(Immunology)---- Lec # 2

III. **ADAPTIVE (SPECIFIC) DEFENSES**: Third line of defense

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.

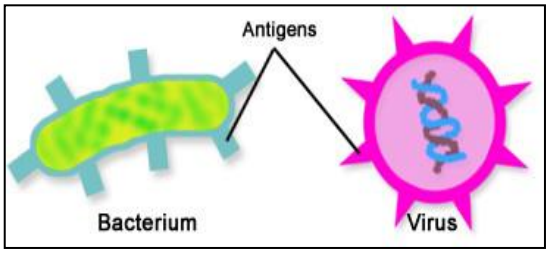
Important Characteristics of the Adaptive Defense System:

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.

Immune Response *(Antigen)*:

Antigens-substances that can mobilize the immune system and provoke an immune response.
Antigen – "any substance when introduced into the body stimulates the production of an antibody"

- Bacteria, fungus, parasite
- Viral particles
- Other foreign material



Pathogen – An antigen which causes disease

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

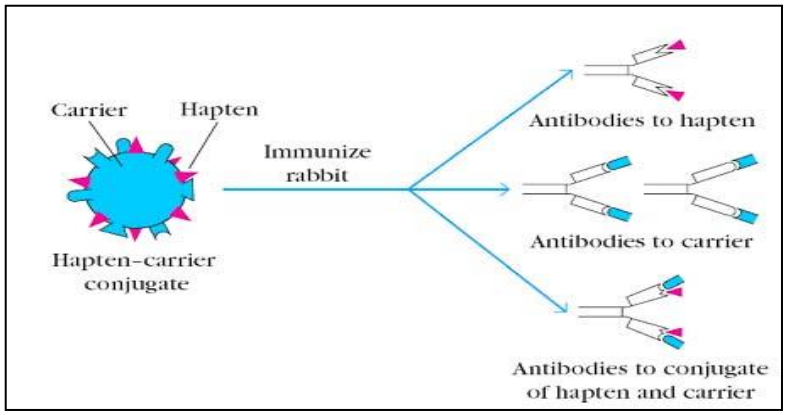
a. Complete Antigens- have 2 key characteristics:

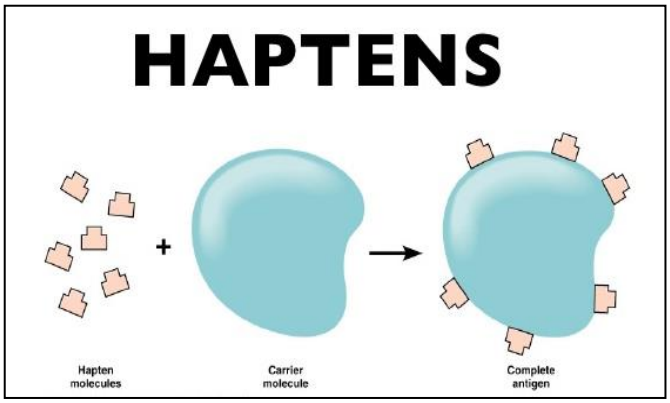
1) Immunogenicity- the ability to stimulate the formation of specific lymphocytes and antibodies. Most proteins, nucleic acids and polysaccharides can serve as complete antigens.

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

b. <u>Incomplete Antigens (Haptens)</u>- are reactive but <u>lack</u> immunogenicity.
1) Small proteins, certain chemicals (found in poison, detergents etc..) can act as haptens.

2. Only certain parts of an antigen are immunogenic. These parts are known as **<u>Antigenic Determinants</u>**. Lymphocytes bind to these sites much like enzymes bind to a substrate.





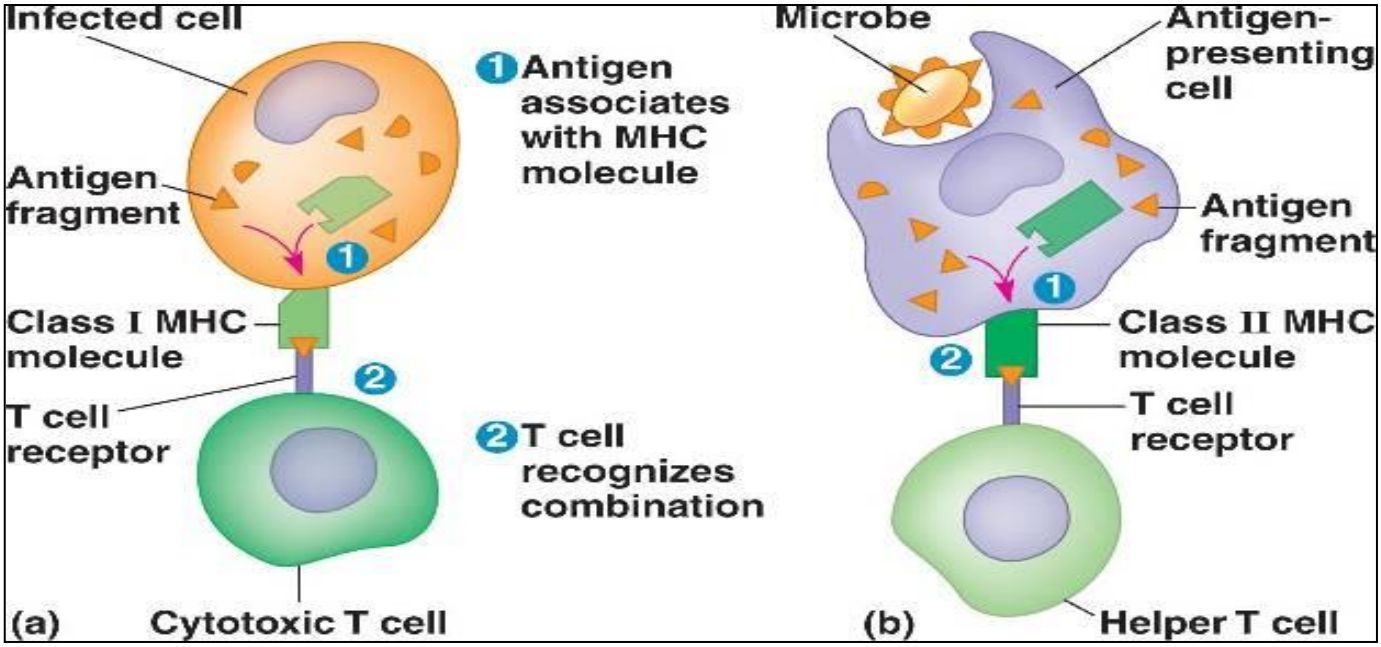
3. **<u>Major Histocompatibility Complex (MHC)</u>-** <u>self antigens</u>, these are a group of proteins that <u>mark cells as ours</u>. These are strongly antigenic to other individuals (<u>this is the basis for rejection of tissues and transfusions</u>). These are generally specific to an individual and the MHC plays a major role in mobilizing the immune response. MHC class I and II are important to T cell activation.

<u>Class I MHC proteins</u> , always recognized by CD8 T cells. Display peptides from endogenous antigens (antigens in the cytosol). **<u>Endogenous antigens</u>** <u>are: antigens that have been generated within the cell, as a result of normal cell metabolism, or because of viral or intracellular bacterial infection.</u>

Class II MHC Proteins, Class II MHC proteins are found only on surfaces of cells that present antigens to helper T cells, e.g. **dendritic cells**, **macrophages**, and **B cells**. Bind longer peptides from exogenous antigens that have been engulfed and broken down in the phagolysosome. A phagosome containing pathogens (with exogenous antigens) merges with a lysosome (phagolysosome). Invariant protein

prevents class II MHC proteins from binding to peptides in the endoplasmic reticulum.

Class II MHC proteins migrate to phagolysosomes where the antigen is degraded and the invariant chain is removed for peptide loading. Loaded Class II MHC molecules then migrate to the cell membrane and display antigenic peptide for recognition by CD4 cells



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. Very little is known about this process, however.

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. Antigen-Presenting Cells:
these engulf antigens and then present fragments of these antigens on their own surface. T cells can then recognize and destroy the antigen.

Two 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.

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 re exposed 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.

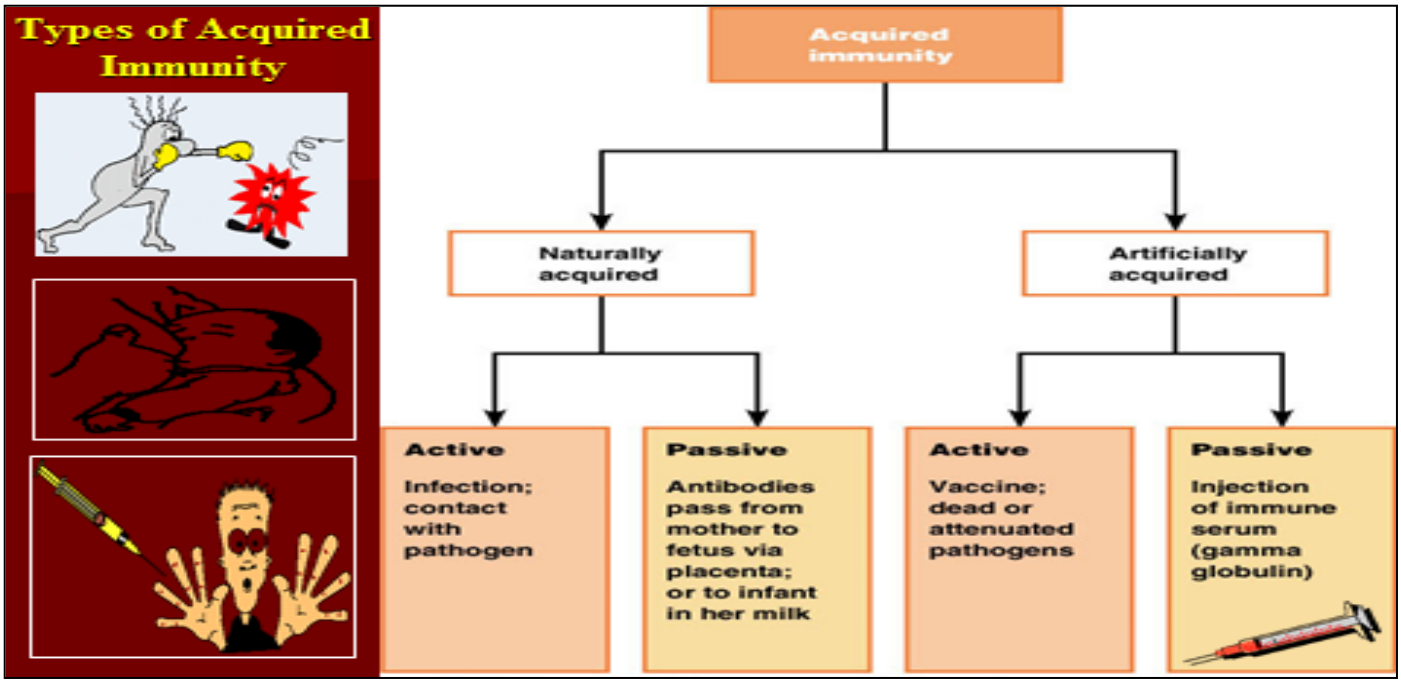
2. Types of Humoral Immunity:

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

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.

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.

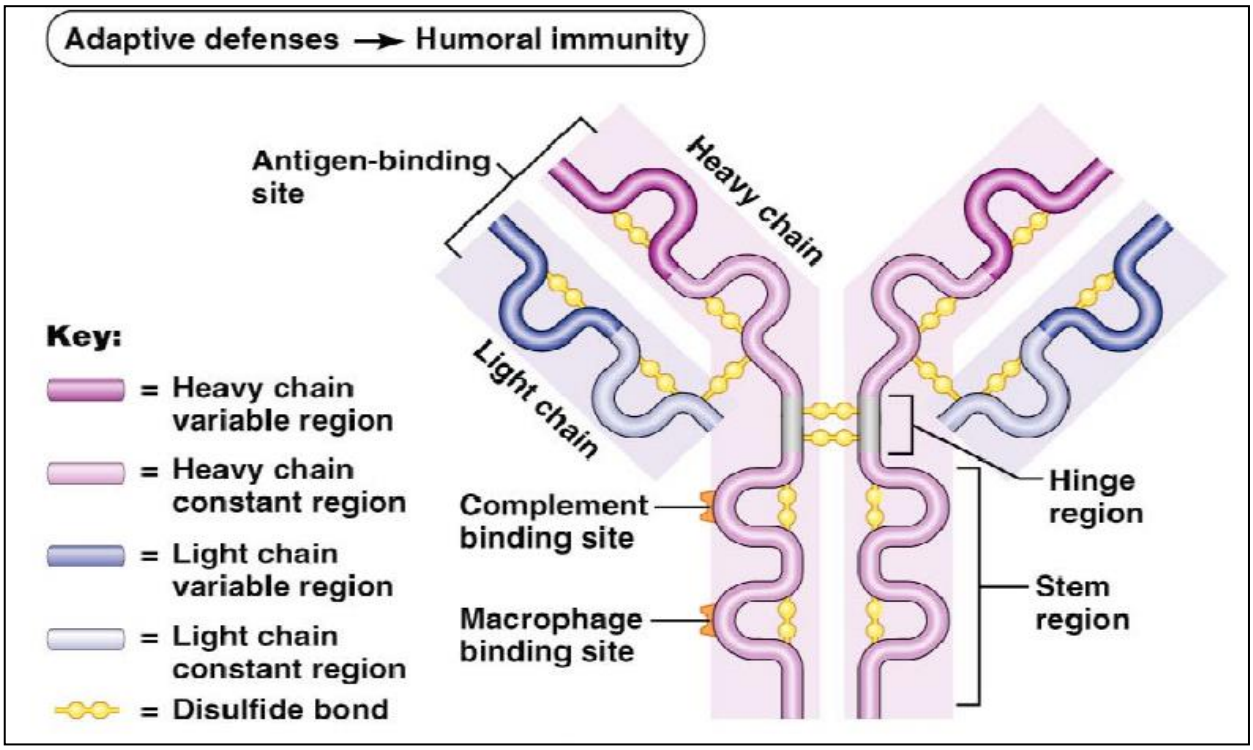


3. Antibodies (Immunoglobulins)- Constitute the gamma globulin portion of blood proteins, are secreted by activated B Cells or Plasma Cells in response to an antigen. These bind to and remove the antigen.

a. Antibody Structure

1) Antibodies have a loop or Y 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) Antigen-binding site- 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. Classes of Antibodies- based on structure and the specific biological role of the antibody. The five major classes of antibodies are: IgG, IgA, IgD, IgM, IgE.

Antibodies do not destroy antigens themselves; however, they do inactivate and tag antigens for destruction. All antibodies form an antigen-antibody (immune) complex.

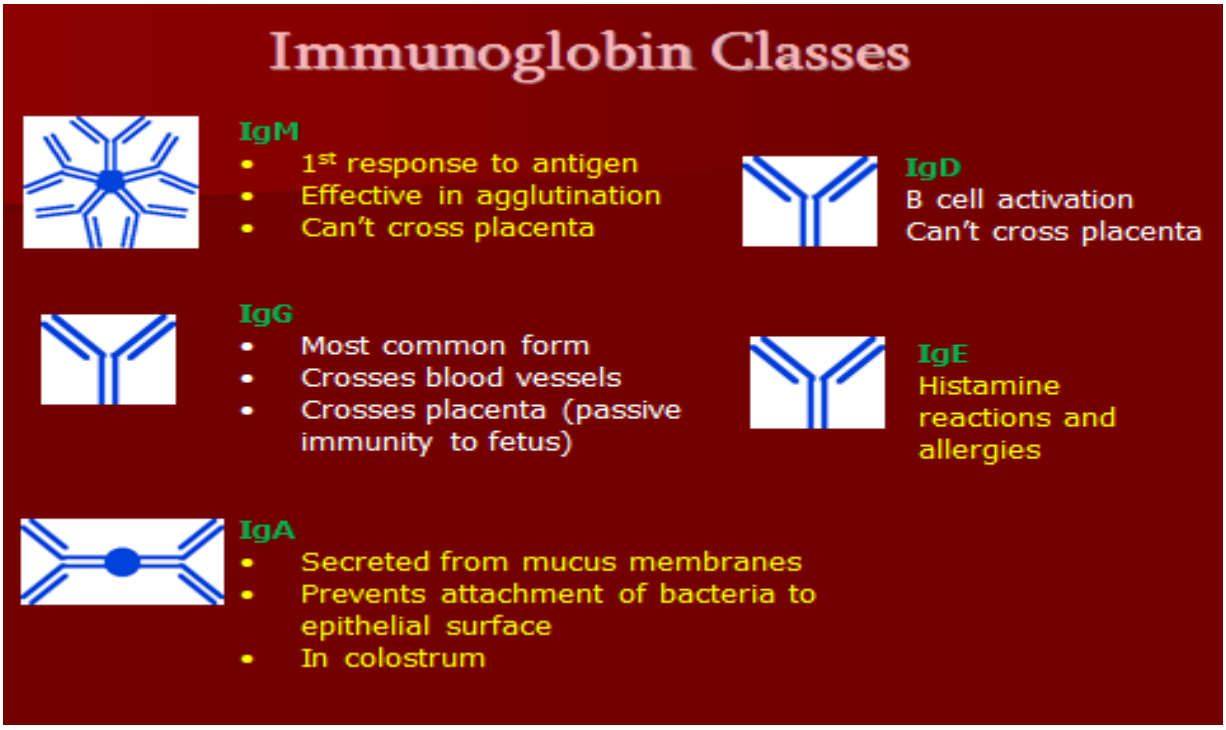
IgD – monomer attached to the surface of B cells, important in B cell activation.

IgM – pentamer released by plasma cells during the primary immune response.

IgG – monomer that is the most abundant and diverse antibody in primary and secondary response. crosses the placenta and confers passive immunity

IgA – dimer that helps prevent attachment of pathogens to epithelial cell surfaces.

IgE – monomer that binds to mast cells and basophils, causing histamine release when activated.



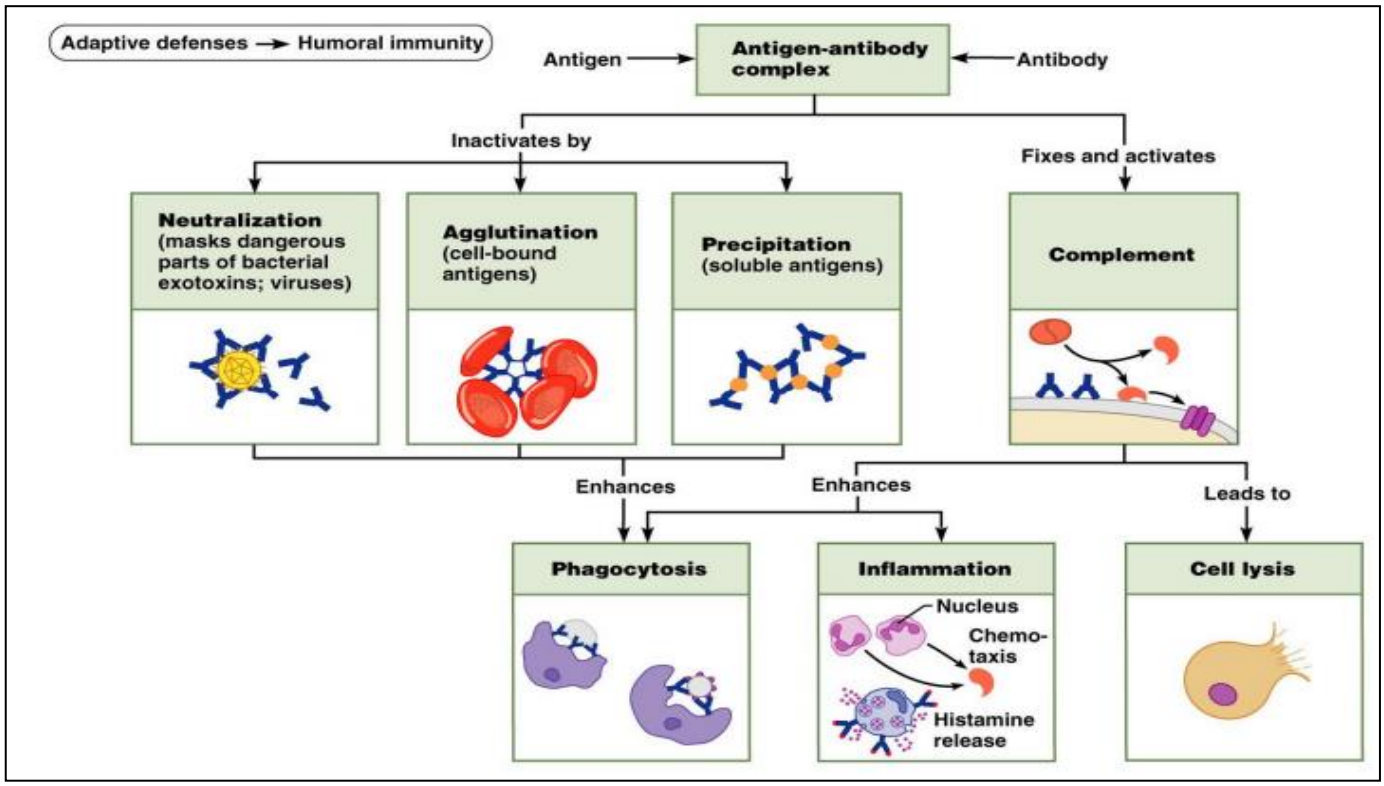
<u>Types of Antigen-Antibody reactions include:</u> Defensive mechanisms used by antibodies are:

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

2) <u>Neutralization</u>- 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) <u>Agglutination</u>- antibodies can cause antigens to clump. This clumping is known *agglutination*. IgM is involved in this process.

4) <u>Precipitation</u>- occurs when large molecules are linked into complexes that settle out of solution. These antigens are then easily removed by phagocytic cells.



<u>Cell-Mediated Immune Response</u>: Since antibodies are useless against intracellular antigens, cell-mediated immunity is needed.

<u>Two major</u> <u>populations of T cells mediate cellular immunity:</u>
- CD4 cells (T4 cells) are primarily helper T cells (TH).
- CD8 cells (T8 cells) are cytotoxic T cells (TC) that destroy cells protecting foreign antigens

Importance of Cellular Response:

- T cells cannot "see" free antigens .
- T cells recognize and respond only to processed fragments of antigen displayed on the surface of body cells.
- T cells are best suited for cell-to-cell interactions, and target: Cells infected with viruses, bacteria, or intracellular parasites.
- Abnormal or cancerous cells. - Cells of infused or transplanted foreign tissue

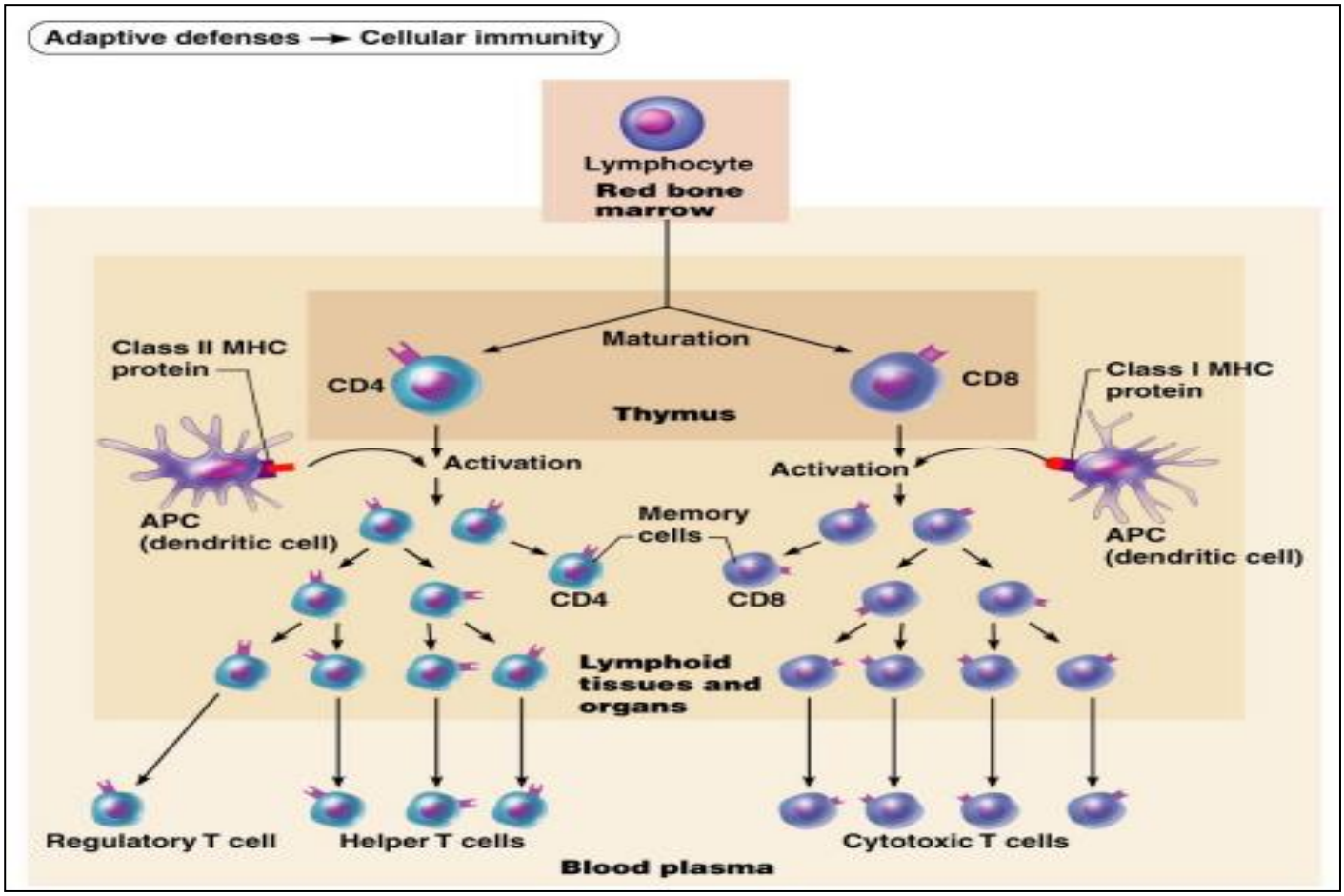
Antigen Recognition and MHC Restriction with T cells:

- Immunocompetent T cells are activated when the V regions of their surface receptors bind to a recognized antigen.

- T cells must simultaneously recognize:

Nonself (the antigen)

Self (a MHC protein of a body cell)



<u>2 Steps in T Cell Activation</u>:

1) <u>Antigen Binding</u>- the attachment of a T cell to an antigen on a body cell.

2) <u>Co-Stimulation</u>-T cells must recognize one or more co-stimulatory agents on cells before they can produce clones.

a) A variety of agents, including proteins and chemicals, can serve as co-stimulating agents.

b) It is thought that this requirement of two stimulators maybe a way to ensure that healthy cells are not attacked.

c) Once activated, a T Cell enlarges and clones itself to carry out its specific duty.

d) Once a T Cell destroys its specific antigen, it is destroyed. However, many of the cloned T cells become Memory T Cells that last for a life time. These cells provide a reservoir of cells that can respond to the antigen if it is encountered again.

Cytokines- Chemicals released by T cells, these help to enhance the immune response.

Specific Roles of T Cells

a. Helper T Cells- Stimulate proliferation of other T Cells and B Cells that are attached to an antigen.

b. Cytotoxic T Cells- Directly attack and kill other cells. Their main targets are virus-infected cells.

c. Suppressor T Cells- Suppress the activity of B Cells and T Cells. Are thought to inhibit autoimmune reactions.

d. Gamma delta T Cells- Live in the intestine, their function is unclear.

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