Introduction

Immunology :- is a broad branch of biomedical science that covers the study of all aspects of the immune system in all organisms. It deals with, among other things, the physiological functioning of the immune system in states of both health and disease; malfunctions of the immune system in immunological disorders (autoimmune diseases, hypersensitivities, immune deficiency, transplant rejection).(is the study of all aspects of host defense against infection and of adverse consequences of immune responses).

The immune system: is biological term used to describe the tissues, cells, and molecules involved in adaptive immunity, or sometimes the totality of host defense mechanisms.

Immunization: is the process of becoming immune to (protected against) a disease. 2 type: active immunization; passive immunization.

The immune response: is the response made by the host to defend itself against a pathogen.

Immune responses can be **innate (non-adaptive)** or **adaptive (acquired).**

Type of immunity:

1- Adaptive immunity (specific immune defense)

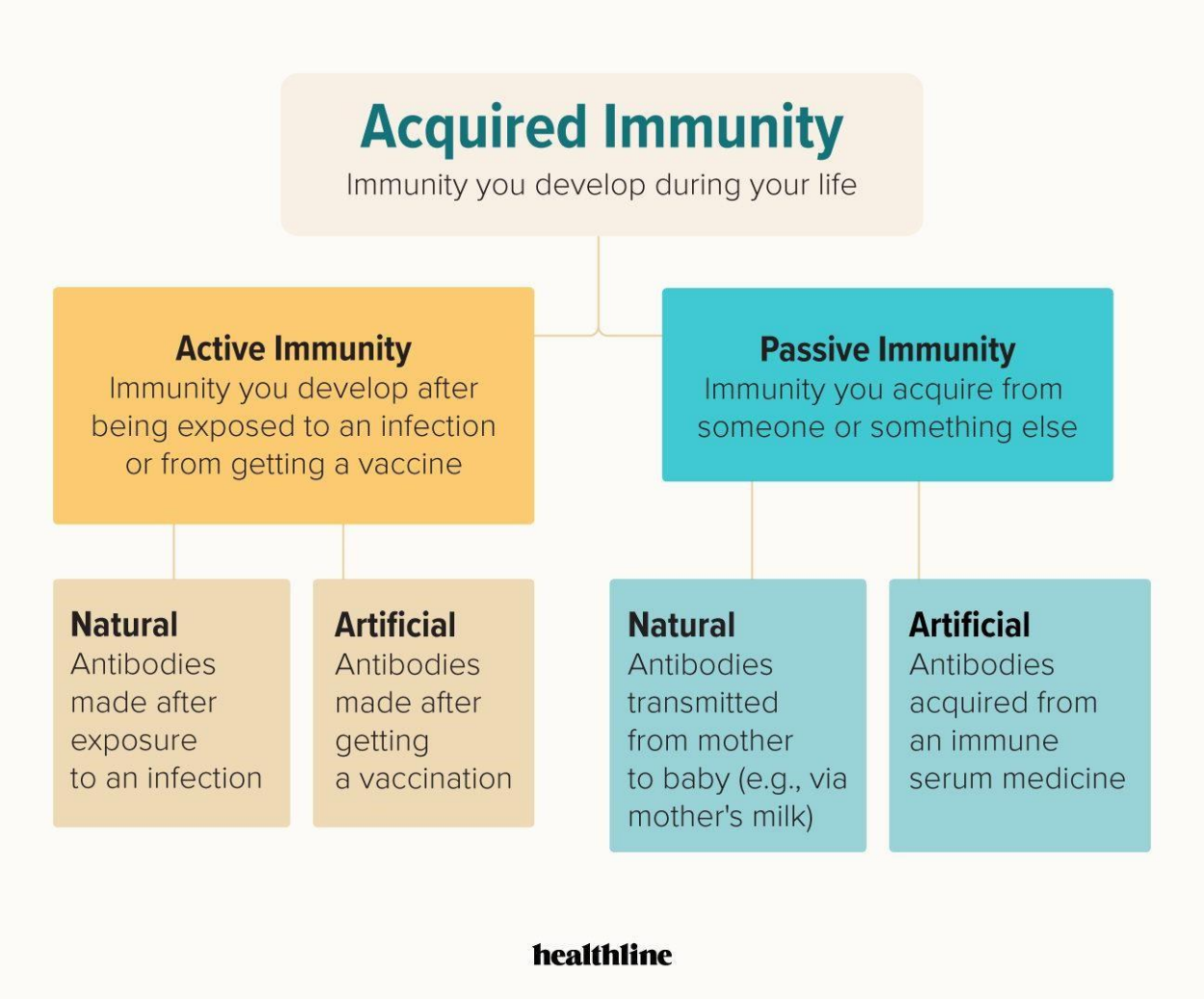
Adaptive immunity, which occurs after exposure to an antigen (eg, an infectious agent) is specific and is mediated by either antibody or lymphoid cells. is described as a dual system, with humoral and cellular components. Humoral immunity primarily involves B cells and neutralizes foreign body outside human cells. Cellular immunity primarily involves T cells and deals with foreign body inside cells. It can be passive or active.

A-Active Immunity

Active immunity is induced after contact with foreign antigens (eg, microorganisms or their products). This contact may consist of clinical or subclinical infection, immunization with live or killed infectious agents or their antigens, exposure to microbial products (eg, toxins, toxoids), or transplantation of foreign cells. In all these instances the host actively produces antibodies, and lymphoid cells acquire the ability to respond to the antigens. Advantages of active immunity include long-term resistance (based on memory of prior contact with antigen and the capacity to respond faster and to a greater extent on subsequent contact with the same antigen); disadvantages include the slow onset of resistance and the need for prolonged or repeated contact with the antigen.

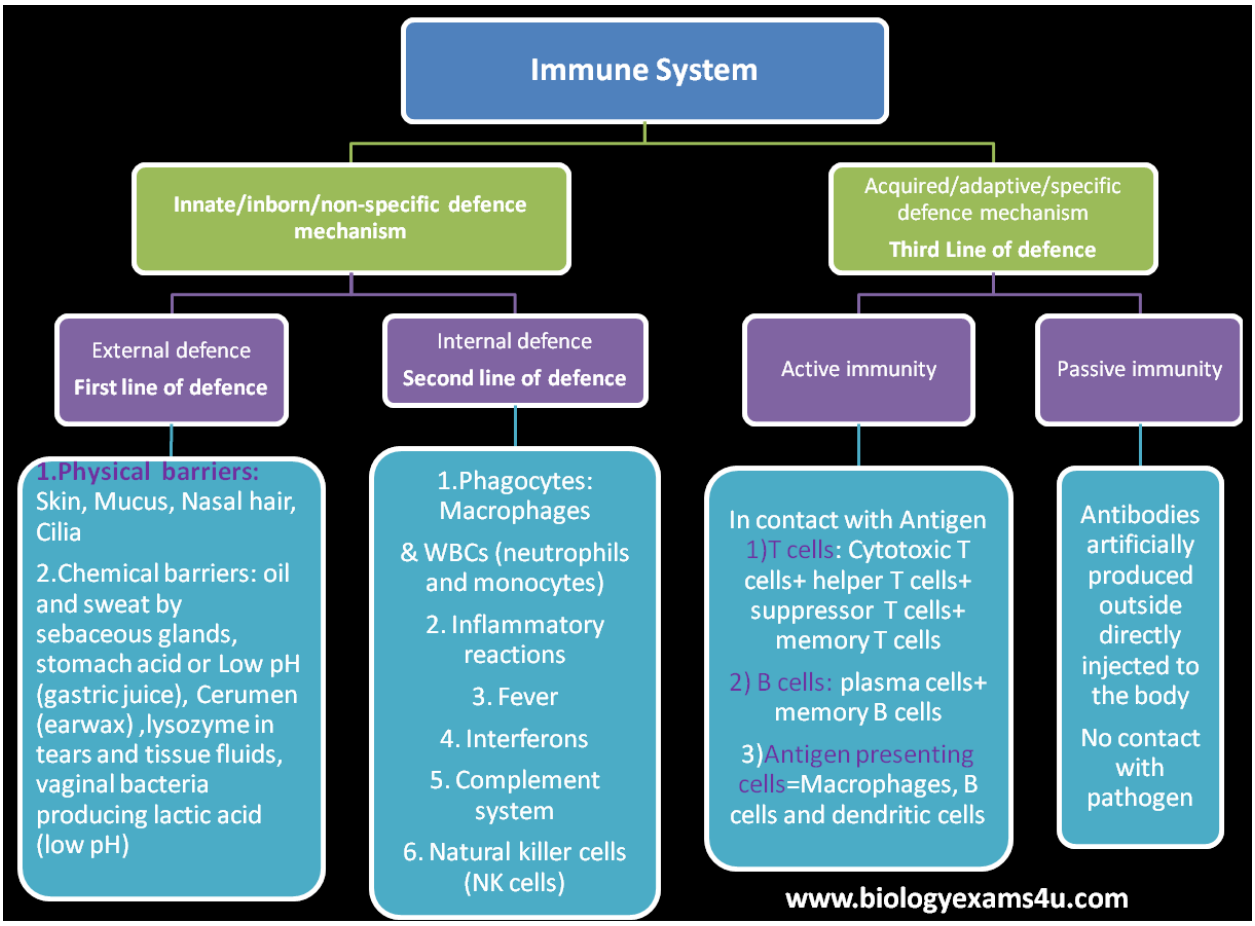
B-Passive Immunity

Passive immunity is transmitted by antibodies or lymphocytes preformed in another host. The passive administration of antibody (in antisera) against certain viruses (eg, hepatitis B) can be useful during the incubation period to limit viral multiplication, eg, after a needle stick injury to someone who has not been vaccinated. The main advantage of passive immunization with preformed antibodies is the prompt availability of large amounts of antibody; disadvantages are the short life span of these antibodies and possible hypersensitivity reactions if antibodies (immunoglobulins) from another species are administered.



2-Innate immunity (also called natural or native or non-specific immunity)

Innate immunity is resistance that is pre-existing and is not acquired through contact with a nonself (foreign) entity known as an antigen. It is nonspecific and includes barriers to infectious agents—eg, skin and mucous membranes, phagocytic cells, inflammatory mediators, and complement components. It may vary with age and with hormonal or metabolic activity.



The principal components of innate immunity are:

(1) Physical and chemical barriers, such as epithelia and antimicrobial chemicals produced at epithelial surfaces; For example, epithelial cells of the nasal passages and bronchi of the respiratory system have cilia (small hair-like structures) that beat in an upward direction to help remove microorganisms that enter during breathing.Some substances are known to directly kill microbes, e.g. lysozyme digests proteoglycans in bacterial cell walls; others compete for nutrients (e.g. transferrin, Fe), and others interfere with ion transport (e.g. NaCl). Mucus (containing mucin) secreted by the mucosal epithelial cells coats their surfaces and makes it difficult for microbes to contact and bind to these cells – a prerequisite for entry into the body. The washing action of tears, saliva and urine also helps to prevent attachment of microbes to the epithelial surfaces. In addition, IgA antibodies in tears and saliva prevent the attachment of microbes. table (1).

Table 1: Secretions at epithelial surfaces

Site	Source	Specific substances secreted
Eyes	Lacrimal glands (tears)	Lysozyme, IgA and IgG
Ears	Sebaceous glands	Oily, waxy secretion, fatty acids
Mouth	Salivary glands (saliva)	Digestive enzymes, lysozyme, IgA, IgG, lactoferrin
Skin	Sweat glands (sweat) Sebaceous glands	Lysozyme, high NaCl, short chain fatty acids Oily secretion and fatty acids (sebum)
Stomach	Gastric juices	Digestive enzymes (pepsin, rennin), acid (low pH, 1–2)

(2) Phagocytic cells (neutrophils, macrophages), dendritic cells, and natural killer (NK) cells and other innate lymphoid cells

Cells of the innate immune response

1-All white blood cells (WBC) are known as leukocytes. Leukocytes are able to move freely and interact with and capture cellular debris, foreign particles, or invading microorganisms. The innate leukocytes include: Natural killer cells, mast cells, eosinophils, basophils; and the phagocytic cells including macrophages, neutrophils, and dendritic cells, and function within the immune system by identifying and eliminating pathogens that might cause infection.

2-Mast cells : Mast cells are a type of innate immune cell that reside in connective tissue and in the mucous membranes. They are intimately associated with wound healing and defense against pathogens, but are also often associated with allergy and anaphylaxis. When activated, mast cells rapidly release characteristic granules, rich in histamine and heparin, along with various hormonal mediators, and chemokines, or chemotactic cytokines into the environment. Histamine dilates blood vessels, causing the characteristic signs of inflammation, and recruits neutrophils and macrophages.

3-Phagocytes : The word 'phagocyte' literally means 'eating cell'. These are immune cells that engulf, i.e. phagocytose, pathogens or particles. To engulf a particle or pathogen, a phagocyte extends portions of its plasma membrane, wrapping the membrane around the particle until it is enveloped (i.e., the particle is now inside the cell). Once inside the cell, the invading pathogen is contained inside an endosome, which merges with a lysosome. The lysosome contains enzymes and acids that kill and digest the particle or organism. In general, phagocytes patrol the body searching for pathogens, but are also able to react to a group of highly specialized molecular signals produced by other cells, called cytokines. The phagocytic cells of the immune system include macrophages, neutrophils, and dendritic cells. By helping to remove dead cells preceding growth and development of new healthy cells, phagocytosis is an important part of the healing process following tissue injury.

4-Macrophages : Macrophages, from the Greek, meaning "large eaters," are large phagocytic leukocytes, which are able to move outside of the vascular system by moving across the walls of capillary vessels and entering the areas between cells in pursuit of invading pathogens. In tissues, organ-specific macrophages are differentiated from phagocytic cells present in the blood called monocytes. Macrophages are the most efficient phagocytes, and can phagocytose substantial numbers of bacteria or other cells or microbes. The binding of bacterial molecules to receptors on the surface of a macrophage triggers it to engulf and destroy the bacteria through the generation of a ―respiratory burst‖, causing the release of reactive oxygen species. Pathogens also stimulate the macrophage to produce chemokines, which summons other cells to the site of infection.

5-Neutrophils : Neutrophils, along with two other cell types; eosinophils and basophils , are known as granulocytes due to the presence of granules in their cytoplasm, or as polymorphonuclear cells (PMNs) due to their distinctive lobed nuclei. Neutrophil granules contain a variety of toxic substances that kill or inhibit growth of bacteria and fungi. Similar to macrophages, neutrophils attack pathogens by activating a respiratory burst. The main products of the neutrophil respiratory burst are strong oxidizing agents including hydrogen peroxide, free oxygen radicals and hypochlorite.

6-Dendritic cells : Dendritic cells (DC) are phagocytic cells present in tissues that are in contact with the external environment, mainly the skin (where they are often called Langerhans cells), and the inner mucosal lining of the nose, lungs, stomach, and intestines.

They are named for their resemblance to neuronal dendrites, but dendritic cells are not connected to the nervous system. Dendritic cells are very important in the process of antigen presentation, and serve as a link between the innate and adaptive immune systems.

7-Basophils and eosinophils : Basophils and eosinophils are cells related to the neutrophil . When activated by a pathogen encounter, basophils releasing histamine are important in defense against parasites, and play a role in allergic reactions (such as asthma). Upon activation, eosinophils secrete a range of highly toxic proteins and free radicals that are highly effective in killing bacteria and parasites, but are also responsible for tissue damage occurring during allergic reactions. Activation and toxin release by eosinophils is, therefore, tightly regulated to prevent any inappropriate tissue destruction.

8-Natural killer cells : Natural killer cells, or NK cells, are a component of the innate immune system that does not directly attack invading microbes. Rather, NK cells destroy compromised host cells, such as tumor cells or virus-infected cells, recognizing such cells by a condition known as "missing self." This term describes cells with low levels of a cellsurface marker called MHC I (major histocompatibility complex) - a situation that can arise in viral infections of host cells. They were named "natural killer" because of the initial notion that they do not require activation in order to kill cells that are "missing self." For many years, it was unclear how NK cell recognize tumor cells and infected cells.

Phagocytosis is a process by which cells ingest large particles (> 0.5 micrometers) into membrane-bound vesicles called phagosomes, which are then targeted to the lysosomes for enzymatic degradation

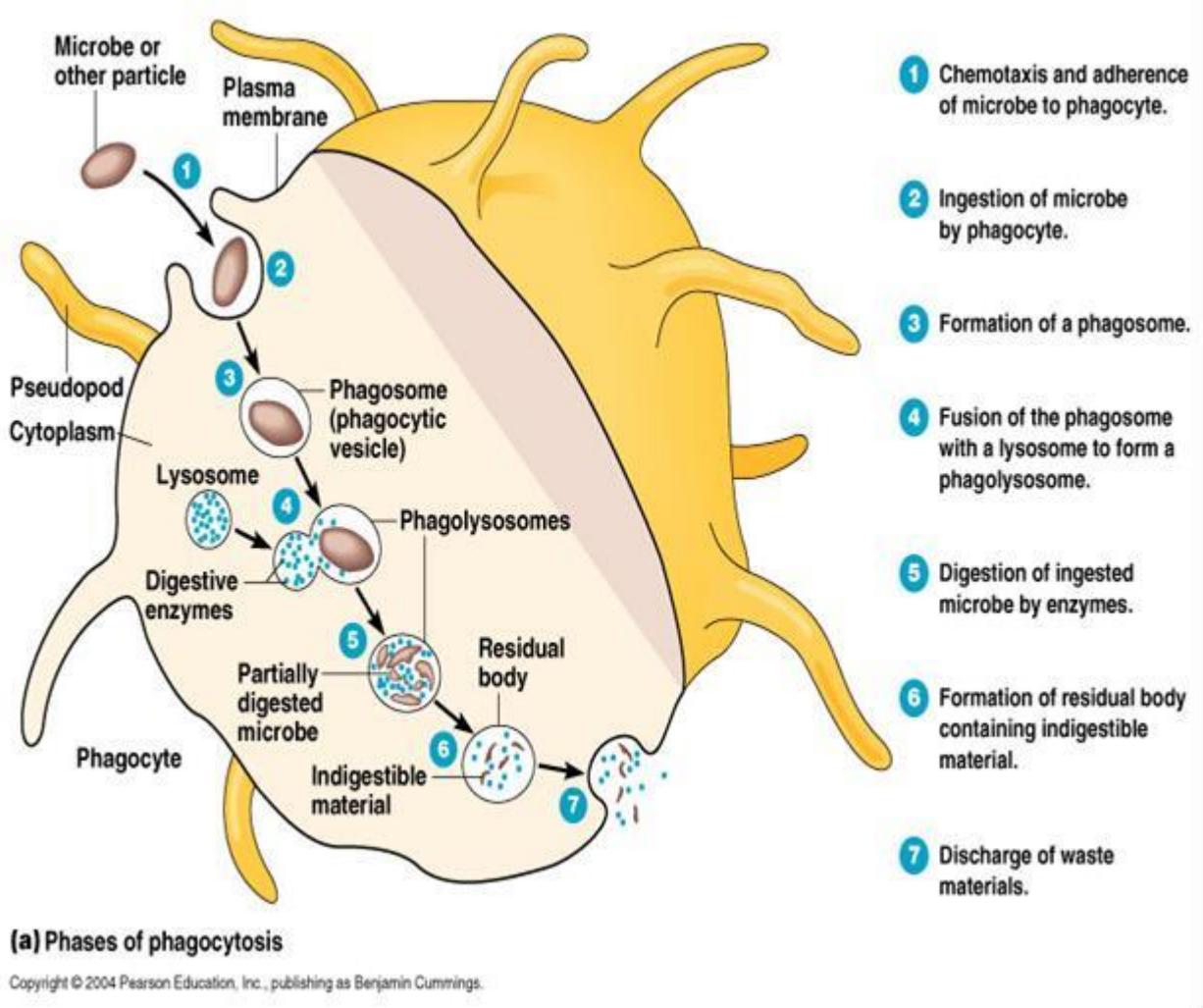
Mechanism of phagocytosis : process by which phagocytes (macrophages and polymorphonuclear leukocytes, PMNs) engulf and destroy microbes. These include:

1- Adhesion (attachment) - phagocyte and pathogen bind to each other.

2- Ingestion (engulfment) - pseudopodia surround the pathogen, then fuse to form a vacuole called a phagosome.

3- killing and digestion - inside phagolysosomes, which are formed by fusion of lysosomes with phagosomes: a-Hydrogen peroxide and related compounds kill microbes. b-Enzymes (proteases, polysaccharidases, lipases, nucleases) digest microbes.

4- Egesting - release of non-digestible material by a process that is essentially the reverse of ingestion.



Several types of cells in the immune system engulf microorganisms via Phagocytosis.

Neutrophils: Neutrophils are abundant in the blood, quickly enter tissues, and phagocytize pathogens in acute inflammation.

Macrophages: Macrophages are closely related to monocytes in the blood. These longer-lived cells predominate in chronic inflammation. They also release some important inflammatory paracrine.

Dendritic Cells: Phagocytosis in these cells is important for the elaboration of a specific immune response rather than for directly destroying the pathogens.

B Lymphocytes: A small amount of phagocytosis in these cells is often necessary in order for them to develop into cells that release antibodies.

Microbial Evasion of Phagocytosis :

1. Some microbes are not killed by phagocytes and can even reproduce in phagocytes.
2. Evasion mechanisms include M protein, capsules, leukocidins, membrane attack complexes, and prevention of phagolysosome formation.