**Host Defense Mechanisms**

When microorganisms attach to cells, chemotactic signals (from chemicals released) attract phagocytes and antigen sensitive T and B lymphocytes (white blood cells) to the area. Phagocytes attach to the microorganisms and antigens are presented to the T and B lymphocytes. The T and B lymphocytes begin to divide and form clones. The B lymphocytes differentiate into plasma cells and memory cells. Plasma cells produce antibody IgM (immunoglobulin) with receptor sites that interact with the microorganism's antigens. An inflammatory response occurs in which plasma seeps into the tissues and redness, heat swelling and pain may occur.

The IgM attaches to the antigen on the microorganism forming immune complexes. The formation of an immune complex activates the formation of complement proteins (specific plasma proteins) which bond to the bacteria and the process is referred to as complement fixation. Phagocytosis, complement fixation and the inflammatory response increase. Complement fixation may cause lesions in the cell wall of the bacteria resulting in lysis.

On the mucosal membranes, IgA is produced instead of IgM and little or no plasma seeps into the area. Phagocytosis occurs but, complement fixation does not occur.

T lymphocytes have also cloned and bonded with antigens by way of protein surface receptors. Various chemicals called lymphokines are released and tissue reactions occur. Macrophages are attracted to and inhibited from leaving the area by lymphokines, lesions form in the cell wall of the bacteria, and some lymphokines act as chemotactic agents by attracting other white blood cells to the area.

When antigens are no longer present, the T and B lymphocytes withdraw from the area and macrophages clean up the dying and dead bacteria and cellular debris. The T and B lymphocytes have a "memory" for the antigen and when it is encountered later in life they will respond more rapidly.

**Immunity and Disease**

Immunity is the ability to recognize and defend against disease.

There are two types of immunity:

a. **innate immunity** - the resistance to infection of an organism due to its genetic inheritance.

b. **acquired immunity** - resistance that develops after antigens have been introduced into the body. Acquired immunity can be active or passive. Active immunity develops after antigens or toxins enter the body and the immune system responds by producing antibodies and immune cells. Passive immunity develops when antibodies enter the body from an outside source.
There are four types of acquired immunity:

1. **naturally acquired active immunity** - the immune system reacts by producing antibodies and T lymphocytes when exposed to antigens. It may last weeks, months, years, or be lifelong for some diseases.

2. **artificially acquired active immunity** - antigens are introduced into the body in the form of vaccines. A vaccine may contain attenuated (weakened) organisms, dead organisms, or their inactivated toxins (toxoids). They protect against future infections.

3. **naturally acquired passive immunity** - the natural transfer of antibodies from a mother to the fetus across the placenta or to the newborn through nursing. It lasts only a short time (3 to 6 months after birth), usually until the baby’s immune system matures. Immunity depends on the infections the mother has had or been immunized against.

4. **artificially acquired passive immunity** - antibodies are received in the form of antiserum from another person or animal already immune to the antigen due to previous infection or by vaccination. They may prevent a disease from developing or lessen its severity and duration of infection and the effects are temporary and short-lived.

**Artificially Acquired Active Immunity**

Vaccines are produced from an infectious organism or its products in such a way that they will not cause disease and it induces immunity in the host.

There are four major types of vaccines:

1. **inactivated (killed) vaccines** - they are prepared in laboratory cultures such as animals, chick embryos, and tissue cultures, and injected and killed by chemicals (formalin and phenol) or heat. Several injections may be required, as well as, "booster" shots. The Salk vaccine for polio and influenza shots are formed from inactivated viruses.

2. **attenuated (living) vaccines** - methods are used to eliminate the pathogenic properties of the organism, but they still mimic the active infection. They provide better immunity than inactivated vaccines. The Sabin polio vaccine and vaccines for measles, rubella, and mumps are formed from attenuated viruses.

3. **toxoids** - bacterial toxins are inactivated by heat or chemicals. They stimulate the immune response which neutralizes the toxin. Toxoids are used for protection against tetanus and diphtheria.
4. **recombinant DNA vaccines** - vaccines are produced by genetic engineering and include a vaccine against the hepatitis B virus which consists of the viral protein coat produced by a genetically engineered yeast.

**Disorders of the Immune System**

An immunological disorder is a condition that results from an inappropriate or inadequate immune response. Inappropriate responses involve a type of **hypersensitivity** ("too much of a good thing") in which either antibodies or T lymphocytes cause significant damage to tissues and inadequate responses are due to an **immunodeficiency**.

There are two types of hypersensitivity:

1. **Immediate Hypersensitivity** - more commonly referred to as **allergy**. It is a rapid response (usually 10-20 minutes) resulting from previous exposure to an antigen, called an **allergen**, to which the body has been **sensitized**. Sensitizing occurs during the first exposure (sensitizing dose) to an allergen and subsequent exposures cause the body to produce harmful reactions. The subsequent dose is an **eliciting dose** if it causes tissue damage. If the damage is profound it is a **shocking dose**.

Three physiologic effects occur with an eliciting or shocking dose:

- a. Antigens combine with the antibody where it is attached to tissue cells.

- b. Granulocytes (leukocytes) release substances, especially **histamine**, from the granules in their cytoplasm, platelets release **serotonin**, and plasma proteins release **kinins**.

- c. The release of histamine, serotonin, and kinins causes sudden dilation of blood vessels, contraction and spasms of smooth muscle in small arteries and bronchioles, and an increase in the permeability of capillaries resulting in edema.

There are three types of immediate hypersensitivity:

1. **anaphylaxis** ("away from protection") - The allergen must be introduced indirectly into the tissues (insect bites, drug injections) and they combine with IgE antibodies. Hives may occur at the site of injection or over large areas of the skin. **Anaphylactic shock** may occur in which the production of **histamine** causes the smooth muscle of the bronchioles to constrict (bronchospasms) making breathing difficult, as well as, constriction of the arteries which increase heart rate followed by vasodilation and an increase in the permeability of capillaries.
which produces edema (swelling), and a drop in blood pressure resulting in shock. Death may occur within minutes or hours.

(2). **atopic allergy** - they are localized reactions caused by inhaling, ingesting, or by contact with an antigen resulting in hives, hay fever, asthma, or gastrointestinal problems. Reactions occur between a small amount of IgE antibodies and the allergen. Hives are caused by a rapid inflammatory response with redness, soreness, and itching at the site of contact. In hay fever, the mucosal membranes of the upper respiratory tract become inflamed, swollen and produce more mucus in reaction to histamine production, resulting in a runny nose and watery eyes. The lower respiratory tract is involved in asthma and results in the constriction of the smooth muscle of the bronchi and edema of the airways in response to epinephrine production. Gastrointestinal food allergies may cause hives and inflammation of the mucosal membranes resulting in abdominal pain and diarrhea.

(3). **immune complex disease** - they result from the formation of antigen-antibody complexes (immune complexes) that are not destroyed by phagocytes. The major antibody involved is IgG and sometimes includes IgM which are found circulating through the blood and lymph. The complexes lodge in capillaries and activate complement proteins and an inflammatory response that attracts leukocytes. The leukocytes release destructive enzymes that damage nearby tissue. **Serum sickness** may occur when animal (usually horse) serum is injected. The symptoms are usually similar to anaphylactic shock but less severe and include sudden fever, edema of the face, hands, and feet, and swollen lymph nodes.

2. **Delayed Hypersensitivity** - These reactions take more than 12 hours to occur, and involve T lymphocytes which circulate in the blood and lymph and have been sensitized to antigens. The T lymphocytes produce lymphokines that attract macrophages, cause cytotoxic effects, and cause the inflammatory response.

There are five types of delayed hypersensitivity:

a. **allergy of infection** - many involve chronic diseases from parasitic worms (trichinosis), fungi (histoplasmosis), bacteria (tuberculosis), and viruses. Skin tests are used to detect infections. Injection of the antigen into the skin (intracutaneous) causes redness, edema, and a hardened area (induration) in the skin.
b. **allergic contact dermatitis (ACD)** - it occurs after exposure of the skin to allergens in clothing, jewelry, insecticides, cosmetics, or plant oils (poison ivy, poison sumac, poison oak). The symptoms may range from an itchy skin rash to large blister-like lesions surrounded by redness.

c. **autoimmune disease** - it is the failure of the immune system to recognize "self" antigens and it produces antibodies which cause damage to the body’s own tissues and organs. They may be caused by genetic factors, antigenic mimicry (antigens similar to pathogenic antigens), antigens released during injury which were hidden in tissues and escaped contact with T and B lymphocytes during immune system development, and mutations.

Autoimmune diseases include:

- **Grave’s disease** - The binding of antibodies to receptors for thyroid-stimulating hormone leads to over-stimulation of thyroid activity. Symptoms include goiter and bulging eyes.

- **Rheumatoid arthritis** - inflammation and destruction of the joints by deposition of IgG and IgM antibodies resulting in chronic infection and damage to cartilage and bone in the joint.

- **Myasthenia gravis** - blocking of acetylcholine production which prevents the transmission of nerve impulses to muscles resulting in muscle weakness and fatigue.

d. **graft rejection** - attraction of T lymphocytes and some antibodies which damage transplanted tissues and organs. All human cells have genetically determined major histocompatibility complex (MHC) proteins on their surface which are also called human leukocyte antigens (HLA) because they were first studied in leukocytes. Transplants occur between individuals with nearly the same MHC’s which reduces the chance of rejection.

e. **tumor immunity** - tumors are formed by rapidly dividing cells which form large growths that crowd and eventually kill normal neighboring cells. The transformed cells contain tumor-specific antigens on their surface which mark cancer cells for destruction. **Immunologic surveillance** occurs by T lymphocytes and macrophages as they move through the body and eliminate most malignant cells before they cause cancer. **Immunologic escape** may occur if a small number of cells fail to stimulate the immune response, the antigens are covered up or masked by other molecules, the tumor cells shed their antigens, or the tumor cells release substances which suppress the activity of T lymphocytes.
Immunodeficiency Disease

Immunodeficiency diseases occur because of a breakdown or deficiency in the immune functions. The deficiency may be complete or it may be selective in which it involves an inability to produce a certain type of antibody or an abnormality in the function of a particular type of T or B lymphocyte. Congenital immunodeficiencies are inherited or develop before birth and usually appear early in life. Acquired immunodeficiencies develop later and are caused by infection, cancer, or the side effects of immunosuppressive medications.

Stages of Infectious Disease

Infectious diseases vary in duration or severity and location in the body. An acute disease develops rapidly, usually has severe symptoms, but lasts a short time. Acute diseases include colds, influenza, and measles. A chronic disease develops slowly, and the body’s reactions may be less severe, but the disease is likely to be continual or recurrent for long periods. There is a rise and fall of signs and symptoms throughout life as antigens become active and then suppressed over and over. Chronic diseases include tuberculosis, leprosy, mononucleosis, and syphilis. A subacute disease is in between an acute and a chronic disease and includes the gum disease gingivitis. A latent disease is one in which the causative agent remains inactive for a time, but then becomes active again when natural and acquired immune responses have been compromised and produces symptoms of the disease. Chicken pox, caused by the herpes zoster virus may reoccur as shingles later in life and the herpes simplex virus causes cold sores and canker sores in the mouth due to stress.

Infections can also be classified according to the extent to which the host’s body is affected. A local infection is one in which the invading microorganisms are limited to a relatively small or specific area of the body such as those which produce boils and abscesses and bladder infections. In a systemic (generalized) infection, microorganisms or their products are spread throughout the body by the blood or lymphatic system, such as in measles and chicken pox. Very frequently, agents of local infection enter the blood or lymph vessel and spread to other specific parts of the body and become systemic infections. They are referred to as a focal infection. Focal infections can arise from infections in the teeth, tonsils, or sinuses. Organisms from an abscess can enter the bloodstream and be carried to other tissues, including the kidneys and the urinary tract.
The state of host resistance also determines the extent of infections. A primary infection is an acute infection that causes the initial illness. A secondary infection is one caused by an opportunistic microorganism after the primary infection has weakened the body's defenses. Influenza (primary) can lead to bacterial pneumonia (secondary), and a common cold (primary) can lead to a middle-ear infection (secondary). An inapparent (subclinical) infection is one that does not cause any noticeable signs or symptoms of illness either because too few organisms are present or because host defenses effectively combat the pathogens. Poliovirus, hepatitis A and hepatitis B virus can be carried by people who never develop the illness.

Stages of Acute Infectious Disease

There are four stages of acute infectious disease based on activity of the invading pathogen and the symptoms produced.

1. incubation period - It is the time between initial infection and the first appearance of signs and symptoms. The pathogen is establishing itself and there are no outward signs of infection. It is determined by the type of pathogen, generation time, virulence, and host resistance. The length of time may be short (2-3 days), moderate (2 weeks), or long (weeks to months). The period ends when the pathogen survives and multiplies.

2. prodromal period ("running before") - Early mild symptoms appear for about 1-2 days. The symptoms may be malaise, general aches, "scratchy" throat, or headache. Infected individuals are contagious at this stage and can spread the disease to others. Some diseases skip this stage.

3. active, acute, or illness period - Interactions between the pathogen and host are at full intensity and there is a peak of prolonged symptoms of illness. The pathogen causes tissue damage. Signs and symptoms appear and may include fever, chills, nausea, muscle pain, sore throat, lymph node swelling, or gastrointestinal disorders (diarrhea). At the end of this stage the host defense mechanisms overcome the pathogen.

4. decline and convalescent period - It is a period of decline and diminishing of signs and symptoms. Tissues are repaired, healing takes place, body systems return to normal, the body regains strength, and recovery occurs.