The human body continually attempts to maintain homeostasis by counteracting harmful or disease-producing organisms called pathogens or the toxins they produce. The ability to fight off disease is known as resistance. Lack of resistance is susceptibility.

Body defenses against disease are divided into two types which may work together:

1. nonspecific body defenses - They consist of a wide variety of general mechanisms which respond immediately to protect the body from a wide range of pathogens.

2. specific body defenses (immune system) - Immunity is the highly specific resistance to disease. The immune system consists of immune cells such as lymphocytes and macrophages, and a wide variety of chemicals and antibodies.

Nonspecific Body Defenses

There are three nonspecific body defenses:

1. species resistance - It is the inherited resistance to diseases that affect other organisms.

2. surface membrane barriers - They include the skin and mucous membranes and function as the body's first line of defense as long as they remain intact. Keratin in the skin provides a physical barrier to organisms and is resistant to weak acids, bases, toxins, and bacterial enzymes. Skin secretions, such as oil and sweat, are toxic to some bacteria and inhibit their growth. Mucous membranes line the respiratory, digestive, urinary, and reproductive tracts and secrete mucus. Mucus traps bacteria and other foreign substances. Some mucous membranes have cilia on their surface which moves the mucus and trapped bacteria or foreign substance along the tract for elimination.
nonspecific cellular and chemical defenses

There are five nonspecific cellular and chemical defenses:

a. phagocytosis - Macrophages are the major phagocytes and they attack and destroy pathogens and other foreign substances that penetrate the skin and mucous membranes. When a pathogen is ingested by a phagocyte it is taken into the cell and surrounded by a membrane forming a vesicle. The vesicle containing the pathogen or foreign substance is specifically called a phagosome. The phagosome fuses with a lysosome forming a larger phagolysosome. The digestive enzymes from the lysosome destroy the pathogen or foreign substance.

Some bacteria are coated with plasma proteins, called complement proteins and antibodies which promotes attachment with receptors on the phagocyte. The process is referred to as opsonization ("to make tasty")

b. natural killer cells (NK) - They are large lymphocytes called null cells which are found circulating in the blood and lymph. Null cells directly attack and lyse virus-infected cells and some cancer cells. Changes in the surface of virus-infected cells and cancer cells are recognized by the null cells.

c. inflammatory response - Inflammation is the body's second line of defense. The four cardinal signs of an inflammatory response are redness, heat, swelling, and pain. Inflammatory chemicals, such as histamine, complement proteins, kinins, prostaglandins, and lymphokines are released from damaged tissue, phagocytes, lymphocytes and plasma proteins. The inflammatory chemicals cause dilation of the blood vessels in the injured area resulting in redness and heat. Permeability of the capillaries increases and fluid seeps into the tissue causing local swelling. The swelling puts pressure on nearby nerve endings, resulting in pain.

The inflammatory chemicals act as chemotactic agents and attract neutrophils and other white blood cells to the area. Neutrophils line up along the surface of the inner walls of the capillaries and the process is referred to as pavementing or margination. The neutrophils then move through the capillary walls and into the tissue by diapedesis.

Monocytes then enter the tissues and enlarge and become macrophages. The macrophages eventually replace the neutrophils and digest dying and dead bacteria and neutrophils, and cellular debris.
d. antimicrobial proteins

There are two major antimicrobial proteins:

(1). complement proteins - They consist of a group of 20 plasma proteins normally found in the blood. Complement proteins can be activated by two pathways:

(a). classical pathway - Antibodies bond with the microorganism, forming an antigen-antibody complex. The complement proteins then bond with the antigen-antibody complex and the process is referred to as complement fixation.

(b). alternative pathway - It occurs when plasma protein factors interact with polysaccharides in the cell walls of some bacteria and fungi.

Both pathways may involve the incorporation of membrane attack complex proteins (MAC) into the plasma membrane of the invading organism. It causes lesions to form in the membrane, resulting in lysis. Activation of both pathways also enhances opsonization, the inflammatory response, phagocytic activity, and chemotactic attraction of other white blood cells to the area.

(2). interferon - Cells infected by viruses form small proteins called interferons. Interferon is secreted by the virus-infected cell and it diffuses into nearby uninfected cells. The uninfected cells are stimulated to produce antiviral proteins that inhibit or "interfere" with viral replication in these cells.

e. fever - A fever is an abnormally high temperature and is usually the result of an infection from bacteria and their toxins, or viruses. Macrophages exposed to the bacteria, toxins, or viruses produce proteins known as pyrogens which affect the hypothalamus and cause it to set its "thermostat" at a higher temperature. As a result, the body temperature rises and will maintain a higher temperature until pyrogens are no longer being produced. The higher body temperature inhibits growth of bacteria and viruses, increases metabolic reactions of tissues which promotes tissue repair, and speeds up nonspecific and specific body defenses.
Specific Body Defenses: Immunity

The immune system is the body's third line of defense, which recognizes and acts against particular pathogens or foreign substances known as antigens and has a "memory" for previous exposure to antigens against which it reacts more vigorously or strongly.

The three types of cells involved in the immune system include T lymphocytes or T cells, B lymphocytes or B cells, and macrophages.

During fetal development, lymphoid stem cells form in the red bone marrow. Many are released into the blood and migrate to the thymus gland where they differentiate into T lymphocytes and develop immunocompetence. Immunocompetence is the ability to recognize a specific antigen. A single unique receptor on the surface of the T lymphocyte allows it to bind with a specific antigen. The T lymphocytes leave the thymus and are transported by the blood to other lymphatic organs and tissues.

The remaining lymphoid stem cells that do not become T lymphocytes are thought to differentiate into B lymphocytes and become immunocompetent in the red bone marrow. The B lymphocytes enter the blood and are transported to other lymphatic tissues and organs.

T and B lymphocytes are also found circulating in the blood and lymph and when they bind with recognized antigens, they complete their differentiation into fully functional T and B lymphocytes.

Monocytes, formed in the red bone marrow, enter the blood and differentiate into macrophages when they enter the tissues. Macrophages may act as antigen presenters. When they ingest foreign substances or antigens by phagocytosis, part of the antigen remains exposed on their surface. The exposed antigen is recognized by immunocompetent T lymphocytes.

Macrophages also secrete proteins that activate T lymphocytes and the activated T lymphocytes then release chemicals that stimulate macrophages to become activated macrophages. Activated macrophages are "killer" phagocytes and they also secrete bacteria-killing chemicals.

Antigens

Most antigens are large complex molecules. When they are introduced into the body, the body produces specific antibodies or activates T and B lymphocytes which react with the antigens.
Complete antigens have two characteristics:

1. **immunogenicity** - The ability to stimulate the formation of specific immunocompetent T and B lymphocytes and the formation of specific antibodies.

2. **reactivity** - The ability of the T and B lymphocytes and specific antibodies to react with the antigen.

Small localized regions on the antigen, called **antigenic determinants**, function as bonding sites for the activated T and B lymphocytes and antibodies. The more bonding sites the antigen has, the higher the immunogenicity and reactivity.

Incomplete antigens have reactivity, but lack immunogenicity and they cause allergic responses.

Immune Responses or Immunity

There are two types of immune responses or immunity:

1. **humoral or antibody-mediated immune responses**

2. **cell-mediated immune responses**

1. **humoral or antibody-mediated immune responses** - They involve B lymphocytes and immunity is provided by antibodies present in the body fluids or "humors". When antigens bind with the specific antigen-receptors of B lymphocytes, the B lymphocyte undergoes rapid divisions by mitosis. A large number of identical cells are formed called a clone. Most of the clone cells differentiate into plasma cells which secrete antibodies that have the same antigen-receptor molecules as the original B lymphocyte. The antibodies circulate in the blood or lymph and bind to the antigens. Specific or nonspecific defense mechanisms then destroy the antigen-antibody complexes. The formation of the clone and plasma cells which secrete antibodies is the **primary immune response**.

The remaining clone cells that do not become plasma cells differentiate into memory cells. When the same antigen is encountered later in life, the memory cells respond by forming a clone of cells which then become plasma cells and memory cells. The formation of a clone from memory cells and their differentiation into plasma cells and memory cells is a **secondary immune response**. It is faster, longer, and more effective than the primary immune response because the memory cells are already "sensitized" to the antigen.
Antibodies

Antibodies are immunoglobulins or IgS which are part of plasma proteins. Most antibodies are made up of four polypeptide chains. Two of the chains are identical to each other and are called heavy or H chains and they consist of about 400 amino acids. The other two chains are also identical to each other, consist of about 200 amino acids and are called light or L chains. Antibodies are Y-shaped molecules and each half of the molecule has a heavy and a light chain. The H chains form the arms and the stem of the "Y" and the light chains are found running parallel along the outside of the H chains of the arms of the "Y". The tops of the H and L chains are called variable or V regions. They function as antigen-bonding sites and are different for each kind of antibody. The remainder of the molecule is the constant or C region which is the same, or nearly the same in all antibodies of a given class. They function as bonding sites for complement proteins, macrophages, chemicals, or cells.

There are five classes of antibodies:

1. IgA - They are found in mucus and other secretions. They function in preventing pathogens from entering the body.

2. IgD - They are attached to the surface of B lymphocytes and function as a receptor of immunocompetent B lymphocytes and in the activation of B lymphocytes.

3. IgE - They are secreted by plasma cells and are involved in allergic responses.

4. IgG - They are the most abundant antibodies and they are the only ones that can cross the placenta. They function in the primary and secondary immune responses and in complement fixation.

5. IgM - They are attached to B lymphocytes and are the first antibody released into the blood by plasma cells during a primary immune response. They function as antigen receptors and in complement fixation.

In humoral immune responses, antibodies do not directly destroy the antigens, they only inactivate them by forming antigen-antibody complexes or immune complexes.

There are two major defensive mechanisms that form the complexes:

1. complement fixation and activation - When antibodies bond to the antigen, their shape changes and complement-bonding sites on the constant regions of the antibody are exposed. Complement fixation occurs in the antigen cell surface and results in lysis. The chemicals released during lysis enhance the non-specific body defenses of the inflammatory response, opsonization, and phagocytosis.
2. **neutralization** - Antibodies bond to sites on viruses or chemicals secreted by bacteria called exotoxins. The virus or exotoxin receptor cells are filled by antibodies and they can no longer bond to receptor sites on tissue cells. The antigen-antibody complexes are destroyed by phagocytes.

2. **Cell-mediated immune responses** - They occur when cells have been invaded by pathogens and they involve T lymphocytes.

Four major types of T lymphocytes are formed which have different functions:

a. **cytotoxic or killer T lymphocytes**
b. **helper T lymphocytes**
c. **suppressor T lymphocytes**
d. **memory T lymphocytes**

Cells of the body have genetically determined cell surface proteins called **major histocompatibility complex (MHC) proteins**.

There are two classes of MHC proteins which are important in activation of T lymphocytes:

a. **Class I MHC proteins** - They are located on the surface of the plasma membrane of most body tissue cells. Cytotoxic T lymphocytes are activated by antigen fragments bonded to Class I MHC proteins on body tissue cells.

b. **Class II MHC proteins** - They are located on the surface of mature B lymphocytes, some T lymphocytes, and macrophages. Class II MHC proteins allow cells of the immune system to recognize one another. Helper T lymphocytes bond with antigens on the surface of antigen-presenting macrophages which contain Class II MHC proteins. Once helper T lymphocytes have been presented the antigen by an antigen-presenting macrophage, they stimulate other T lymphocytes and B lymphocytes that are bonded to an antigen. When helper T lymphocytes bond with the antigen-presenting macrophage the macrophage releases a lymphokine called interleukin 1. Interleukin 1 stimulates the helper T lymphocyte to release interleukin 2 which stimulates the production of more helper T lymphocytes, activates cytotoxic T lymphocytes, and B lymphocytes. In some cases, helper T lymphocytes bond directly with B lymphocytes and interleukin 2 is released. The activated B lymphocytes produce humoral immune responses. Other lymphokines released by helper T lymphocytes also attract other white blood cells, especially neutrophils, to the area and enhance non-specific body defense mechanisms.
Cytotoxic T lymphocytes

Cytotoxic T lymphocytes are the only T lymphocytes that can directly attack and kill other cells. They circulate in the blood and lymph, and through lymphatic tissues and organs in search of body tissue cells displaying antigens. The process is referred to as immunologic surveillance. The target cells are usually virus infected cells, cancer cells, cells infected by bacteria or parasites, and foreign cells from blood transfusions or organ transplants.

Cytotoxic T lymphocytes release several kinds of lymphokines:

1. **perforin** - It is a cytotoxic substance which bonds to the surface of an antigen-bearing cell and causes lesions in the plasma membrane. The antigen is destroyed by lysis, similar to that produced by complement fixation.

2. **transfer factor** - It is a protein that is released and it reacts with nonsensitized lymphocytes at the site of invasion. It causes them to take on the same characteristics as the sensitized cells, resulting in an increase in the number of cytotoxic T lymphocytes.

3. **macrophage activating factor (MAF)** - When it is released it increases phagocytic activity of macrophages at the area of infection.

4. **migration inhibitory factor (MIF)** - When released it prevents the activated macrophages from leaving the area of infection.

5. **chemotactic factors** - They attract macrophages, neutrophils, and other white blood cells to the area of invasion.

6. **tumor necrosis factor (TNF)** - It slowly works on tumor cells and causes selective vascular damage to the blood vessels which are feeding the tumor, activates T lymphocytes, and attracts other white blood cells to the area.

Suppressor T lymphocytes

Suppressor T lymphocytes regulate the immune response by releasing lymphokines that inhibit the activity of B and T lymphocytes when the antigen has been inactivated or destroyed.

Memory T lymphocytes

Memory T lymphocytes recognize the original invading antigen during later infection and since they are sensitized to the antigen they cause a faster, more effective reaction.