elicited the production of a specific **antibody**. Ehrlich hypothesized that these antibodies were specialized molecular structures with specific receptor sites that fit each pathogen like a **lock and key**. Thus, the first realization that the body had a **specific defense system** was introduced.

A representation by Robert Seymour of the cholera epidemic of the 19th century depicts the spread of the disease in the form of poisonous air.

The most important scientists in immunology are **Paul Ehrlich** and **Élie Metchnikoff .**
The idea that specific cells could be directly involved with defending the body was first suggested in 1884 by **Élie Metchnikoff**.

he conducted experiments on animals where he would inflict some injuries, and he would later on notice while examining under the microscope that there are some cells trying to treat the injury.

However, it was not until the 1940s that his theories were accepted and the **cell mediated**, as opposed to the **humoral**, immune response was recognized.

(The two types of adaptive immunity, called humoral immunity and cell- mediated immunity, are mediated by different cells and molecules and they provide defense against extracellular microbes and intracellular microbes, respectively)

the invention of the microscope contributed to developments in discovering the immune system.

Humoral immunity : is the aspect of **immunity** that is mediated by macromolecules found in extracellular fluids.

The immune system includes the role of 1- **physical** 2- **cellular** 3- **chemical systems**, that are in place and that respond to all aspects of **foreignness**.

The immune system targets any "foreign" object, so the first step is to **recognize** what is self and non- self.

This step 'recognition' is very important and to make this step successful, the immune system has **receptors** and **certain molecules.**

The second step is to **restore** homeostasis by eliminating the foreign object.

The third step is to **remember** the invading pathogen to respond better the next time it is encountered.

If we want to summarize the mechanism of the immune system:

1-recognise

2-restore

3-remember.

The immune system is not **only** active when danger arises, but is constantly sensing danger and is **important for normal physiology and homeostasis** similar to the cardiovascular and renal systems.

***Immune system exists in all organisms even in bacteria.**

Virtually all organisms have at least one form of defence that helps repel disease-causing organisms.

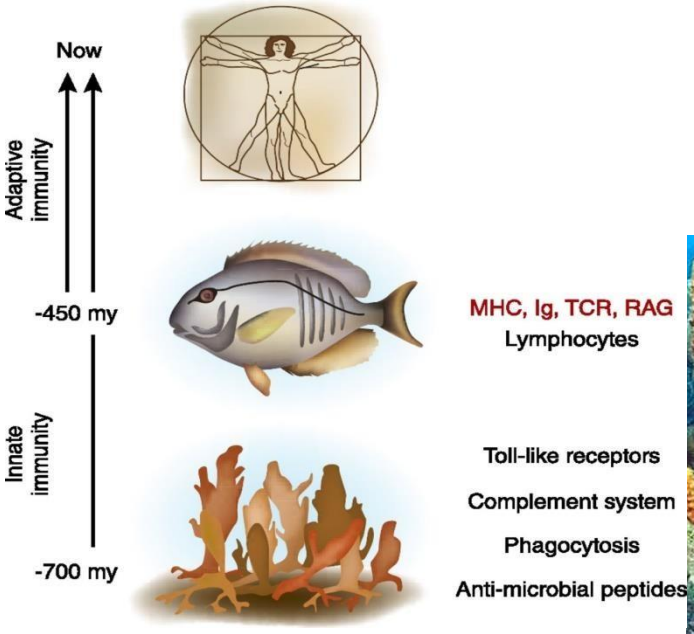
Mechanisms for discriminating "**self" from "non-self"** evolved to accomplish the task of fighting pathogens, launching a long history of **host-pathogen co-evolution.**

There are two divisions of immune system:

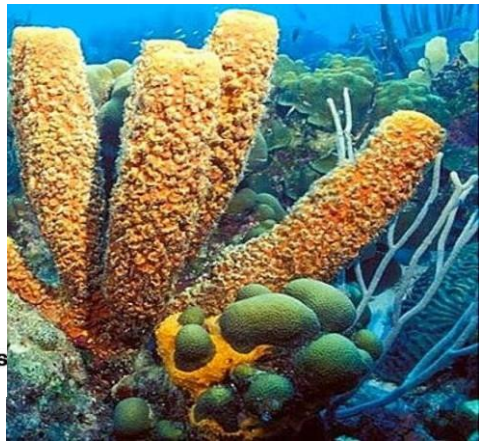
1- **The innate immune** response (faster): is activated by chemical properties of the antigen.

2- **Adaptive immunity** (slower): refers to antigen-specific **immune** response.

Pathogens evolve new strategies to overcome immune mechanisms, and so the host defence becomes more complex to defend against invading pathogens.



Jawed vertebrates have developed higher complexity of defence reflected in the **adaptive immune response** .



In the figure above: Transplantation of parts of a sponge to other sponges is met by an immune response.

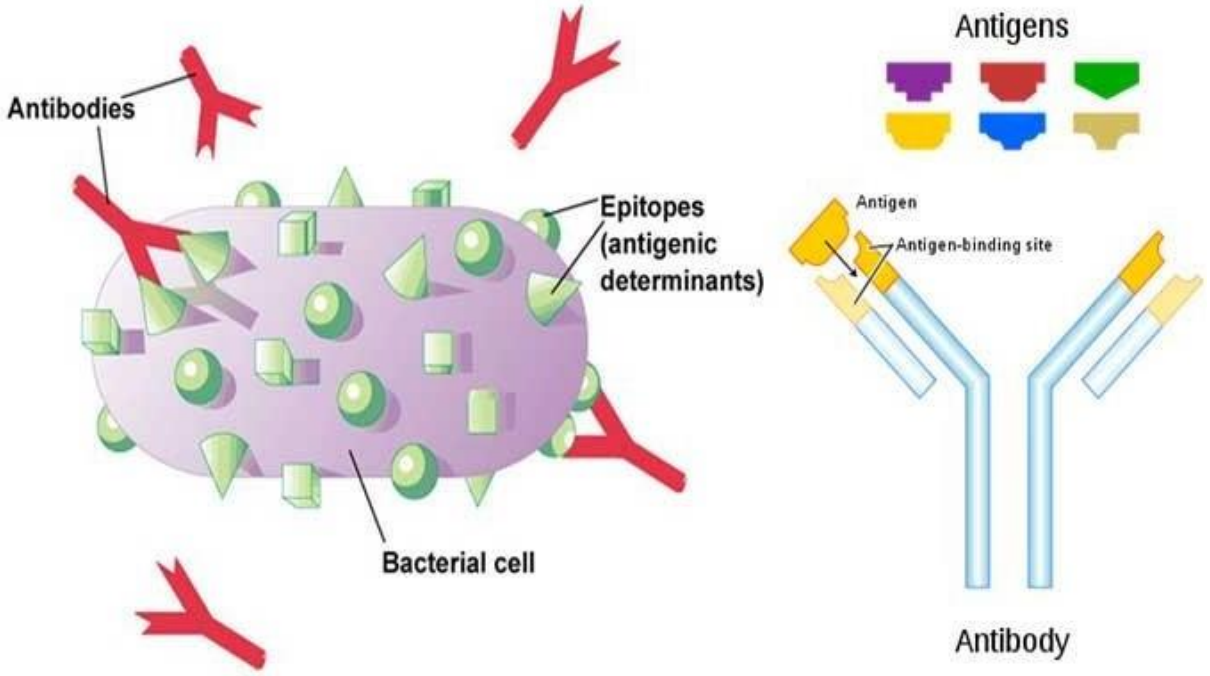
with time, the immune system becomes more complex because of the huge number of bacteria, and as a result, both the bacteria and the immune system are always becoming more complex.

Antigen: antibody generating molecule

Antigens are any substance that stimulates the immune system to produce **antibodies**.

Antigens can be bacteria, viruses, or fungi that cause infection and disease. They might also originate from within the body ("self-antigen"), but should not be attacked by the immune system in normal situations.

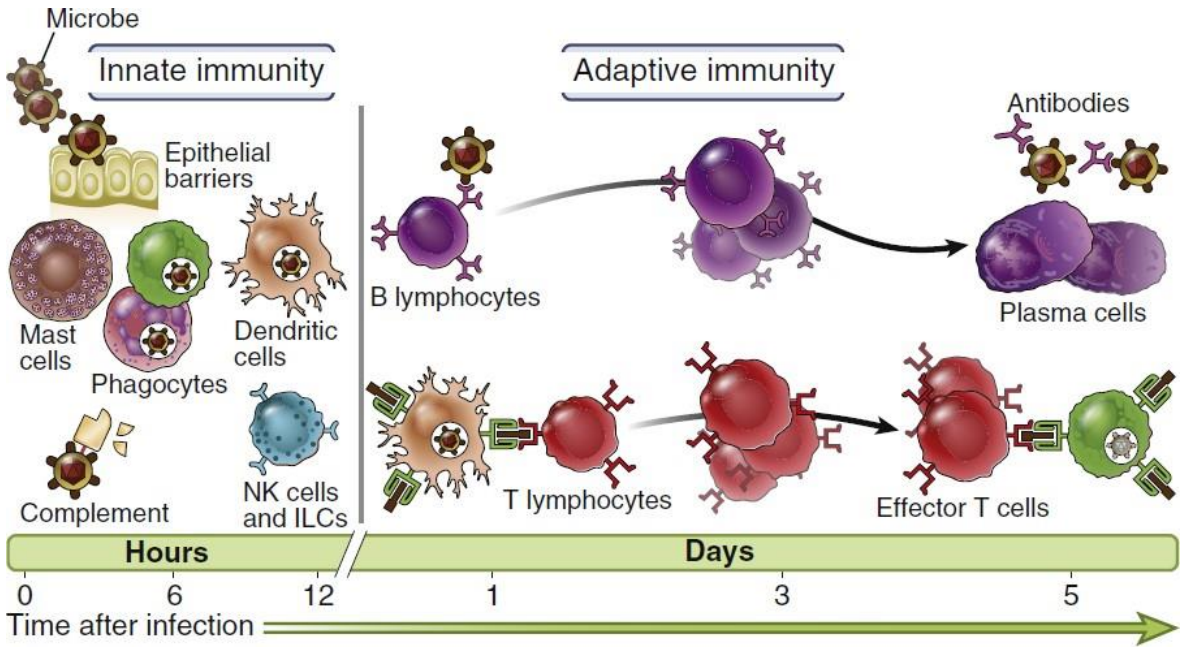
Antibodies, also called immunoglobulins: the Y-shaped molecules are proteins that are manufactured by the body that help fight against **antigens**.



Epitope also known as **antigenic determinant**, is the part of an antigen that is recognized by the immune system.

In general: innate immunity works within hours, whereas adaptive immunity takes days.

*there is somehow communication between innate and adaptive immunity.



Host defenses are grouped under:

innate immunity, which provides **immediate** protection against microbial invasion, and **adaptive** immunity, which develops **more slowly** and provides more specialized defense against infections.

The Innate immune system is active all the time and is non-specific, if it can't overcome the microbes, the adaptive immune system will be activated.

	Innate immunity	**Adaptive Immunity**
Components	1. Physical and chemical barriers 2. Phagocytic leukocytes 3. Dendritic cells 4. Natural Killer cells 5. Plasma proteins (complement)	1. Humoral immunity (B cells, which mature into antibody secreting plasma cells) 2. Cell-mediated immunity (T cells, which mature into effector helper and cytotoxic T cells)
Activity	Always present	Normally silent
Response and potency	Immediate response, but has a limited and lower potency	Slower response (over 1-2 weeks, but is much more potent
Specificity	General: can recognize general classes of pathogens (i.e. bacteria, viruses, fungi, parasites) but cannot make fine distinctions	Recognizes highly specific antigens
Course	Attempts to immediately destroy the pathogen, and if it can't, it contains the infection until the more powerful adaptive immune system acts.	Slower to respond; effector cells are generally produced in 1 week and the entire response occurs over 1-2 weeks. However, this course can vary somewhat during different responses in an individual.

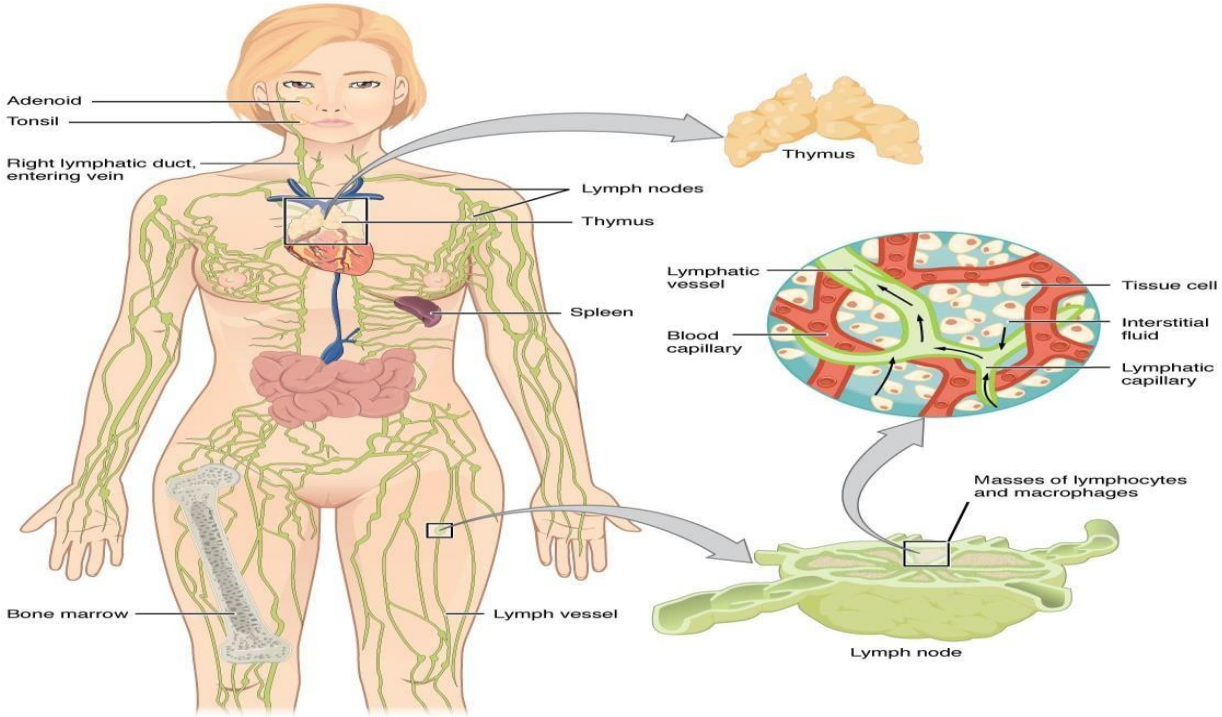
((**Principal mechanisms of innate and adaptive immunity**. The mechanisms of innate immunity provide the initial defense against infections. Some mechanisms (e.g., epithelial barriers) prevent infections, and other mechanisms (e.g., phagocytes, natural killer [NK] cells and other innate lymphoid cells [ILCs], the complement system) eliminate microbes.
Adaptive immune responses develop later and are mediated by lymphocytes and their products. Antibodies block infections and eliminate microbes, and T lymphocytes eradicate intracellular microbes. The kinetics of the innate and adaptive immune responses are approximations and may vary in different infections))

Location of immune system:

The duty of the immune system is to survey the whole body so it should be present **everywhere**. There are sites where immune cells collect to fulfil their function (e.g. lymph nodes).

For example, in the small intestine there is a lymphatic tissue that surveys intestinal pathogens called Peyer's patches.

The bone marrow is an important place for the generation of immune and non-immune blood cells.



The cells of the immune system originate from the bone marrow, in the bone marrow there are stem cells which can differentiate into **lymphoid stem cells** and **myeloid stem cells.**

Cellular components of the immune system

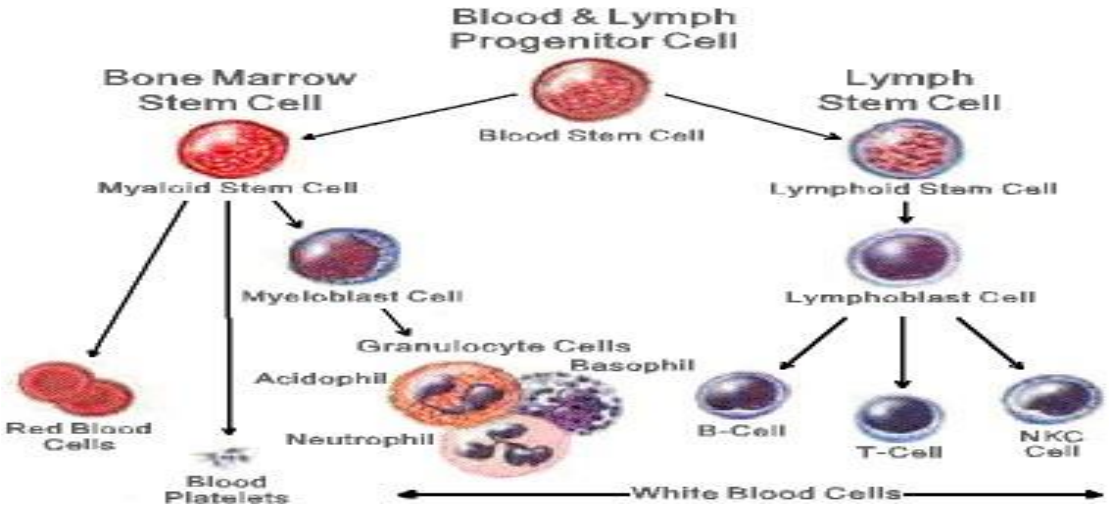


Table 2.

Normal White Blood Cell Distribution

WHITE BLOOD CELL LINE	*NORMAL PERCENTAGE*
Neutrophils	40 to 60
Lymphocytes	20 to 40
Monocytes	2 to 8
Eosinophils	1 to 4
Basophils	0.5 to 1

Quick summary: Immunology is a relatively **recent science** with **applications** that extend to other medical sciences. Thus, it is important for medical students.
The immune system in an **ancient** defence mechanism composed of tissues, cells and molecules that interact with each other with **great complexity**.
Parts of the immune system are continuously active, and help in maintaining **homeostasis**.
Specialized immune cells are mainly in the **bone marrow** and then circulate the blood or aggregate in lymph nodes.
The **immune system's arms** can be divided in general into **innate** and **adaptive**.

Good Luck ☺