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عنوان المحاضرة باللغة العربية: المناعة و الامراض

عنوان المحاضرة باللغة الإنكليزية: **Immunity and Diseases**

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محتوى المحاضرة:

# Lec # : Immunity and Diseases

**Immunology:** Study of the components and function of the immune system.

**Immunity:** Is the body's ability to fight off harmful micro-organisms- PATHOGENS- that invade it. The immune system produces antibodies or cells that can deactivate pathogens.

**The central question? How does the immune system respond to different infections?**

- Microbes are recognized by two mechanisms, evolved broad recognition mechanisms (innate immunity), and by highly specific lymphocyte antibodies and T cell receptors (adaptive immunity).

- Different types of microbes are eliminated by different effector mechanisms, which are designed to best combat each type of microbe.

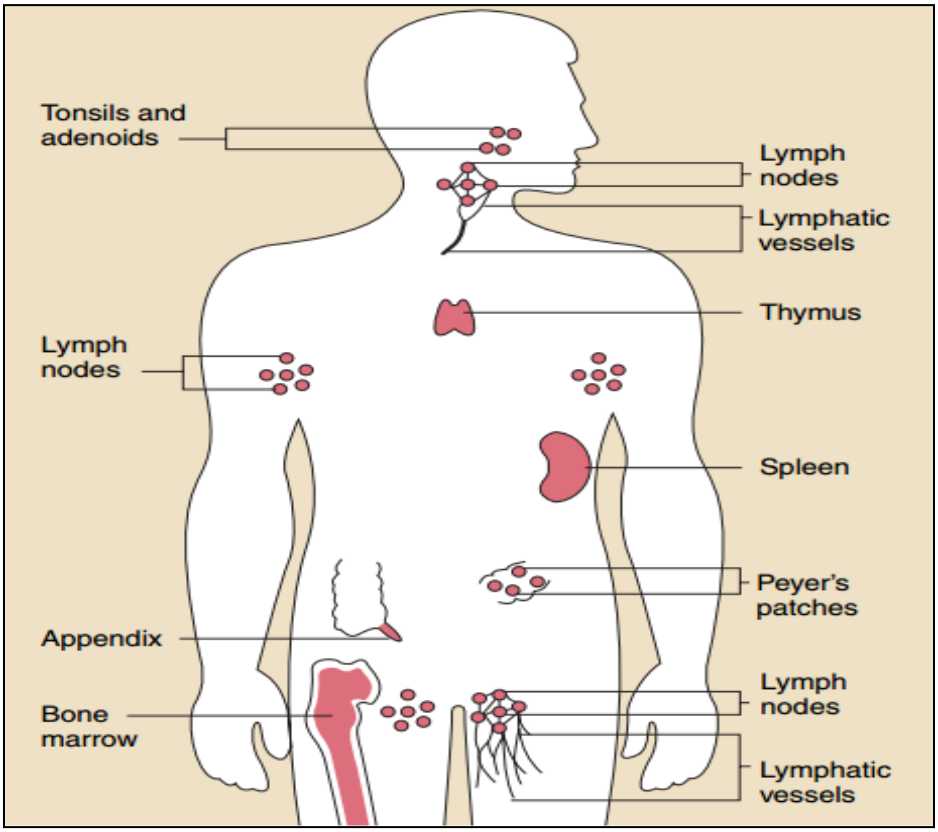
To understanding the **immunology**, in this and the next lecture, we will help you understand the basic features of **normal immune responses** and **immune-mediated diseases**. Here will discuss how the immune system fights microbes and how its abnormalities cause a variety of diseases. So, you need to know the following:

I- **Part (I) The Normal Immune Response**
II- **Part (2) How The Immune System Causes Disease?**

**The Structure of the Immune System:**

The organs of the immune system are positioned throughout the body. They are called **lymphoid organs** because they are home to lymphocytes, small white blood cells that are the key players in the immune system.

**Bone marrow**, the soft tissue in the hollow center of bones, is the ultimate source of all blood cells, including white blood cells designed to become immune cells. The **thymus** is an organ that lies behind the breastbone; lymphocytes known as **T lymphocytes**, or just "T cells," mature in the thymus. **Lymphocytes** can travel throughout the body using the blood vessels. The cells can also travel through a system of lymphatic vessels that closely parallels the body's veins and arteries. Cells and fluids are exchanged between blood and lymphatic vessels, enabling the lymphatic system to monitor the body for invading microbes. The lymphatic vessels carry **lymph**, a clear fluid that bathes the body's tissues.

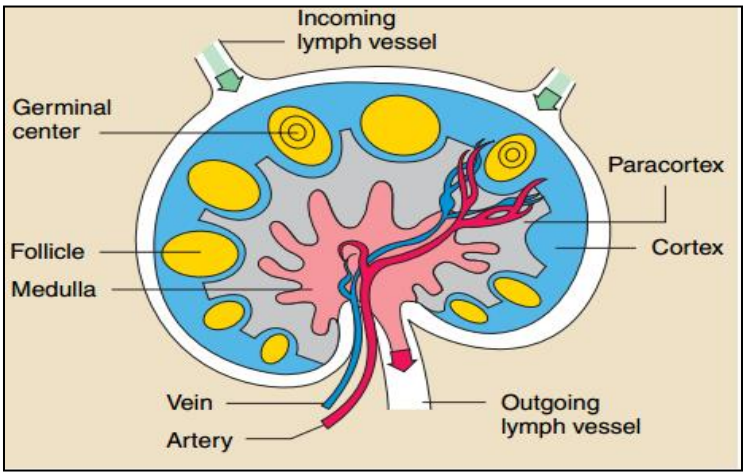



**(The organs of the immune system are positioned throughout the body)**

Small, bean-shaped **lymph nodes** are laced along the lymphatic vessels, with clusters in the neck, armpits, abdomen, and groin. Each lymph node contains specialized compartments where immune cells congregate, and where they can encounter antigens.

The **spleen** is a flattened organ at the upper left of the abdomen. Like the lymph nodes, the spleen contains specialized compartments where immune cells gather and work, and serves as a meeting ground where immune defenses confront antigens. Clumps of lymphoid tissue are found in many parts of the body, especially in the linings of the digestive tract and the airways and lungs- territories that serve as gateways to the body. These tissues include the **tonsils**, **adenoids**, and **appendix**.

The **lymph node** contains numerous specialized structures. **T cells** concentrate in the paracortex, **B cells** in and around the germinal centers, and plasma cells in the medulla.




## Part (1): INNATE AND ADAPTIVE BODY DEFENSES

**I. Introduction**: A variety of cells and structures work together to protect the human body from bacterial, fungal, parasitic and viral infection. This resistance to disease (also known as **immunity**) allows the body to maintain its health.

***** There are two primary defense systems in the body that work both independently and cooperatively to provide resistance to disease.

Those two systems are:

1. **The Innate (Nonspecific) System**
2. **The Adaptive (Specific) System**

***** The immune system is considered to be a *functional system* instead of an organ system. It is composed of chemicals and trillions of immune cells that occupy lymphoid tissue and circulate in body fluids. When functioning

properly, this system protects the body from infectious microorganisms and cancer cells.

**II. INNATE (NONSPECIFIC) DEFENSES**- This system responds quickly to protect the body from pathogens and infection.

**A.** There are two major lines of defense that make up the Innate Defensive System:

**1. Surface barriers or external body membranes** which prevent the penetration

of pathogens into the body. These barriers can produce a number of chemicals

that provide protection for the body (acids, enzymes, mucin, defensins).

**2. Inflammation**-which includes a variety of proteins, cells and phagocytes which

work together to prevent the spread of pathogens throughout the body.

**B. Surface Barriers: Skin and Mucosae**

**1. Skin**

**a.** This system works well as long as the thick keratinized epithelial tissue of the

skin is not broken.

**b.** The thick protein keratin is also resistant to the acids and bases secreted

by most bacteria. Recall that this protein is abundant in the skin.

**2. Mucous Membranes** line body cavities that open directly to the outside of the body. Specific functions of mucous membranes in innate body defense include:

**a.** Serving as sticky surfaces to trap microorganisms before they enter body systems (such as the digestive and respiratory systems).

**b.** Some membranes secrete chemicals that are toxic to some bacteria. For example the skin secretes sebum which kills some bacteria.

**c.** Mucosa in the stomach secrete hydrochloric acid and protein-digesting enzymes, both of which act to kill microorganisms.

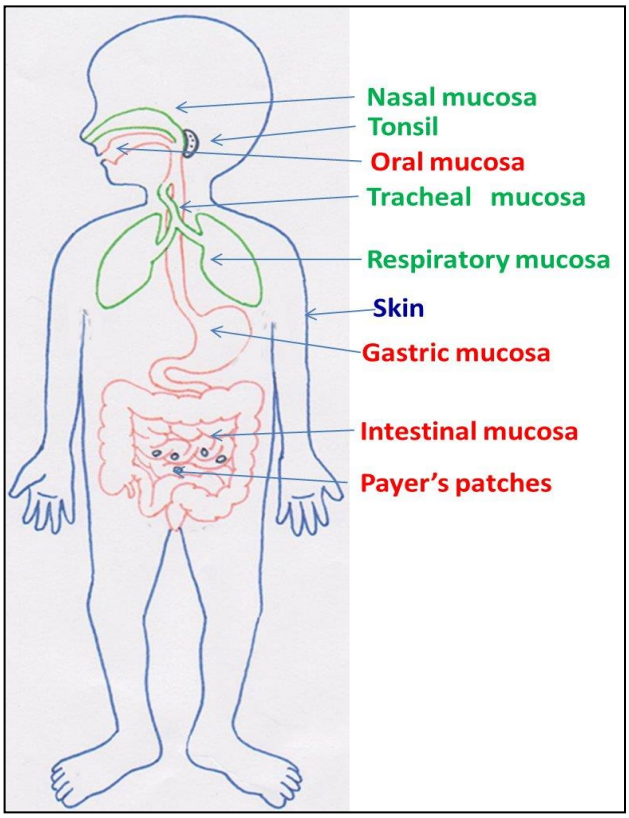
**d.** Saliva cleanses the oral cavity and teeth.

**e.** Lysozyme is secreted onto the surface of the eye. This enzyme functions by destroying bacteria.

**3. On occasion**, the various membranes of the body are nicked, scratched and cut. When this occurs, microbes can invade deeper into the human body. At this point, the internal innate defenses take over to fight off the invaders.

**C.** There are a number of internal innate defenses that help to fight off invading

microorganisms. These include **phagocytic cells**, natural killer cells, antimicrobial proteins, fever and inflammation.




## D. Cells and Chemicals Involved In Internal Innate Defense

**1. Phagocytes**- cells that feed on and destroy invading microorganisms.

### a. Types of Phagocytic Cells

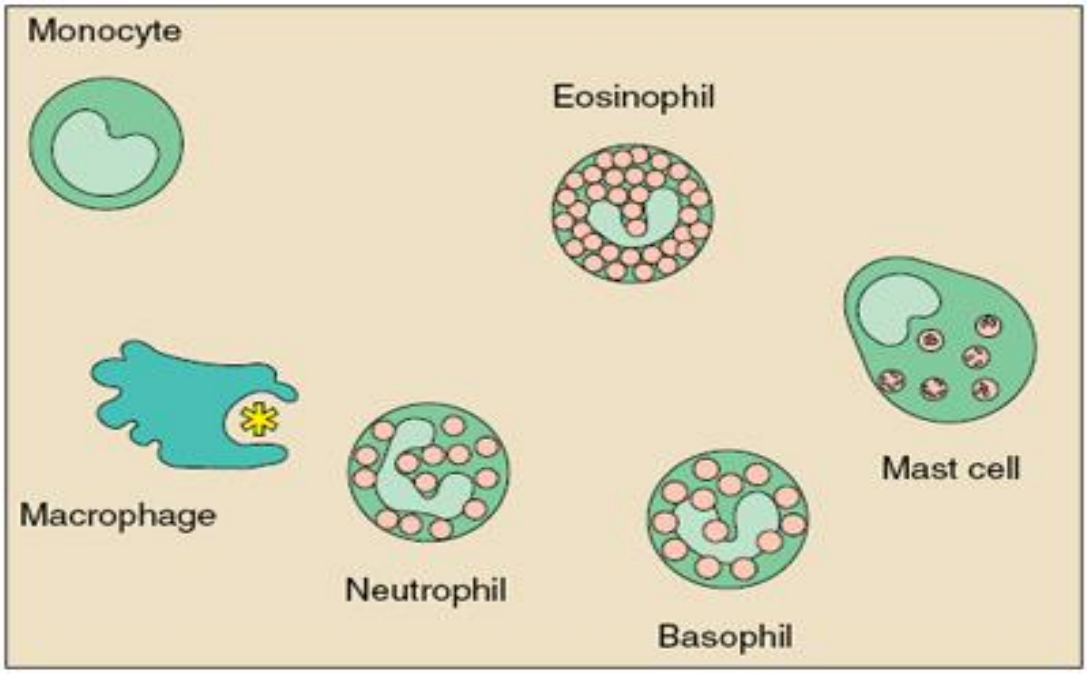
**1) Macrophages**- primary phagocytes in the body. These are derived from leukocytes known as **monocytes** which leave the bloodstream, enter tissues and develop into macrophages.

**2) Neutrophils**- most abundant type of leukocyte in the body, these become phagocytic upon encountering infectious materials in the body.

**3) Eosinophils**- another type of leukocyte in the body, these can be phagocytic but they are best known for fighting parasitic worms.

**4) Free Macrophages**- can move throughout the body searching for and destroying foreign invaders. Alveolar macrophages in the lungs are examples of free macrophages.

**5) Fixed Macrophages**- are permanent residents of specific organs in the body. Kupffer Cells in the liver and microglia in the brain are examples of fixed macrophages.




**Events That Occur In Phagocytosis**

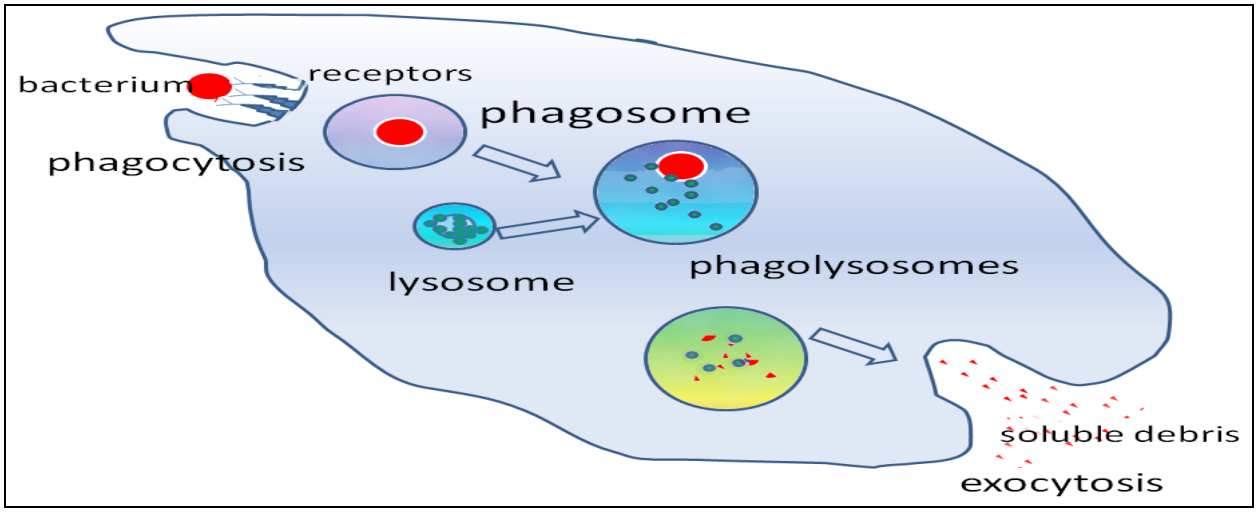
**a) Adherence**- the phagocyte adheres to the pathogen. This is accomplished when the phagocyte recognizes either the protein or carbohydrate signature of the pathogen.

**b) Opsonization**- process in which proteins and antibodies coat the outer covering around a pathogen. This provides "handles" for the phagocyte to attach to, thus increasing the efficiency of phagocytosis.

# Stages in phagocytosis

- Pathogens are recognised by antigens on their surface
- Phagocyte moves towards pathogen and receptors on the cell surface membrane attach to antigens on the pathogen
- Phagocyte engulfs the pathogen creating a phagosome
- Lysosomes fuse with the phagosome releasing digestive enzymes
- End products absorbed into the cytoplasm.

**Phagocytosis of the pathogen**




**Natural Killer Cells**- Cells in the blood and lymph that can lyse and kill cancer

cells and virus-infected cells before the adaptive immune response is initiated.

**a**. These are not specific and they develop from granular leukocytes.

**b**. Again, proteins on the specific cell identify those cells for the natural killer cells.

**c**. These destroy cells by releasing chemicals known as perforins which destroy the nucleus of cells (Killer Cells are not phagocytic). Natural killer cells are not phagocytic.

## Inflammation

**1.** The inflammatory response is initiated when body tissues are injured. The

primary goal of inflammation is to clear the injured area of pathogens, dead

cells and any other debris so that tissue repair can begin.

## Benefits of Inflammation:

a. Prevents the spread of damaging agents into the body.

b. Removes cell debris and pathogens

c. Sets the stage for repair.

d. Turns on the adaptive immune system

e. Redness, heat, pain and swelling are considered to be the key indicators of inflammation.

**Fever** - Abnormally high body temperature. This is another defense against infection.

**1.** The hypothalamus regulates body temperature. In response to microbial invasion, leukocytes and macrophages secrete chemicals known as **pyrogens** which initiate the hypothalamus to raise body temperature.

**2.** Mild fever appears to have a positive effect on the body since it:

**a.** Reduces release of certain nutrients by the liver and spleen (Microbes require these nutrients to grow and multiply).

**b.** Increases metabolism; thus increasing repair processes.

**3.** Extreme fever can be dangerous since it denatures enzymes.

### III. ADAPTIVE (SPECIFIC) DEFENSES:

This specific system protects the body from a wide range of microorganisms and abnormal body cells. This system is turned on by exposure to a foreign substance. Adaptive responses were first documented in dogs during the 1800's.

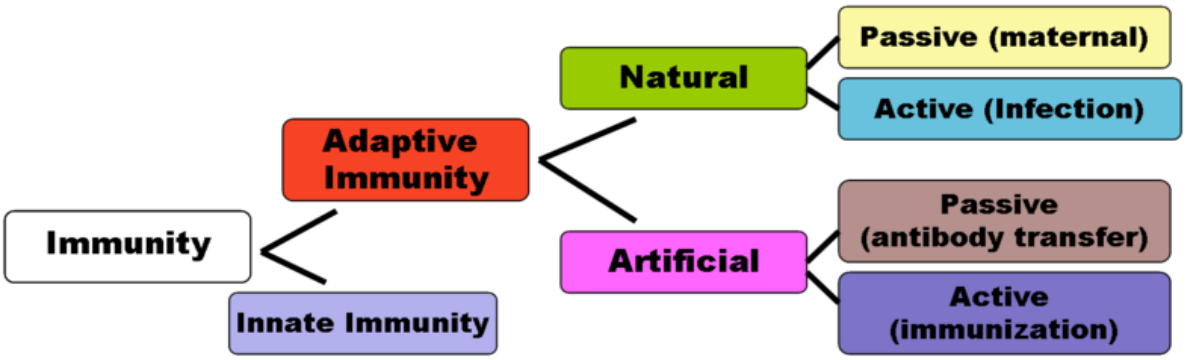
**Important Characteristics of the Adaptive Defense System**

**1. It is specific**- It recognizes and attacks particular pathogens or foreign debris

in the body.

**2. It is systemic**- Immunity is not restricted to the site of the initial infection.

**3. It has memory**- after an initial exposure, it recognizes and strongly attacks a




previously encountered pathogen.

**Antigens**- Substances that can mobilize the immune system and provoke an immune response.

1. Antigens are classified as being either **complete** or **incomplete**.

**a. Complete Antigens**- have 2 key characteristics:

**1) Immunogenicity**- the ability to stimulate the formation of specific lymphocytes and antibodies. Most proteins, nucleic acids and polysaccharides can serve as complete antigens.

**2) Reactivity**- the ability to react with the activated lymphocytes and the antibodies released by immunogenic reactions.

**b. Incomplete Antigens (Haptens)**- are reactive but lack immunogenicity.

1) Small proteins, certain chemicals (found in poison ivy, detergents etc..) can act as haptens.

2. Only certain parts of an antigen are immunogenic. These parts are known as

Antigenic Determinants. Lymphocytes bind to these sites much like enzymes bind to a substrate.

**3. Major Histocompatibility Complex (MHC)**-self antigens, these are a group of

proteins that mark cells as ours. These are strongly antigenic to other individuals (this is the basis for rejection of tissues and transfusions).

a. These are generally specific to an individual and the MHC plays a major role in mobilizing the immune response.

## D. Overview of Cells in the Adaptive Immune System

### 1. Lymphocytes

a. Originate in the bone marrow from hematopoietic stem cells. When released, lymphocytes mature into either **B cells** or **T cells**.

1) **T cells** become **immunocompetent** (able to recognize a specific antigen by binding to it) in the thymus gland. Only 2% of the T cells that are produced in the thymus are released into the blood. The others are selected against since they cannot actively attach to and destroy antigens.

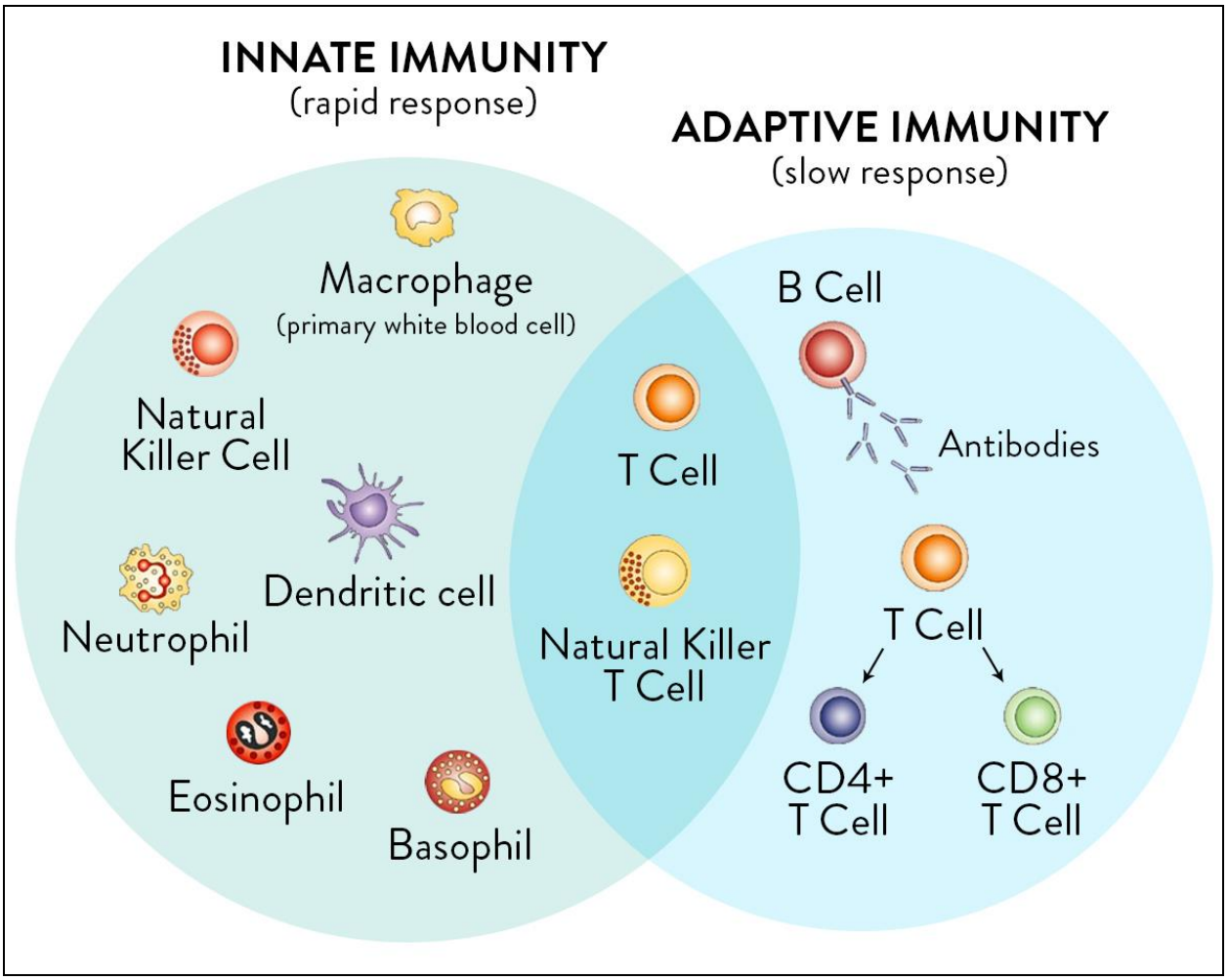
2) **B cells** become immunocompetent in bone marrow.

b. Lymphocytes become immunocompetent before meeting the antigens that they must attack and destroy. Thus, it is our genes that determine what specific foreign substances our immune system will be able to recognize and resist.

c. After becoming immunocompetent, lymphocytes are transported to the spleen, lymph nodes and other lymphoid structures where encounters with antigens can occur.

**2. <u>Antigen-Presenting Cells</u>**- These engulf antigens and then present fragments of

these antigens on their own surface. T cells can then recognize and destroy the antigen.




**2 Major Types of Immunity in the Adaptive Defense System**

**1. Humoral (Antibody-Mediated) Immunity**- produced by antibodies present in the body's fluids. Antibodies bind to pathogens, inactivating them and marking

them for destruction by phagocytes or the complement system.

**2. Cell-Mediated Immunity**- occurs when lymphocytes themselves defend the

body from microbial invasion. These cells can produce cell lysis or they can initiate an inflammation response.

**Humoral Immune Response**- In this system, antibodies are produced against a pathogen.

**1. Differentiation of B Cells**

**B Cells** are activated when antigens bind to their surface. This leads to clonal selection in which numerous B Cells are formed resulting in cloned cells that are capable of destroying a particular antigen.

**1)** Most of these activated B Cells develop into **Plasma Cells** which are able to secrete antibodies. These cells survive for only 4 or 5 days. (Plasma cells, also called plasma B cells, plasmocytes, plasmacytes, or effector B cells, are white blood cells that secrete large volumes of antibodies. They are transported by the blood plasma and the lymphatic system. Plasma cells originate in the bone marrow; B cells differentiate into plasma cells that produce antibody molecules closely modelled after the receptors of the precursor B cell. Once released into the blood and lymph, these antibody molecules bind to the target antigen (foreign substance) and initiate its neutralization or destruction)

**2)** Some of the B Cells develop into Memory Cells which can lead an immediate attack if they encounter the same antigen again in the future. This proliferation and differentiation of Plasma and Memory Cells is known as the Primary Immune Response which occurs on the first exposure to an antigen.

**3)** Secondary Immune Response-occurs when someone is reexposed to a particular antigen. This response is fast and extremely effective since the immune system is on alert for the antigen. This is known as Immunological Memory.

**2. Types of Humoral Immunity:**

**a. Active Humoral Immunity**- occurs when B Cells encounter antigens and produce antibodies against them (as just described). Active immunity is *naturally* acquired when you are exposed to pathogens. It can also be *artificially* acquired when you receive **vaccines**.

**1) Vaccines**- contain dead or weak pathogens or their components. Vaccines provide two benefits: they spare us of many of the symptoms of an illness and they provide us with immunity against an antigen. Booster shots may be given to provide extensive immunity to a particular microbe.

**b. Passive Humoral Immunity**- antibodies in this case are made from the serum of an immune human or animal donor. As a result, B cells are not challenged by antigens. Memory does not occur but protection occurs when the borrowed antibodies degrade in the body.

1) This occurs naturally in a fetus when the mother's antibodies cross the placenta. Immune sera are also used to treat snake bites, botulism and rabies. In each of these cases, the protection is short-lived.

**3. <u>Antibodies (Immunoglobulins)</u>**- are secreted by activated B Cells or Plasma Cells in response to an antigen. These bind to and remove the antigen.

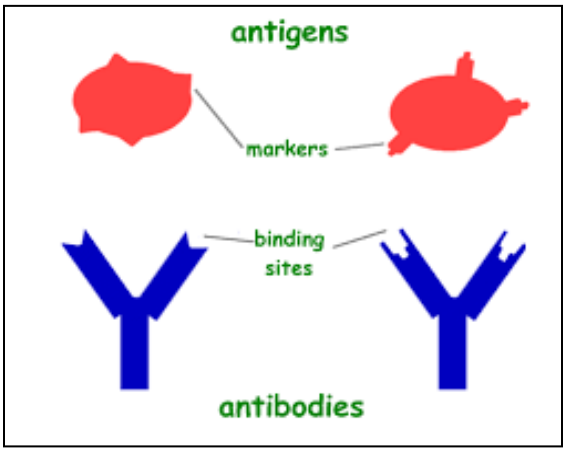
**a. <u>Antibody Structure</u>**

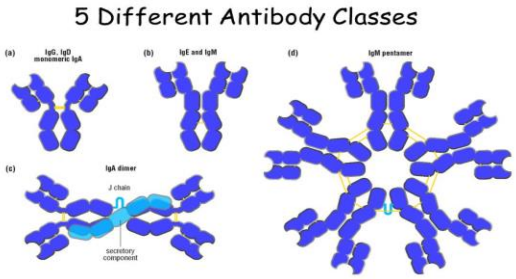
1) Antibodies have a loop shape and are composed of 2 heavy chains and 2 light chains. They also contain a C region and a V region. Disulfide bonds hold the heavy and light chains together.

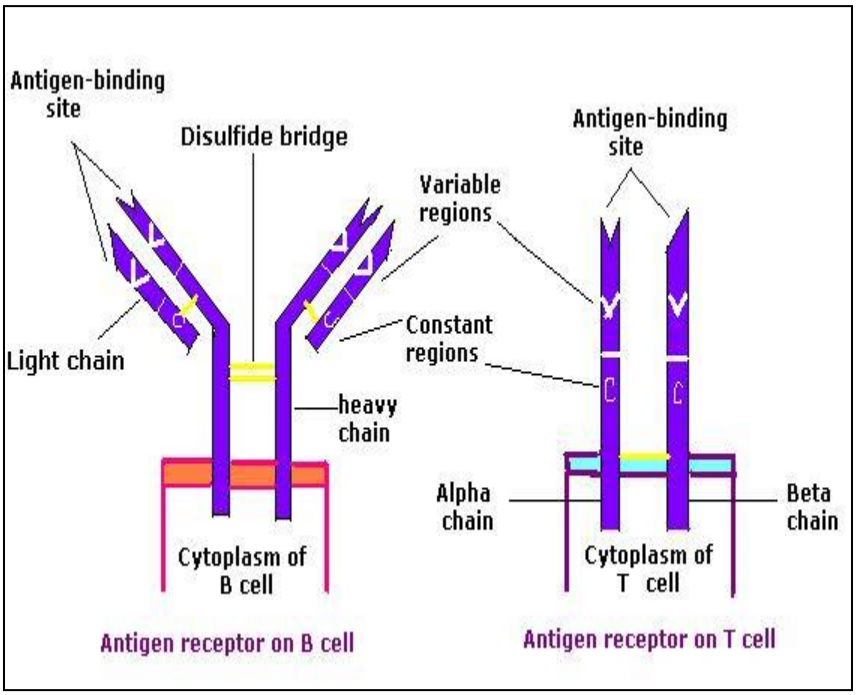
**2) <u>Antigen-binding site</u>**-shaped to fit a specific antigen. These are located at the ends of each of the arms that make up the V region of the antibody. Each antibody has 2 antigen- binding sites.

**b. <u>Classes of Antibodies</u>**- based on structure and the specific biological role of the antibody. The five major classes of antibodies are: IgG, IgA, IgM, IgD and IgE.

**c. Antibodies** do not destroy antigens themselves; however, they do inactivate and tag antigens for destruction.






**Types of Antigen-Antibody reactions include:**

**1) Complement Fixation and Activation**- antibodies bind to cells and change shape. This triggers complement fixation and cell lysis.

**2) Neutralization**-occurs when antibodies block specific sites on viruses or toxins. This prevents the antigen from attaching to tissue receptors; thus, preventing injury to the tissue.

**3) Agglutination**-antibodies can cause antigens to clump. This clumping is known as *agglutination*.

**Cell-Mediated Immune Response**

1. This involves the use of lymphocytes (T Cells) to attack and destroy pathogens.

2. T Cells generally recognize and respond to protein antigens displayed on body

cell surfaces. Therefore, T cells are geared to attack and destroy body cells infected by pathogens, cancer cells and transplanted cells.

3. T Cells are activated by a recognized antigen. T Cells also must identify the

antigen and normal, healthy body cells.

MHC Proteins-on cells, act to signal foreign invaders are present in the body.