Immunology:

The modern word "immunity" derives from the Latin *immunis*, meaning exemption from military service, tax payments or other public services.The first written descriptions of the concept of immunity may have been made by the Athenian, in 430 B.C, described that when the plague hit Athens: "the sick and the dying were tended by the pitying care of those who had recovered, because they knew the course of the disease and were themselves free from apprehensions. For no one was ever attacked a second time, or not with a fatal result".

The first clinical description of immunity which arose from a specific disease causing organism is probably *Kitab fi al-jadari wa-al-hasbah* ('A Treatise on Smallpox and Measles', translated 1848[4]) written by the Islamic physician Al-Razi in the 9th century. In the treatise, Al Razi describes the clinical presentation of smallpox and measles and goes on to indicate that that exposure to these specific agents confers lasting immunity (although he does not use this term).[2]

The first scientist who developed full theory of immunity was Ilya Mechnikov after he revealed phagocytosis in 1882.

With Louis Pasteur's germ theory of disease, the fledgling science of immunology began to explain how bacteria caused disease, and how, following infection, the human body gained the ability to resist further infections. In 1891, Pasteur widened the definition of vaccine in honour of Jenner and it then became essential to qualify the term, by referring to polio vaccine, measles vaccine etc.

Introduction:

In biology, **immunity** is the state of having sufficient biological defenses to avoid infection, disease, or other unwanted biological invasion.

It is the capability of the body to resist harmful microorganisms or viruses from entering it. Immunity involves both specific and non-specific components.

The non-specific components act either as barriers or as eliminators of wide range of pathogens irrespective of antigenic specificity.

Other components of the immune system adapt themselves to each new disease encountered and are able to generate pathogen-specific immunity.

A-Innate immunity, or nonspecific immunity is the natural resistances with which a person is born. It provides resistances through several physical, chemical and cellular approaches.

Microbes first encounter the epithelial layers, physical barriers that line skin and mucous membranes. Subsequent general defences include secreted chemical signals (cytokines), antimicrobial substances, fever, and phagocytic activity associated with the inflammatory responses. The phagocytes express cell surface receptors that can bind and respond to common molecular patterns expressed on the surface of invading microbes.

Through these approaches, innate immunity can prevent the colonization, entry and spread of microbe

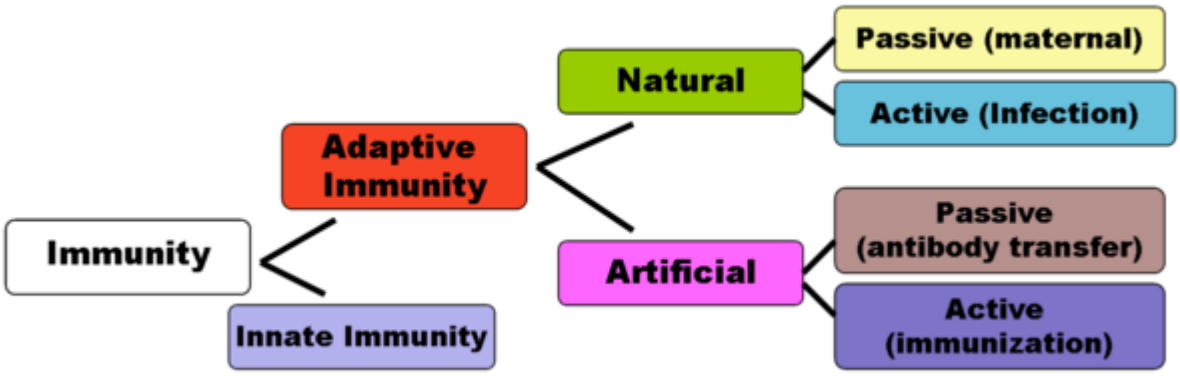
B-Adaptive immunity is often sub-divided into two major types depending on how the immunity was introduced.

1- 'Naturally acquired immunity' occurs through contact with a disease causing agent, when the contact was not deliberate,

Whereas 2- 'artificially acquired immunity' develops only through actions such as vaccination.

Both naturally and artificially acquired immunity can be further subdivided depending on whether immunity is induced in the host or passively transferred from an immune host.

'Passive immunity' is acquired through transfer of antibodies or activated T-cells from an immune host, and is short lived—usually lasting only a few months—whereas 'active immunity' is induced in the host itself by antigen and lasts much longer, sometimes lifelong. The diagram below summarizes these divisions of immunity.



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The Immune System:

The Blood System

--The 5 liters of blood of a 70 kg person constitute about 7% of the body's total weight..

- Blood is composed of 52–62% liquid plasma and 38–48% cells.

-The plasma is mostly water (91.5%) and acts as a solvent for transporting other materials (7% and 1.5% other stuff).

- Blood is slightly alkaline (pH = 7.40 □ .05) and a tad heavier than water

All blood cells are manufactured by stem cells, which live mainly in the bone marrow, via a process called **hematopoiesis**.

The stem cells produce **hemocytoblasts** that differentiate into the precursors for all the different types of blood cells.

Hemocytoblasts mature into three types of blood cells:

1- **erythrocytes** (red blood cells or RBCs),

2-leukocytes (white blood cells or WBCs), and

3- **thrombocytes** (platelets).

The leukocytes are further subdivided into

A- **granulocytes** (containing large granules in the cytoplasm)

The granulocytes consist of neutrophils (55–70%), eosinophils (1–3%), and basophils (0.5–1.0%).

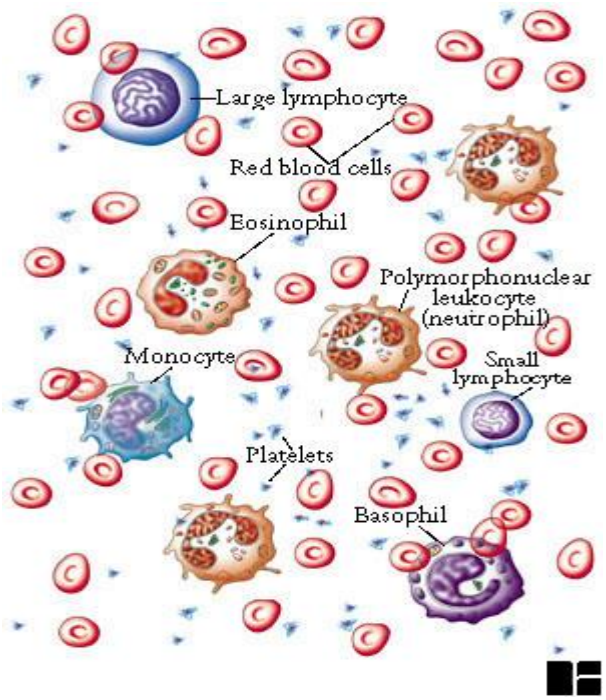
B-agranulocytes (without granules).

The agranulocytes are **lymphocytes** (consisting of B cells and T cells)

and **monocytes**.

Lymphocytes circulate in the blood and lymph systems, and make their home in the lymphoid organs.

All of the major cells in the blood system are illustrated below.



There are 5000–10,000 WBCs per mm^3 and they live 5-9 days.

About 2,400,000 RBCs are produced each second and each lives for about 120 days (They migrate to the spleen to die.

A healthy male has about 5 million RBCs per mm^3, whereas females have a bit fewer than 5 million.

Normal Adult Blood Cell Counts			
Red Blood Cells		$5.0*10^6/mm^3$	
Platelets		$2.5*10^5/mm^3$	
Leukocytes		$7.3*10^3/mm^3$	
	Neutrophil		50-70%
	Lymphocyte		20-40%
	Monocyte		1-6%
	Eosinophil		1-3%
	Basophil		<1%

The goo on RBCs is responsible for the usual ABO blood grouping, among other things. The grouping is characterized by the presence or absence of A and/or B antigens on the surface of the RBCs. Blood type AB means both antigens are present and type O means both antigens are absent. Type A blood has A antigens and type B blood has B antigens.

Some of the blood, but not red blood cells (RBCs), is pushed through the capillaries into the interstitial fluid.

The Lymph System

Lymph is an alkaline (pH > 7.0) fluid that is usually clear, transparent, and colorless. It flows in the lymphatic vessels and bathes tissues and organs in its protective covering. it has a lower protein content than blood. Like blood, it is slightly heavier than water (density = 1.019 □ .003).

The lymph flows from the interstitial fluid through lymphatic vessels up to either the thoracic duct or right lymph duct, which terminate in the subclavian veins, where lymph is mixed into the blood.

Lymph carries lipids and lipid-soluble vitamins absorbed from the gastrointestinal (GI) tract. Since there is no active pump in the lymph system, there is no back-pressure produced. The lymphatic vessels, like veins, have one-way valves that prevent backflow.

, along these vessels there are small bean-shaped **lymph nodes** that serve as filters of the lymphatic fluid. It is in the lymph nodes where antigen is usually presented to the immune system.

The human lymphoid system has the following:

- **primary organs**: bone marrow and the thymus gland (located behind the breastbone above the heart), and
- **secondary organs** at or near possible portals of entry for pathogens:
- adenoids,
- tonsils,
- spleen (located at the upper left of the abdomen),
- lymph nodes (along the lymphatic vessels with concentrations in the neck, armpits, abdomen, and groin),
- Peyer's patches (within the intestines), and the appendix.

Innate Immunity

The innate immunity system is what we are born with and it is nonspecific; all antigens are attacked pretty much equally. It is genetically based and we pass it on to our offspring.

1-Surface Barriers or Mucosal Immunity

1. The first and, arguably, most important barrier is the **skin**. The skin cannot be penetrated by most organisms unless it already has an opening, such as a nick, scratch, or cut.
2. **Mechanically**, pathogens are expelled from the lungs by ciliary action as the tiny hairs move in an upward motion; **coughing** and **sneezing**; the **flushing action of tears**, saliva, and urine also force out pathogens.

3-Sticky mucus in respiratory and gastrointestinal tracts traps many microorganisms.

4-Acid pH (< 7.0) of skin secretions inhibits bacterial growth.

5- **Hair follicles** secrete sebum that contains **lactic acid** and **fatty acids** both of which inhibit the growth of some

(pathogenic bacteria and fungi. Areas of the skin not covered with hair, such as the palms and soles of the feet, are most susceptible to fungal infections. Think athlete's foot.)

6-Saliva, tears, nasal secretions, and perspiration contain **lysozyme**, an enzyme that destroys Gram positive bacterial cell walls causing cell lysis. **Vaginal secretions** are also slightly).

7- **Spermine and zinc** in **semen** destroy some pathogens.

8- **Lactoperoxidase** is a powerful enzyme found in **mother's milk**.

9-The stomach is a formidable obstacle insofar as its mucosa secrete hydrochloric acid **(HCl)** ($0.9 < pH < 3.0$, very acidic that kill many pathogens.

10-Normal flora are the microbes, mostly bacteria, that live in and on the body with, usually, no harmful effects to us.

- We have about 10^{13} cells in our bodies and 10^{14} bacteria, most of which live in the large intestine.

- There are 10^3–10^4 microbes per cm^2 on the skin (*Staphylococcus aureus*, *Staph. epidermidis*, diphtheroids, streptococci, *Candida*, etc.).

-Various bacteria live in the nose and mouth.

- Lactobacilli live in the stomach and small intestine.

- The upper intestine has about 10^4 bacteria per gram of which 95–99% are anaerobes

The urogenitary tract is lightly colonized by various bacteria

Normal flora produce (**bacteriocidins, defensins, cationic proteins, and lactoferrin)** all of which work to destroy other bacteria

The resident bacteria can become problematic when they invade spaces in which they were not meant to be. As examples:

(a) staphylococcus living on the skin can gain entry to the body through small cuts/nicks.

(b) Some **antibiotics**, (clindamycin), kill some of the bacteria in our intestinal tract. This causes an overgrowth of (*Clostridium difficile*,) which results in **colitis**, a rather painful condition wherein the inner lining of the intestine cracks and bleeds

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11- **phagocyte : is a cell that attracts (by chemotaxis), adheres to, engulfs, and ingests foreign bodies.**

made in the bone marrow, after which they are released into the blood and called ***monocytes*****,** which mature into **macrophages** .

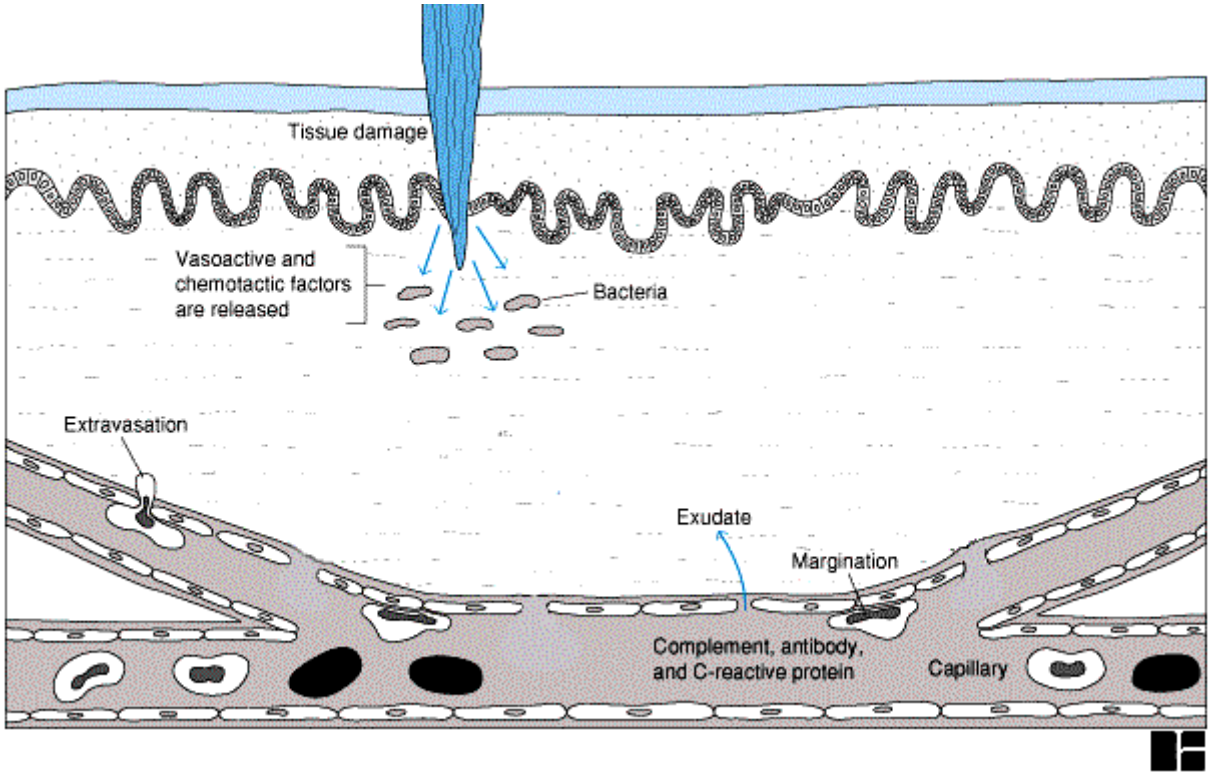
-Some **macrophages** are concentrated in the lungs, liver (**Kupffer cells),** lining of the lymph nodes and spleen, brain, kidney mesoangial cells,

. They are long-lived,. Once a macrophage phagocytizes a cell, it places some of its proteins, called **epitopes,** on its surface.

These surface markers serve as an alarm to other immune cells that then infer the form of the invader.

All cells that do this are called antigen presenting cells (APCs).

The *wandering macrophages* roam the blood vessels and can even leave them to go to an infection site where they destroy dead tissue and pathogens. Emigration by squeezing through the capillary walls to the tissue is called **diapedesis** or **extravasation**. The presence of histamines at the infection site attract the cells to their source.



- **Natural killer cells** move in the blood and lymph to lyse cancer cells and virus-infected body cells. They are large granular **lymphocyte.**
- **neutrophils**, , are phagocytes that have no mitochondria., short-lived (half-life of 6–8 hours, 1–4 day lifespan), and have a segmented nucleus.

. The neutrophils provide the major defense against pyogenic (pus-forming) bacteria and are the first on the scene to fight infection.

They are followed by the wandering macrophages about three to four hours later

Eosinophils are attracted to cells coated with complement C3B, where they release major basic protein (MBP), which work together to burn holes in cells and helminths (worms).

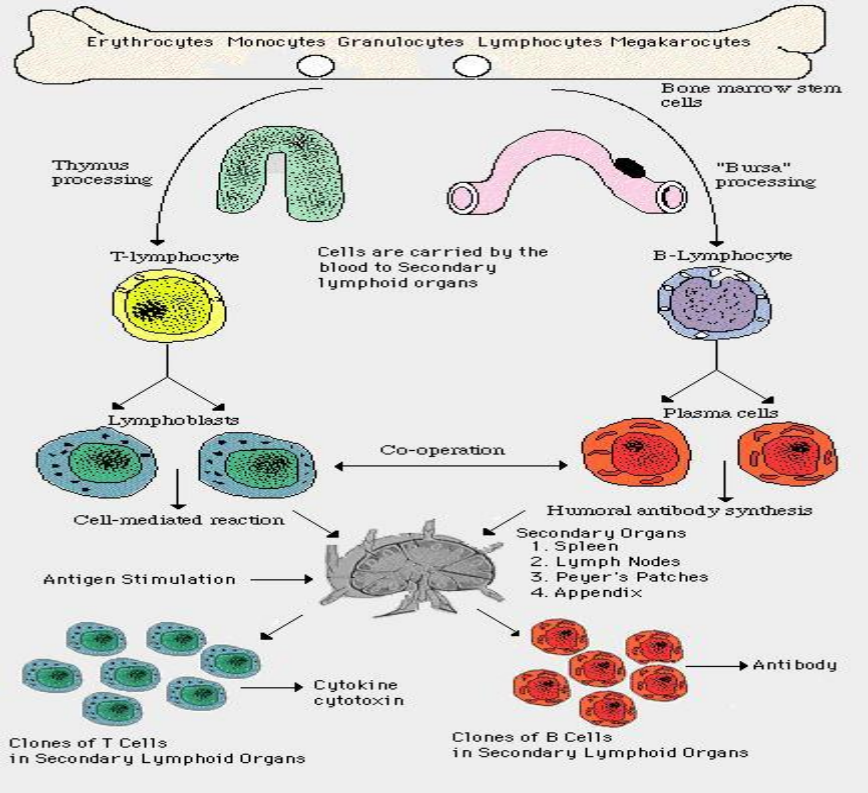
Neutrophils, eosinophils, and macrophages are all phagocytes.

The **complement system** is a major triggered enzyme plasma system. It coats microbes with molecules that make them more susceptible to engulfment by phagocytes

Dendritic cells are covered with a membranous processes that look like **nerve cell dendrites**.

Most of them are highly efficient **antigen presenting cells**. There are four basic types:.

Our major concern will be **Langerhans cells**, which are found in the epidermis and mucous membranes, especially in the anal, vaginal, and oral cavities. These cells make a point of attracting antigen and efficiently presenting it to T helper cells for their activation



Each of the cells in the innate immune system bind to antigen using **pattern-recognition receptors**. These receptors are encoded in the germ line of each person. This immunity is passed from generation to generation. Over the course of human development these receptors for pathogen-associated molecular patterns have evolved via natural selection to be specific to certain characteristics of broad classes of infectious organisms. There are several hundred of these receptors and they recognize patterns of bacterial lipopolysaccharide, peptidoglycan, bacterial DNA, dsRNA, and other substances. Clearly, they are set to target both Gram-negative and Gram-positive bacteria.

Adaptive or Acquired Immunity

. Lymphocytes constitute 20–40% of the body's WBCs. Their total mass is about the same as that of the **brain or liver.** (Heavy stuff!)

Lymphocytes come in two major types:

1- B cells 15%**, B cells** are produced in the **stem cells** of the bone marrow; they produce antibody and oversee humoral immunity. ,
2- T cells. 80% of them ,**T cells** are nonantibody-producing lymphocytes which are also produced in the bone marrow but sensitized in the **thymus** and constitute the basis of cell-mediated immunity

Parts of the immune system are changeable and can adapt to better attack the invading antigen. There are two fundamental adaptive mechanisms:

A- cell-mediated immunity and B- humoral immunity.

Humoral immunity

An immunocompetent but as immature **B-lymphocyte** is stimulated to maturity when an **antigen** binds to its surface receptors in the**(APC)**

and there is a **T helper** cell nearby (to release a **cytokine).**

This **sensitizes** the B cell and it undergoes **clonal selection**, which means it reproduces asexually by mitosis

1-. Most of the family of clones become **plasma cells**. These cells produce highly specific **antibodies** at a rate of as many as 2000 molecules per second for four to five days.

2- The other B cells become long-lived **memory cells**.

Cell-mediated immunity

Macrophages engulf antigens, process them internally, then display parts of them on their surface together with some of their own proteins.

-This sensitizes the **T cells** to recognize these antigens. All cells are coated with various substances, each of which is a different chemical molecul that coats the surface. CD8+ is read "CD8 positive." Every T and B cell has about 10^5 molecules on its surface.

Essentially, an antigen may find a near-perfect fit with a very small number of lymphocytes, perhaps as few as one.

Helper T cells (CD4+) serve as managers, directing the immune response. They secrete chemicals called **lymphokines** that::

stimulate **cytotoxic T cells** and B cells to grow and divide, attract neutrophils, and enhance the ability of macrophages to engulf and destroy microbes.

Cytotoxic or **killer T cells** (CD8+) do their work by releasing **lymphotoxins**, which cause cell lysis.

Suppressor T cells inhibit the production of cytotoxic T cells once they are unneeded, lest they cause more damage than necessary.

Memory T cells are programmed to recognize and respond to a pathogen once it has invaded and been repelled.

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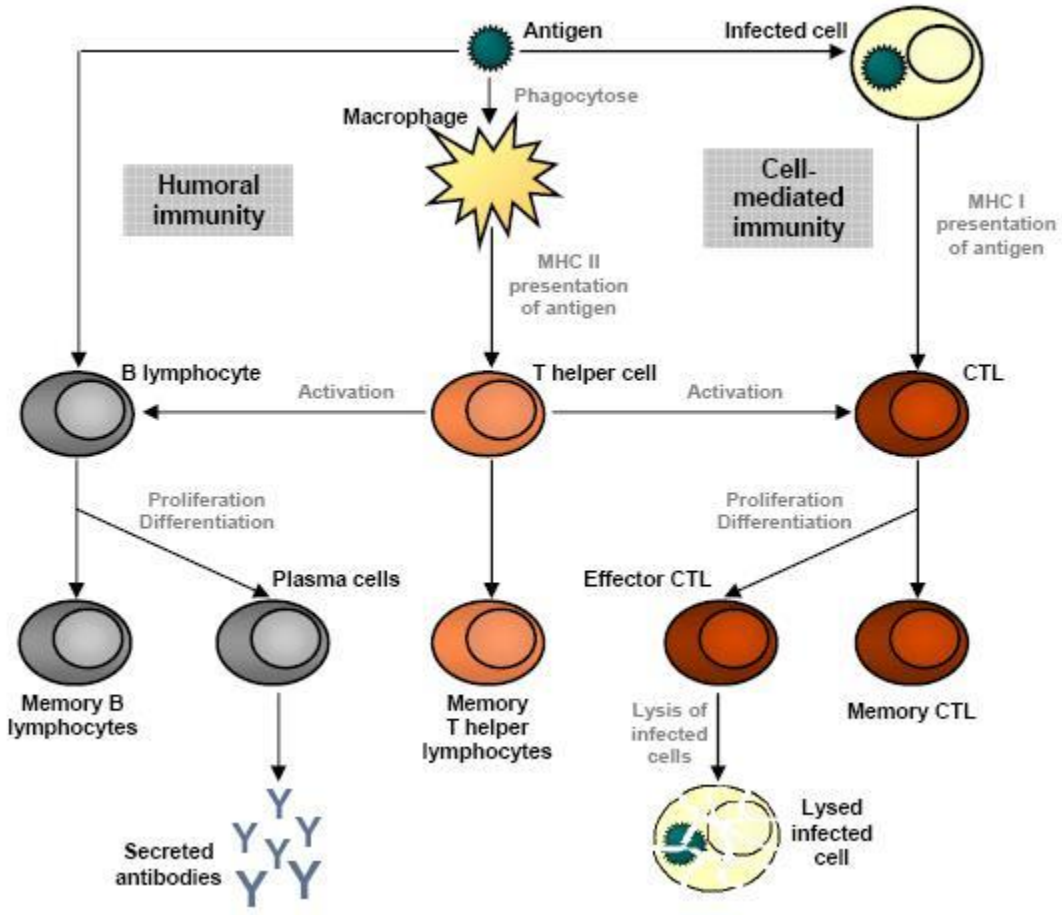

The table below shows the differences between innet and adaptive immunity:

Table 1

Innat immunity	Adaptive immunity
Response is **antigen-independent**	Response is **antigen-dependent**
There is **immediate** maximal response	There is a **lag time** between exposure and maximal response
Not antigen-specific	**Antigen-specific**
Exposure results in **no immunologic memory**	Exposure results in **immunologic memory**